ABSTRACT

Optical coherence tomography (OCT) is a novel biomedical imaging technique that functions as a type of “optical biopsy” by using low coherence interferometry to non-invasively generate high resolution cross-sectional images of tissue in real time. OCT has become a standard diagnostic tool in ophthalmology and investigators have demonstrated OCT in a variety of biomedical applications including cardiology, gastroenterology, dermatology, and urology. Recent research advances in swept source lasers have enabled swept source OCT (SS-OCT) to achieve imaging speeds 5-50x faster than commercially available spectral domain OCT (SD-OCT) systems.

This thesis describes the design of a handheld SS-OCT instrument for portable-real-time imaging in situ at the point of care. Traditional OCT devices require bulky table-mounted systems, but the handheld device has the potential to be used as an advanced point-of-care diagnostic instrument in primary care settings or intraoperatively. The combination of the wide scanning angle in the handheld and the high imaging speed of SS-OCT could allow for screening of pathology with a single volumetric data set spanning the areas of interest on the patient. The compact, easy-to-use form factor could enable the adoption of SS-OCT in settings like primary care clinics or the surgical theater where space is limited. Emergent applications can include intraoperative assessment of kidney transplant viability, as many donor kidneys suffer ischemic insult while awaiting transplant and there is a critical clinical need for a reliable, real-time assay to evaluate donor kidney viability and predict post-transplant outcome.

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Chapter 1
Introduction and Overview
1.1 Introduction and Specific Aims

Optical coherence tomography (OCT) is an established medical imaging technology that uses light to perform high-resolution, non-invasive, cross-sectional and three-dimensional imaging of biological tissues in situ and in real time. Recent advances in hardware have dramatically improved the imaging speed and resolution of OCT, enabling its application in a wide variety of medical fields. OCT has been adapted for use in a multitude of instruments and form factors, ranging from the standard ophthalmoscope down to endoscopes, catheters, and needle probes. The objective of this thesis is to construct a swept source OCT instrument and handheld device for high-speed, non-invasive, three-dimensional imaging of human tissue in situ as an advanced point-of-care diagnostic instrument. By constructing a portable system, OCT imaging can be performed in primary care settings or intraoperatively with minimal disruption to existing clinical/surgical procedure. This has the potential to enable earlier detection of diseases and potentially predict surgical outcomes with accurate image-based diagnostics.

Aim 1. Develop a compact, high-speed swept source OCT instrument. Traditional OCT imaging systems require a variety of bulky and complex tabletop laser light sources, optical elements, and supporting electronics to perform high-resolution, high-speed imaging. A point-of-care imaging system must be compact and robust without sacrificing speed, resolution, or ease of use. Recent advances in hardware have dramatically miniaturized many of these components, enabling development of a much more compact OCT imaging system that can fit into a single tabletop enclosure. Successful reduction of the size and complexity of the system is crucial for meeting the space and reliability constraints of deployment in clinical/surgical settings.

Aim 2. Develop a handheld probe interface that allows for ease of alignment and imaging. A handheld imaging system must have a patient interface that is easy to use with patients in primary care settings or with a sterile covering for imaging in the operating room. The optical components must fit in a compact, lightweight probe that is ergonomically designed to be gripped with the hand to minimize strain on the operator. This mandates the use of small scanning optics. An adjustable element can be included to aid in alignment and to adjust the working distance between the lens and tissue.

Aim 3. Perform imaging of human tissue with the handheld device as proof-of-principle. The handheld imaging system must be tested on human tissue to evaluate the image quality and ease of imaging. Modifications and changes will require several iterations of the device.

1.2 Background

The work in this thesis was performed in collaboration with Prof. Peter Andrews from Georgetown University and Prof. Yu Chen from the University of Maryland, under support from the National Institutes of Health program 5R01DK094877-04 “Non-invasive evaluation of transplant kidney using OCT.” The objective was to develop OCT for imaging transplant kidneys as a potential approach to predict transplant function. The subcontract work at M.I.T. focused on
developing a high speed OCT instrument capable of three dimensional imaging, while ongoing work at Georgetown University utilized commercial OCT technology for preoperative and intraoperative imaging in kidney transplant.

1.2.1 OCT Background

OCT is a technique for performing subsurface imaging of optical scattering media (such as biological tissue) and functions by directing an optical beam at the media and using optical interferometry to image reflections from within the media. OCT systems can resolve the depth that light reflects from within the media by implementing a Michelson interferometer and using optical interference between light traveling to/from the sample and light traveling down a reference path [1]–[4]. With this method, focusing an optical beam to a single point on the sample yields a one-dimensional data set (1-D image) of the sample’s depth-dependent reflectance. Scanning the beam in a line across the surface of the sample yields a two-dimensional data set (cross-sectional image), whereas an area scan will yield a three-dimensional data set (volumetric image).

State-of-the-art OCT systems implement swept-source OCT (SS-OCT), which offers significant speed and sensitivity advantages over early implementations [5]–[7]. SS-OCT performs imaging with a broadband light source to create spectrally encoded interference patterns (i.e. the reflected sample depths are encoded in wavelength). This is achieved by using a laser that sweeps a span of wavelengths at high frequency [8]–[10] and sampling the interference pattern with a detector as the light source sweeps through different wavelengths over time. The bulk optics configuration of an SS-OCT interferometer using a dual-balanced detector can be seen in Figure 1-1. The schematic of a typical fiber optics configuration of an SS-OCT system can be seen in Figure 1-2.

In SS-OCT, scanning speed is limited by the sweep frequency of the light source (i.e. the frequency at which the light source can sweep through the entire band of output wavelengths). Recent literature has demonstrated SS-OCT with ultra-high imaging speeds made possible by ultra-high speed swept source light sources. For example, Fourier domain mode-locked (FDML) lasers have been demonstrated in retinal OCT imaging with 1.37 MHz sweep rates [11]. Members of our group have also developed vertical cavity surface emitting laser (VCSEL) devices sweeping from 60 kHz – 1 MHz and demonstrated these devices in ophthalmic and dermal OCT imaging [12].
Figure 1-1 Bulk optics setup of SS-OCT interferometer with balanced detection. The light source sweeps through a wide band of wavelengths over time. Just like in an SD-OCT system, the light is split into a reference arm path and a sample arm path to produce a spectrally-encoded interference pattern at the beam splitter. However, instead of a spectrometer, the interfered light is sent to a 50/50 beam splitter where the light is split into two beams which are separately detected by photodiodes. By measuring the difference signal between the two photodiodes, a balanced detector is capable of eliminating the DC component (i.e. the constant term) of the interference pattern. Since the light source sweeps through wavelengths in time, the spectrally-encoded interference pattern is a time-varying signal. Consequently, the output of the balanced detector is a single time-varying signal where spectral information is distributed temporally. Thus, spectral information in the interference pattern is extracted by sampling the signal in time with an A/D acquisition card from a computer (not shown).
Figure 1-2 Fiber optics setup of SS-OCT system with balanced detection. Note the use of fiber optic couplers with uneven split ratios instead of bulk-optics beam splitters. Five percent of light from the swept source laser is coupled into a Mach-Zehnder interferometer (MZI) for calibration of acquired OCT interference patterns. The remaining ninety-five percent of light is split between the sample and reference arm paths – ten percent is coupled into the reference arm path and ninety percent is coupled into the sample. Light reflected from the sample and reference arm paths pass through an optical circulator, a special fiber-optic component designed such that light entering a port exits from the next (clockwise in the schematic). The sample and reference arm light is interfered at the 50/50 fiber coupler and evenly split into two paths for the balanced detectors. The balanced detectors measure the difference signal between the two inputs, eliminating the DC component (i.e. the constant term) and extracting the OCT interference pattern. Spectral information in the interference pattern is obtained by sampling the balanced detector with an A/D acquisition card from a computer. The A/D acquisition card has a finite sample rate so a low pass filter (LPF) is placed on each balanced detector output to prevent aliasing. Acquisition is synchronized with the start of each sweep of the laser by a trigger signal produced by the swept source laser and a scan signal produced by the multifunction I/O card.

The imaging range of SS-OCT is limited by the instantaneous linewidth of the swept source light source and the acquisition rate of the A/D card. When compared against commonly used OCT systems, most of which implement spectral domain OCT (SD-OCT), SS-OCT generally offers a greater imaging range because swept source light sources often have a narrower linewidth than the resolution of a spectrometer used in SD-OCT and the narrow linewidth enables light to remain coherent over longer distances [13].
SS-OCT has the potential for superior sensitivity compared to commonly used SD-OCT systems because SS-OCT detectors are more efficient than SD-OCT line scan cameras and there are no spectrometer losses in SS-OCT. Additionally, sensitivity in SD-OCT suffers when imaging deeper into the sample. This sensitivity roll-off with depth is caused by the use of a line scan camera in the spectrometer, where higher spatial frequencies are averaged due to the finite pixel size and pixel crosstalk results in degradation of signal quality [14], [15]. The use of a balanced detector in SS-OCT avoids this sensitivity roll-off with depth and enables a greater dynamic range due to the elimination of the DC component of the signal.

1.2.2 OCT in Renal Medicine

End stage renal disease (ESRD) affects over 600,000 U.S. residents and is associated with high mortality rates (136 deaths per 1,000 patient years) and an enormous economic burden on the U.S. healthcare system (over $30 billion per year) [16]. Treatment options for ESRD include dialysis and kidney transplantation, but transplantation is often preferred for its ability to extend patients’ lives and improve their quality of life. However, organ shortages pose a major problem as more than 88,000 patients annually wait for kidney transplants, with the active waiting list 2.8 times larger than the supply of donor kidneys [16]. Many kidneys used for transplantation are obtained from living donors and heart-beating cadavers. There are also many kidneys from non-heart-beating cadavers that are not utilized due to their unknown status. However, the majority of kidneys used for transplantation are obtained from deceased donors [16]. As they await transplantation, these kidneys are frequently subject to long storage times and suffer ischemic insult (lack of blood perfusion) leading to acute tubular necrosis (ATN). ATN often results in varying degrees of delayed graft function (DGF), representing a significant risk for eventual graft and patient survival [17]–[21]. Furthermore, DGF can be difficult to discern from rejection. In present clinical practice, there is no reliable real-time assay for evaluating viability of donor kidneys and assessing whether donor kidneys may develop DGF. Therefore, there is a critical clinical need for objective and reliable real-time tests to predict post-transplant outcome.

Previous efforts to develop such a test have focused on biochemical analysis of kidneys but this work has been largely disappointing as no biochemical criteria were found to be accurate [22]. Current efforts now focus on imaging and investigators have examined light microscopy of excisional kidney biopsies as a more conventional means to evaluate kidney pathology. However, excisional biopsies take time to process, are destructive to kidneys, and are subject to sampling errors since they only permit imaging of small regions of the kidney [23], [24]. To mitigate some of these downsides, techniques such as tandem scanning confocal microscopy (TSCM) [25], [26], near-infrared confocal microscopy [27], and multi-photon microscopy [28]–[30] have been investigated and demonstrated the ability to perform non-invasive imaging of kidney structure and function in animal models. However, the limited penetration depths of these microscopy procedures (roughly 100-200 μm) makes it nearly impossible to image the human kidney, especially if the kidney is still surrounded by an intact renal capsule. Furthermore,
conventional microscopy instruments are bulky and unsuitable for use in the surgical suite, where kidney specimens will need to be imaged in situ.

These concerns can be addressed by optical coherence tomography (OCT), a non-invasive imaging modality first developed in 1991 by the Fujimoto group at MIT [1] that can function as a type of “optical biopsy”. OCT functions analogously to ultrasound except that OCT images are created using backscattered light from the sample instead of sound. Many OCT systems employ broadband optical light sources in the near-infrared, allowing OCT to achieve resolutions more than an order of magnitude finer than ultrasound while being much less expensive than MRI devices and much safer than X-ray technologies. When compared against non-invasive light microscopy, OCT offers imaging with superior penetration depth and longer working distances without the need for tissue contact. OCT can also provide three-dimensional imaging with virtual sectioning in arbitrary planes.

Investigators have demonstrated that OCT is able to assess the status of kidneys in animal models [31]–[33] and OCT also possesses the penetration depth and resolution to visualize human kidney microstructures through the intact renal capsule [34]–[37]. Dimensional changes in renal blood vessels and other tubular structures can be visualized in real-time and volumetrically rendered using OCT [38]. OCT is also capable of very high acquisition rates, potentially enabling evaluation of the entire kidney within a short timeframe [39].

1.2.3 Portable/Handheld OCT

While OCT is a promising option for kidney imaging and evaluating physiological function, a major limitation of current OCT devices is that they are bulky table mounted systems requiring a host of complex supporting electronics. This precludes them from use in the operating room or clinical settings where space is often extremely limited. Thus, a handheld OCT device would enable deployment in cramped surgical/clinical environments, providing clinicians with the ability to perform high-speed, three-dimensional, non-invasive imaging of human tissue in situ. For example, this would enable clinicians to image human kidneys in situ during transplant procedures. This would be an effective tool for evaluating the global status of a kidney and the information obtained by OCT may be useful for developing a method to predict post-transplant outcome. Success here will have tremendous clinical impact, enabling optimal utilization of existing donor organs and potentially expanding the pool of donor organs that can be safely used for transplantation. Successful development of a portable handheld OCT device could also expand OCT imaging to primary care settings with minimal disruption to existing clinical procedure. This has the potential to enable earlier detection of diseases with accurate image-based diagnostics.

Creating a handheld OCT device for point-of-care imaging will be challenging and success will require careful consideration of optical, ergonomic, and clinical workflow requirements. First, optical components must be carefully selected to achieve acceptable imaging performance. Generally, a wide laser beam incident on a focusing lens is necessary to produce a
small beam spot on the tissue and improve transverse resolution. The laser beam diameter in an
OCT system is often limited by the scanning mechanism. Galvanometer scanners offer high
performance and support driving large mirrors (for large beam diameters) without sacrificing
acceleration or velocity. However, these scanners require two sets of actuators housed in an
aluminum block and are bulky compared to alternatives such as MEMS scanning mirrors. While
MEMS scanners are more compact, they also have lower resonance frequencies and must use
smaller mirrors, thus trading off scanning speed and transverse resolution for size and weight. An
optical design must be created to obtain an acceptable spot size without sacrificing speed and
imaging length/angles on the tissue. This is important, as the number of resolvable spots on the
tissue is determined by the imaging length divided by the spot size and a high number of
resolvable spots is necessary for detection of tissue features for diagnosis. The choice of
scanning mechanism will thus need to be made carefully as it affects the power of the optics
needed in addition to the size, weight, and performance of the handheld device.

The optical design considerations will inform the ergonomics of the device, as there are
multiple ways a handheld device could be used. For example, the handheld device could be held
like a pen, grasped like a camcorder, or pointed at the tissue with a pistol style grip for imaging.
The intended grip must be sufficiently balanced and stable to minimize operator motion without
degrading imaging capability. Additionally, the handheld device must be made of durable
materials that can be easily sterilized whilst remaining lightweight enough to prevent operator
fatigue, especially when multiple imaging sessions are expected. While heavy, glass for optical
elements cannot be avoided without sacrificing performance. However, commonly used optical
mounts are made of aluminum and these can be substituted with rapid-prototyped plastic to
reduce weight. The handheld device can be designed to provide tissue contact for stability but the
handheld device is still subject to operator motion while imaging and this potentially introduces
motion artifacts. To alleviate this, the OCT system can be designed with a higher imaging rate to
reduce overall imaging time and prevent operator fatigue. Additionally, post processing
techniques such as registration using orthogonal data sets have been demonstrated to correct
motion [40].

Finally, the device must be easy to use in a clinical setting and its impact on existing clinical
workflow must be minimized in order to achieve success. For example, alignment feedback is
necessary to find regions of interest and target specific areas of the tissue for imaging. This can
be achieved using a visible optical path for direct or indirect viewing of the targeted area. A
direct view would provide a visible optical path from the tissue to the operator’s eye, similar to a
microscope. An indirect view would use a camera in this path and display the targeted area on a
computer screen. Both of these would require the introduction of a second (visible) optical
pathway to the handheld device on top of the existing OCT pathway. To avoid the additional
weight and complexity of a second pathway, OCT preview scans displayed on a computer screen
can be used instead for alignment. Typically, orthogonal cross sections are taken in real time to
check for off axis alignment of the imaging plane. An enface preview of the entire imaging
surface can also be performed in real time for 2-D alignment data by taking a quick raster scan of the tissue and summing the data.

1.3 Scope of Thesis

Conventional OCT devices are bulky table mounted systems requiring a host of complex supporting electronics that preclude OCT from use in the operating room or clinical settings where space is limited. This thesis focuses on the development of a handheld OCT device utilizing high-speed swept source lasers for non-invasive, three-dimensional imaging and diagnostics of human tissue in situ at the point of care. Through rapid prototyping and the use of printed plastic, a lightweight and compact OCT handheld device can be constructed to meet clinical requirements for speed and ease-of-use without sacrificing alignment requirements for OCT image quality. A combination of high-speed imaging and motion correction post-processing techniques can enable acquisition of motion-free volumetric scans of tissue. Volumetric scans can potentially be used for evaluating the global status of a transplant kidney or detecting disease in primary care settings.

Chapter 2 reviews the theoretical background of swept source OCT and describes the low-coherence interferometry techniques that form the basis for axial ranging in OCT. The relationship between the axial resolution of an OCT system and the spectral bandwidth of its light source is derived for media both with and without dispersion. Fundamental noise sources and their impact on system sensitivity are also discussed.

Chapter 3 discusses the design parameters and requirements for the sample arm of a handheld OCT device. Several common scan patterns and optical scanning elements are considered. The fundamental performance limits of the sample arm are examined through theoretical analysis of the optical design. Requirements for alignment to achieve optimal imaging are also discussed.

Chapter 4 discusses and characterizes the different modules of the SS-OCT system used to acquire images with the handheld device.

Chapter 5 discusses the iteration of the OCT handheld device and characterizes its optical performance. The optical setup, physical design, and imaging results of the handheld device are analyzed and an analysis of its effectiveness and limitations is performed.

1.4 References


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Chapter 2
Swept Source Optical Coherence Tomography Theory
2.1 Overview

This chapter reviews the theoretical background of swept source OCT and describes the low-coherence interferometry techniques that form the basis for axial ranging in OCT. The relationship between the axial resolution of an OCT system and the spectral bandwidth of its light source is derived for media both with and without dispersion. Fundamental noise sources and their impact on system sensitivity are also discussed.

2.2 The Michelson Interferometer and Axial Resolution

OCT images are produced by processing the interference fringes created by the combination of light traveling from two optical paths in a Michelson interferometer. This section describes the principles of low-coherence interferometry governing operation of a Michelson interferometer. The axial resolution of the interferometer is shown to exhibit a Fourier transform relationship with the spectral bandwidth of the light source. The spectral bandwidth of the light source is also shown to exhibit an inverse relationship with the coherence length of the light source in non-dispersive media.

2.2.1 Interferometer with Coherent Light

Consider the simplified schematic of a Michelson interferometer consisting of a light source, beam splitter, two mirrors, and a detector shown in Figure 2-1. Light is emitted from the source and divided into reference and sample beams at the beam splitter. The reference and sample beams are reflected from the reference and sample mirrors, respectively, and recombined at the beamsplitter. The combined beam is then incident on the detector for subsequent digitization. If the light source is monochromatic (i.e. perfectly coherent), then the electric field incident on the detector $E_{\text{det}}$ is the sum of two monochromatic field components $E_R, E_S$ at the beamsplitter from light reflected by the reference and sample mirrors, respectively. These fields can be expressed by the phasors

$$ E_{\text{det}} = E_R + E_S $$

$$ E_R = A_R e^{-j(2\beta_R L_R - \omega t)} \quad E_S = A_S e^{-j(2\beta_S L_S - \omega t)} $$

where $\omega$ denotes the optical frequency of the light source and $\beta$ is the propagation constant (angular wavenumber). Note the factor of two multiplying the propagation constants – this reflects the roundtrip path taken by light to and from the reference and sample mirrors.
Figure 2-1 The Michelson interferometer. The reference and sample mirrors are positioned at distances $L_R, L_S$ from the beamsplitter, respectively.

At the detector, only the intensity of the beam can be sensed and the time averaged photocurrent is given by

$$I_{det} = \left( \eta q \right) \frac{|E_{det}|^2}{2n_0}$$  \hspace{1cm} (2.3)

where $\eta$ is the detector quantum efficiency, $q$ is the elementary charge, $h\nu$ is the single photon energy, and $n_0$ is the intrinsic impedance of free space. Substituting Equations (2.1) and (2.2), this becomes

$$I_{det} = \frac{\eta q}{h\nu} \cdot \frac{1}{n_0} \left[ \frac{1}{2} |A_R|^2 + \frac{1}{2} |A_S|^2 + \Re \{E_S E_R^*\} \right]$$  \hspace{1cm} (2.4)

Note that we have defined $E_R, E_S$ as the field components in the interferometer after reflection at the mirrors and recombination at the beamsplitter. That is, $A_R, A_S$ incorporate the split ratio and phase-shift of the beamsplitter in addition to the reflectivity of the mirrors. Taking a closer look at the last term
\[ \Re \left\{ E_S E_R^* \right\} = A_R A_S \cos \left(2 \beta_R L_R - 2 \beta_S L_S \right) \]  

(2.5)

this describes the variation of the photocurrent with respect to the reference and sample mirror positions. This simplifies further by noting that in free space, \( \beta = \frac{2\pi}{\lambda} = k \) and Equation (2.5) can be rewritten as

\[ \Re \left\{ E_S E_R^* \right\} = A_R A_S \cos \left(2k\Delta L \right) \]  

(2.6)

where \( \Delta L = L_S - L_R \) is the path length difference between the reference and sample mirrors. Altogether, the photocurrent is given by

\[ I_{det} = \frac{\eta q}{h \nu} \frac{1}{\eta_0} \left[ \frac{1}{2} \left| A_R \right|^2 + \frac{1}{2} \left| A_S \right|^2 + A_R A_S \cos \left(2k\Delta L \right) \right] \]  

(2.7)

and this equation shows that the photocurrent contains several constant terms and a single sinusoidally varying term. The constant terms (known as the DC component) represent the power reflectivities of the reference and sample mirrors. The sinusoidally varying term (known as the AC component) represents the interference between the sample and reference fields and is a sinusoid in the \( k \) domain with frequency proportional to the path length difference between the sample and reference arms.

### 2.2.2 Interferometer with Low-Coherence Light

The analysis in Section 2.2.1 only considers a perfectly coherent (i.e. monochromatic) light source. In practice, the output from a light source often consists of a finite bandwidth of optical frequencies rather than a single frequency. These are known as low-coherence light sources and the analysis in Section 2.2.1 can be extended to these sources by integrating the interference term in Equation (2.4) over the finite band of frequencies present in the light source. Note that only the AC term given by Equation (2.5) is examined as this is the only term containing interference information. The use of a low-coherence light source means that the reference and sample fields will be functions of frequency:

\[ E_R(\omega) = A_R(\omega) e^{-j\left[2\beta_R(\omega) L_R - \omega t\right]} \]

\[ E_S(\omega) = A_S(\omega) e^{-j\left[2\beta_S(\omega) L_S - \omega t\right]} \]  

(2.8)

The total photocurrent at the detector resulting from the interference signal is proportional to the superposition of the interference due to each monochromatic plane wave. This is found by integrating the interference term from each monochromatic plane wave:
\[ I_{\text{det}} \propto \Re \left\{ \int_{-\infty}^{\infty} E_S(\omega) E_R^*(\omega) \frac{d\omega}{2\pi} \right\} \] (2.9)

Substituting Equation (2.8), the photocurrent is given by

\[ I_{\text{det}} \propto \Re \left\{ \int_{-\infty}^{\infty} A_S(\omega) A_R^*(\omega) e^{-j2\left[ \beta_S(\omega)L_S - \beta_R(\omega)L_R \right]} \frac{d\omega}{2\pi} \right\} \] (2.10)

Note the argument of the phasor represents the phase mismatch \( \Delta \phi \) of each frequency component in the interference signal. Note also that if the sample/reference mirrors and the beamsplitter are all spectrally uniform (i.e. have a flat spectral response) then the magnitude of the phasor will be equivalent to the power spectrum of the light source such that

\[ A_S(\omega) A_R^*(\omega) = S(\omega) . \] In Section 2.2.3, it will be shown that the axial resolution of the interferometer exhibits a Fourier transform relationship with the power spectrum of the light source.

2.2.3 Non-Dispersive Media and Gaussian Light Sources

Consider a Michelson interferometer where the sample and reference mirrors consist of a uniform, linear, non-dispersive material. Assume the propagation constants in the sample and reference arms are equal, such that \( \beta_S(\omega) = \beta_R(\omega) = \beta(\omega) \), and let the spectrum of the light source \( S(\omega - \omega_0) \) be bandlimited and centered at a frequency of \( \omega_0 \). The phase mismatch \( \Delta \phi \) in Equation (2.10) is then set entirely by the path length mismatch between the sample and reference arms \( \Delta L = L_S - L_R \), such that

\[ \Delta \phi(\omega) = 2\beta(\omega) \Delta L \] (2.11)

Equation (2.10) then becomes

\[ I_{\text{det}} \propto \Re \left\{ \int_{-\infty}^{\infty} S(\omega - \omega_0) e^{-j\Delta \phi(\omega)} \frac{d\omega}{2\pi} \right\} \] (2.12)

The propagation constant \( \beta(\omega) \) can be rewritten as a first-order Taylor expansion around the center frequency \( \omega_0 \) so that

\[ \beta(\omega) = \beta(\omega_0) + \beta'(\omega_0)(\omega - \omega_0) \] (2.13)

This enables rewriting Equation (2.12) to obtain
where the variables $\Delta \tau_p, \Delta \tau_g$ representing the phase delay mismatch and group delay mismatch, respectively, have been introduced and are defined as

$$
\Delta \tau_p = \frac{\beta(\omega_0)}{\omega_0} \cdot 2\Delta L = \frac{2\Delta L}{v_p}
$$

$$
\Delta \tau_g = \beta'(\omega_0) \cdot 2\Delta L = \frac{2\Delta L}{v_g}
$$

In this form, it is clear to see that $v_p = \frac{\omega_0}{\beta(\omega_0)}$ corresponds to the phase velocity of the center frequency and $v_g = \frac{1}{\beta'(\omega_0)}$ corresponds to the group velocity. It is also clear that the interferometric term of the photocurrent at the detector consists of a carrier and an envelope. The carrier oscillates on the path length mismatch $2\Delta L$ with spatial frequency $\beta(\omega_0)$. The envelope is the inverse Fourier transform of the light source power spectrum $S(\omega - \omega_0)$. For simplicity, suppose the light source is Gaussian with power spectral density given by

$$
S(\omega - \omega_0) = \sqrt{\frac{2\pi}{\sigma^2}} e^{-\frac{(\omega - \omega_0)^2}{2\sigma^2}}
$$

where $\omega_0$ is the center frequency of the light source and $\sigma_\omega$ is the standard deviation of the Gaussian. Under this definition, the power spectral bandwidth is given by $2\sigma_\omega$. Note also that the Gaussian has been normalized to unit power

$$
\int_{-\infty}^{\infty} S(\omega) \frac{d\omega}{2\pi} = 1
$$

Substitution into Equation (2.14) and evaluation of the integral yields the following interferometric term for the photocurrent

$$
I_{det} \propto \Re \left\{ e^{-j\omega_0 \Delta \tau_p} e^{-\frac{1}{2}(\sigma_\omega \Delta \tau_g)^2} \right\}
$$

(2.15)
This can be rewritten as

\[ I_{\text{det}} \propto \Re \left\{ e^{-j\omega_0 \Delta \tau} e^{-\frac{1}{2} \left( \frac{\Delta \tau_g}{\sigma_t} \right)^2} \right\} \]  

(2.19)

using the substitution

\[ \frac{1}{\sigma_t} = \sigma_\omega \]  

(2.20)

Equation (2.19) shows that the photocurrent has a Gaussian envelope with temporal bandwidth given by \(2\sigma_t\), and Equation (2.20) shows that the temporal bandwidth of the envelope is inversely proportional to the power spectral bandwidth. An interference fringe oscillating with increasing phase delay mismatch modulates the envelope and the envelope quickly drops off as the group delay mismatch \(\Delta \tau_g\) increases. Due to the finite quantum efficiency of a detector, the interference fringe can only be sensed when the envelope is sufficiently large. Thus, we see that Equation (2.19) defines the axial resolving capabilities of the Michelson interferometer. The envelope is only large enough for detection of the interference fringe when the group delay mismatch falls within the Gaussian envelope (i.e. when the reference and sample arm lengths are sufficiently matched). Recall Equation (2.15) and this condition is expressed by the following relation

\[ |\beta'(\omega_0) \cdot 2\Delta L| < \sigma_t \]  

(2.21)

The axial resolution of a Michelson interferometer is defined by the width of the axial point spread function (in units of length mismatch). This is determined from the width of the interference fringe envelope and in this instance, the width of the Gaussian envelope can be found using Equations (2.15), (2.20), (2.21), and the following condition:

\[ \Delta \tau_g = 2\sigma_t \]

\[ \beta'(\omega_0) \cdot 2\Delta L_{AR} = 2\sigma_t \]

(2.22)

\[ \Delta L_{AR} = \frac{\sigma_t}{\beta'(\omega_0)} = \frac{1}{\beta'(\omega_0) \sigma_\omega} = \frac{v_g}{\sigma_\omega} \]
Note that the phase velocity and group velocity are both equal to the speed of light \( c \) for propagation through free space and the axial resolution is thus given by

\[
\Delta L_{AR} = \frac{c}{\sigma_\omega}
\]  

(2.23)

Therefore, we see that the axial resolution of a Michelson interferometer is inversely proportional to the power spectral bandwidth of the low-coherence light source.

Additionally, the above analysis shows that the spectral bandwidth of the light source exhibits an inverse relationship with the coherence length of the light source. Recall that the coherence length is the propagation distance over which an electromagnetic wave maintains the degree of coherence necessary for interference. As seen in Equation (2.19), interference occurs only over a certain distance where the envelope is strong. The length of this interfering region is the coherence length of the light source and from Equation (2.23), the coherence length is equal to the axial resolution. Beyond this region, the envelope falls off and the wave interference is drastically weaker. This is known as coherence gating, where the low coherence of the light source only allows interference of light from a very short path length mismatch between the sample and reference arms. Any light from a path outside of this coherence gate (e.g. light from the sample arm that has traveled much farther/shorter than light from the reference arm) is incoherent and does not interfere with the reference beam.

2.2.4 Group Velocity Dispersion and Gaussian Light Sources

Until now, the analysis has considered only situations where light from both sample and reference arms have propagated through the same non-dispersive materials. In reality, many materials exhibit group velocity dispersion (GVD), which creates a nonlinear relationship between the propagation velocity of light in a material and wavelength. This produces a wavelength dependent phase delay determined by the type and length of material that the light is traveling through. Significant GVD can result in broadening and degradation of the axial point spread function, leading to poor axial resolution. Since GVD can be present in fiber optics and in many sample materials, it is important to consider GVD in the analysis. GVD can be incorporated by examining the second-order Taylor expansion of the propagation constants around the center frequency \( \omega_0 \)

\[
\beta(\omega) = \beta(\omega_0) + \beta'(\omega_0)(\omega - \omega_0) + \frac{1}{2} \beta''(\omega_0)(\omega - \omega_0)^2
\]  

(2.24)

Note that the previous analysis in Section 2.2.3 has only considered a first-order Taylor expansion. Now consider a GVD mismatch \( \Delta \beta''(\omega_0) = \beta''(\omega_0) - \beta''(\omega_0) \) exists between the sample and reference paths along some length \( L_{GVD} \). The frequency phase mismatch from Equation (2.11) is thus given by
\[ \Delta \phi(\omega) = 2 \left[ \beta(\omega_0) + \beta'(\omega_0)(\omega - \omega_0) \right] \Delta L + \frac{1}{2} \Delta \beta''(\omega_0)(\omega - \omega_0)^2 \cdot 2L_{GVD} \quad (2.25) \]

Note that the phase mismatch is only affected by the difference in GVD between the sample and reference arms. This means that the degrading effects of GVD can be mitigated by balancing the GVD between the sample and reference paths. While this may be unintuitive, Equation (2.25) suggests that for some sample materials, the performance of the Michelson interferometer can be improved by introducing GVD instead of attempting to remove it. Following the analysis in Section 2.2.3, the interference term of the photocurrent becomes

\[ I_{det} \propto \mathcal{R} \left\{ e^{-j\omega_0 \Delta \tau_p} \int_{-\infty}^{\infty} S(\omega - \omega_0) e^{-j\frac{1}{2} \beta''(\omega_0)(\omega - \omega_0)^2 \cdot 2L_{GVD}} e^{-j(\omega - \omega_0) \Delta \tau_g d(\omega - \omega_0)} \frac{d(\omega - \omega_0)}{2\pi} \right\} \]

(2.26)

where the phase delay mismatch and group delay mismatch are defined as they were in Equation (2.15). Note that the GVD mismatch introduces a quadratic frequency-dependent phase for the power spectral density of the source \( S(\omega - \omega_0) \). From Equation (2.26), the interferometric signal is a short pulse with an envelope given by the Fourier transform \( S(\omega - \omega_0) \) propagating through a medium with second order dispersion. Just as short pulses broaden and chirp following propagation through dispersive media, so too will the interferometric signal as a result of the GVD mismatch between the reference and sample paths. Now suppose that the light source is Gaussian like before with power spectral density given by Equation (2.16). Substituting back into Equation (2.26), the interferometric signal is given by

\[ I_{det} \propto \mathcal{R} \left\{ e^{-j\omega_0 \Delta \tau_p} \frac{\sigma_t}{\Gamma(2L_{GVD})} e^{-\frac{1}{2} \left( \frac{\Delta \tau_g d(\omega - \omega_0)}{2L_{GVD}} \right)^2} \right\} \]

(2.27)

where \( \sigma_t \) is defined as it is in Equation (2.20) and the width of the envelope is given by

\[ \Gamma(2L_{GVD})^2 = \sigma_t^2 + j\Delta \beta''(\omega_0) \cdot 2L_{GVD} \quad (2.28) \]

Note this is a complex value, where the real and imaginary components describe the broadening and chirping of the interferometric signal. To simplify, define the dispersion parameter

\[ \tau_{critical} = \sqrt{\Delta \beta''(\omega_0) \cdot 2L_{GVD}} \quad (2.29) \]
and Equation (2.28) can be rewritten as

\[
\frac{1}{\Gamma(2L_{GVD})^2} = \frac{\sigma_t^2}{\sigma_t^4 + \tau_{\text{critical}}^4} - j \frac{\tau_{\text{critical}}^2}{\sigma_t^4 + \tau_{\text{critical}}^4}
\]  

(2.30)

Thus the width of the Gaussian envelope has been broadened (and the axial resolution degraded) by GVD, with the new width given by

\[
2\sigma_{GVD} = 2\Re \left[ \Gamma(2L_{GVD}) \right] = 2\sigma_t \sqrt{1 + \left( \frac{\tau_{\text{critical}}}{\sigma_t} \right)^4}
\]  

(2.31)

Note GVD also reduces the peak height of the Gaussian envelope, where the reduction in height can be seen in Equation (2.27) and is described by the multiplicative factor

\[
\frac{\sigma_t}{\Gamma(2L_{GVD})} = \left[ 1 + \left( \frac{\tau_{\text{critical}}}{\sigma_t} \right)^4 \right]^{-1/4}
\]  

(2.32)

In addition to broadening the envelope, the presence of GVD also introduces a chirp to the interferometric signal. The interferometric carrier signal now chirps, as it no longer oscillates at a steady frequency with respect to the path length mismatch \( \Delta L \). This can be observed by differentiating the phase in Equation (2.27)

\[
\frac{d\phi}{d\Delta L} = 2\beta(\omega_0) - 4\Delta \beta'(\omega_0) \left( \frac{\tau_{\text{critical}}^2}{\sigma_t^4 + \tau_{\text{critical}}^4} \right) \Delta L
\]  

(2.33)

Note that GVD has only modified the phase of the interference signal and not the bandwidth.

2.2.5 Higher Order Dispersion

Section 2.2.4 considered the effect of second-order dispersion (GVD) on the interferometric component of the photocurrent at the detector. In reality, there are many higher order terms present in the Taylor expansion of the propagation constant \( \beta(\omega) \) that can affect the signal. For example, the third order term is analogous to cubic dispersion (variation of GVD with wavelength).

Analysis of these higher order terms can be conducted by performing a higher order Taylor expansion of the propagation constant \( \beta(\omega) \) and repeating the analysis in Section 2.2.4. Generally, only the second and third order terms are considered as they are dominant once the
sample and reference paths are properly dispersion matched. Physical matching of the dispersion between the sample and reference arms is often achieved by inserting compensation glass or other materials into the reference path to better match the material in the sample path.

2.3 Swept Source OCT

This section describes the Michelson interferometer as the functional unit of swept source OCT (SS-OCT) and discusses the principles of low-coherence interferometry that enable precise location of reflective boundaries in tissue. This section expands on Section 2.2 to discuss integration of Michelson interferometry for swept source OCT and analyzes a host of parameters affecting OCT image quality.

2.3.1 Integration of Michelson Interferometer and Balanced Detection

The principles of swept source OCT are fundamentally described by a Michelson interferometer, where OCT images are produced by interfering light from two different optical paths (the sample and reference arms) and processing the resulting interference fringes. The schematic of a typical SS-OCT configuration can be seen in Figure 2-2.

![Figure 2-2 Bulk optics setup of SS-OCT interferometer with balanced detection.](image)

Note that this schematic is nearly identical to that of a Michelson interferometer in Figure 2-1 and the same principles discussed in Section 2.2 still apply. Notable differences include the use of a swept source light source, the use of balanced detection, and the presence of multiple reflectors in biological tissue samples.
2.3.2 Swept Source OCT for a Single Reflector

Swept source OCT derives its name from its use of a swept source light source, a laser that rapidly sweeps through a band of wavelengths over a period of time. For simplicity, assume that the instantaneous linewidth of the laser is infinitely narrow (i.e. the laser output is monochromatic at any point in time) and the laser has infinite bandwidth (i.e. it sweeps through all wavenumbers). Assume also that the wavenumber \( k = \frac{2\pi}{\lambda} \) of the laser output sweeps linearly in time with the following relation

\[
k(t) = k_0 + k't
\]  

(2.34)

where \( k_0, k' \) denote the initial wavenumber and the wavenumber rate of change, respectively. In practical swept source lasers, the wavenumber does not sweep in a perfectly linear fashion and higher order modes exist, but this linear approximation is used for simplicity.

If the sample is reflective at only one depth (i.e. assume the sample is a simple, uniform mirror), then the resulting interference fringe can be found using the same analysis as in Section 2.2.1. From Equation (2.7), the photocurrent produced by the interference fringe incident on a single detector is given by

\[
I_{\text{det}} = \frac{\eta q}{h \nu} \cdot \frac{1}{\eta_0} \left[ \frac{1}{2} |A_R|^2 + \frac{1}{2} |A_S|^2 + A_R A_S \cos \left( 2(k_0 + k't)\Delta L \right) \right]
\]  

(2.35)

It is important to note that the swept source laser power output, the Michelson beam splitter, and the sample/reference mirror reflectivities can exhibit a wavelength dependence. Therefore, the photocurrent is more accurately described by

\[
I_{\text{det}} = \frac{\eta q}{h \nu} \cdot \frac{1}{\eta_0} \left[ \frac{1}{2} |A_R(k(t))|^2 + \frac{1}{2} |A_S(k(t))|^2 + A_R(k(t)) A_S(k(t)) \cos \left( 2(k_0 + k't)\Delta L \right) \right]
\]  

(2.36)

For simplicity, assume the laser power spectral density, beam splitter split ratio, sample reflectivity, and reference reflectivity are all uniform in wavenumber so that Equation (2.35) can be used.

It is also important to note that SS-OCT uses balanced detection instead of a single detector. The interfered light from the Michelson beamsplitter is sent to a 50/50 beam splitter where light is equally split into two beams for separate detection by two different photodiodes.
The 50/50 beam splitter transmits half the AC component of the interference power into one photodiode and reflects the other half with a $\pi$ phase shift into the second photodiode. By measuring the difference signal between the two photodiodes, a balanced detector cancels the DC component (i.e. the constant terms) and extracts the AC component (the AC components combine due to the phase shift). As a result, only the AC component remains in the interference pattern

$$I_{\text{det}} = \frac{\eta q}{h \nu} \frac{1}{\eta_0} \left[ A_R A_S \cos \left( 2 \left( k_0 + k' t \right) \Delta L \right) \right]$$ (2.37)

The output signal is thus a sinusoid in $k(t)$ oscillating with a frequency given by the path length mismatch $\Delta L$ between the sample and reference arms. The magnitude of the oscillation is set by the cross-correlation between the sample and reference reflections (i.e. the product of the sample and reference reflectivities, encapsulated by $A_R A_S$). To recover the depth of the sample reflection (relative to the reference reflection), one needs only to extract the frequency of the sinusoid in $k$ given by Equation (2.37). This can be achieved with a Fourier transform, where the Fourier transform of a function is defined as

$$F(\omega) = \mathcal{F} \{ f(k) \} = \int_{-\infty}^{\infty} f(k) e^{-i \omega k} dk$$ (2.38)

The Fourier transform of Equation (2.37) is thus

$$\mathcal{F} \{ I_{\text{det}}(k) \} \propto \mathcal{F} \{ \cos(2k\Delta z) \} \propto \frac{1}{2} \delta(z + 2\Delta z) + \frac{1}{2} \delta(z - 2\Delta z)$$ (2.39)

where the Fourier inverse of the wavenumber $k$ is position in space given by $z$, the path length mismatch has been substituted with a change of variable $\Delta L = \Delta z$, and $\delta(z)$ is the Dirac delta function. The location of the Dirac delta peaks is thus proportional to the displacement between the two arms $\Delta z$. This is the SS-OCT signal and this relationship is illustrated in Figure 2-3.
Figure 2-3 SS-OCT signal produced by imaging a simple mirror. The interference pattern observed by the balanced detector is on the left and is a function of wavenumber. The Fourier transform of the fringe signal can be seen on the right. Note the absence of a DC peak (due to the use of balanced detection) and the peak spacing is set by the path length mismatch between the sample and reference arms.

When imaging with SS-OCT, the reference mirror is kept stationary. The $z = 0$ position corresponds to the sample mirror position when the sample and reference arm paths are matched (i.e. $\Delta z = 0$). This is known as the zero delay position. Thus, when imaging a single reflector with SS-OCT under ideal conditions, the output signal is a single sinusoidal waveform encoding the position and reflectivity of the sample reflector. The amplitude of the sinusoid encodes the sample reflectivity and the oscillation frequency encodes the position of the sample reflector relative to the zero delay position.

2.3.3 Point Spread Function

Following the analysis of the SS-OCT interferometric signal in Section 2.3.2, the point spread function can now be characterized. The point spread function describes the response of the SS-OCT to a point source (in this case, a single ideal reflector) and analysis of the point spread function is important for understanding the precision with which SS-OCT can locate sample reflectors.

Note that the analysis in Section 2.3.2 assumed the use of a uniform laser light source with infinite bandwidth. This meant that Fourier transformation of the SS-OCT signal produced infinitely narrow Dirac delta peaks (i.e. the point spread function is infinitesimally thin), providing infinite axial resolving power for perfect location of a sample reflector. In reality, laser sources have limited optical bandwidth and non-uniform power output. Recall from Section 2.2.3 that axial resolution was demonstrated to exhibit an inverse relationship with bandwidth. Consequently, limited optical bandwidth will limit the axial resolving power of SS-OCT and the point spread function must have finite width.

To illustrate this point, suppose now that the SS-OCT system analyzed in Section 2.3.2 now has a light source with Gaussian power spectral density given by

$$S(k - k_c) = \frac{2\pi}{\sigma_k^2} e^{-\frac{(k - k_c)^2}{2\sigma_k^2}}$$  \hspace{1cm} (2.40)

where $k_c$ denotes the wavenumber at the center of the swept range and $\sigma_k$ is the standard deviation of the Gaussian. From Equation (2.37), the amplitude of the interferometric signal should now exhibit a dependence on $k$ given by the power spectral density. In other words, the power spectral density becomes the envelope of the interferometric signal such that
\[ I_{\text{det}} \propto A_R(k) A_S(k) \cos(2k\Delta L) \propto e^{-\frac{(k-k_c)^2}{2\sigma_k^2}} \cos(2k\Delta L) \]  

Recall that the Fourier transform of a Gaussian remains a Gaussian function, but the Fourier transformed Gaussian has an inversely proportional standard deviation relative to the original Gaussian function. The effect of the Gaussian envelope on the interferometric signal is illustrated in Figure 2-4.

![Figure 2-4 SS-OCT signal produced by imaging a simple mirror using a Gaussian swept source laser. The interference pattern observed by the balanced detector is on the left and is a function of wavenumber. The Fourier transform of the fringe signal can be seen on the right. Note the Gaussian envelope of the fringe results in a broadened point spread function compared to Figure 2-3.](image)

The envelope on the interferometric signal results in a broadened point spread function compared to Figure 2-3. If the optical bandwidth of the Gaussian light source is increased, then the Gaussian envelope of the fringe will be broadened. Consequently, the width of the point spread function will be reduced (broadening the Gaussian in \(k\) will result in a narrowing the Gaussian in the Fourier space \(z\)). This corresponds with the result in Section 2.2.3 where axial resolution was shown to be inversely proportional to the bandwidth of the laser. In fact, Figure 2-4 shows that the shape and spread of the laser power spectrum \(S(k-k_c)\) sets the shape of the point spread function \(\mathcal{F}\{S(k-k_c)\}\).

2.3.4 Multiple Reflectors in Biological Tissue and Axial Resolution

The point spread function defines the axial resolving power of SS-OCT and this can be best understood by considering SS-OCT imaging of biological tissue. Biological specimens are composed of multiple layers and types of cells, each of which scatter and reflect light to varying degrees. Thus, multiple reflections from different layers must be considered when imaging tissue. If the point spread function of the system is too broad, then the axial resolution is poor and the system will be unable to distinguish closely spaced layers. To understand this, consider
the interferometric signal at the balanced detector, which can now be described as the superposition of the signals from the different layers in the tissue

\[ I_{\text{det}} = \frac{\eta q}{h} \cdot \frac{1}{\eta_0} \left[ \sum_{n=1}^{\infty} A_R(k) A_{S,n}(k) \cos(2k\Delta L_n + \theta_n(k)) + \right. \]

\[ \left. \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} A_{S,m}(k) A_{S,n}(k) \cos \left[ 2k(\Delta L_n - \Delta L_m) + \theta_{n,m}(k) \right] \right] \]

where \( A_{S,n}(k) \) incorporates the sample reflectivity at differing depths \( \Delta L_n \) relative to the reference arm position.

The beam splitter is assumed to be uniform in wavenumber, enabling the balanced detection scheme to suppress the DC (autocorrelation) components from the signal. The phase term \( \theta(k) \) describes the difference in phase between reflectivities. This is important to consider, as the previous analysis in Sections 2.3.2 and 2.3.3 only considered imaging simple, uniform mirrors (i.e. samples with purely real reflectivities). However, biological tissue samples often exhibit complex reflectivities and introduce a wavelength-dependent phase delay upon reflecting incident light.

Note also that the signal now contains a cross-correlation component produced by interference of reflections from different layers of the sample. Each tissue layer produces a reflection that interferes with reflections from every other tissue layer. In standard SS-OCT operation, there is much more light reflected by the reference arm than from the tissue layers. Thus \( A_R(k) \gg A_{S,n}(k) \) and Equation (2.42) simplifies to

\[ I_{\text{det}} \propto \sum_{n=1}^{\infty} A_R(k) A_{S,n}(k) \cos(2k\Delta L_n + \theta_n(k)) \]

The signal is a superposition of sinusoids where the frequency of each sinusoid encodes the depth of the reflecting layer (relative to the reference arm) and the amplitude of each sinusoid describes the layer reflectivity. Again, just like in the case of a single reflector, taking a Fourier transform of Equation (2.43) with respect to \( k \) will enable recovery of the depth and amplitude of each reflection. To simplify this calculation, assume that the tissue reflectivity and phase delay are independent of wavelength (i.e. \( A_{S,n}(k) \rightarrow A_{S,n} \) and \( \theta_n(k) \rightarrow \theta_n \)) such that

\[ \mathcal{F}\{I_{\text{det}}\} \propto \mathcal{F}\left\{ A_R(k) \sum_{n=1}^{\infty} A_{S,n} \cos(2k\Delta L_n + \theta_n) \right\} \]

(2.44)
For more insight, Equation (2.44) can be rewritten in terms of the spectrum of the swept source laser \( S_s(k) = A_s^2(k) \), the sample power reflectivity \( R_s(k) \), and the reference mirror power reflectivity \( R_r(k) \). Recall that the responses of the beamsplitter, reference mirror, and sample tissue are assumed to be uniform in wavelength such that Equation (2.44) becomes

\[
\mathcal{F}\{ I_{\text{det}} \} \propto \mathcal{F}\left\{ \left( A_s(k) \sqrt{R_r} \right) \sum_{n=1}^{\infty} \left( A_i(k) \sqrt{R_{s,n}} \right) \cos(2k\Delta L_n + \theta_n) \right\} \tag{2.45}
\]

Recall from the convolution theorem that the Fourier transform of a product is equivalent to the convolution of the Fourier transforms. Thus, Equation (2.45) can be written as

\[
\mathcal{F}\{ I_{\text{det}} \} \propto \mathcal{F}\left\{ A_i^2(k) \right\} \otimes \sqrt{R_r} \sum_{n=1}^{\infty} \sqrt{R_{s,n}} e^{\pm j\theta_n} \delta(z \pm 2\Delta z_n) \tag{2.46}
\]

where the different depths of each layer have been substituted with a change of variable \( \Delta L_n = \Delta z_n \) and \( \delta(z) \) is the Dirac delta function. Note that Equation (2.46) is Hermitian symmetric – this is to be expected since the detectors can only sense light intensity, a real-valued signal. Consequently, the symmetry creates an ambiguity in ranging and it is not possible to distinguish whether a tissue layer is located a positive or negative distance from the reference arm. This can potentially create overlapping artifacts in the image, so it is crucial that the sample is positioned such that all layers are positive or negative distances from the zero delay position (i.e. all \( \Delta z_n \) are the same sign).

Equation (2.46) also shows that the reflection from each layer in tissue is convolved with the point spread function. The point spread function (given by the Fourier transform of the spectrum of the laser) has a direct effect on the axial resolving power of SS-OCT and this is illustrated in Figure 2-5. The spectrum of the laser is assumed to be Gaussian and consequently, the point spread function is also assumed to be Gaussian.
The result of convolving the point spread function with Dirac delta functions representing reflections from different layers in the sample. The SS-OCT signal is the Fourier transform of the detected interference fringes and well-spaced layers are clearly distinguishable while closely spaced layers cannot be resolved.

Taking a closer look at Figure 2-5, the Dirac delta functions represent the reflections from each layer of the sample. Layers that are more reflective will have a stronger Dirac delta peak. The output SS-OCT signal is the convolution of this Dirac delta peak pattern with the system point spread function. Recall that the shape of the point spread function is set by the shape and spread of the laser power spectrum. If the point spread function is narrow, then the system has good axial resolution and reflections from different layers in the tissue can be resolved. However, if the point spread function is too broad, then the system has poor axial resolution and it is not possible to distinguish reflections from closely-spaced layers.

The axial resolution of an SS-OCT system thus defines its ability to distinguish closely spaced reflective layers in tissue samples. In SS-OCT, the axial resolution is typically reported as the full width half maximum (FWHM) of the point spread function. For a swept source laser with a Gaussian power spectrum given by

$$A_i^2(k) = e^{-\frac{(k-k_c)^2}{2\Delta k^2}}$$

(2.47)

where $k_c, \Delta k$ denote the center wavenumber of the swept range and standard deviation of the Gaussian, respectively, the point spread function is given by
\[
F\left\{ A_i^2(k) \right\} = \sqrt{\frac{2\pi}{\Delta k}} e^{-j k_c z} e^{-\frac{z^2}{2\Delta k^2}}
\]

(2.48)

and the FWHM is thus

\[
FWHM = \frac{2\sqrt{2\ln 2}}{\Delta k}
\]

(2.49)

The FWHM can also be written as a function of wavelength by substituting the relationship

\[
\Delta k = 2\pi \frac{\Delta \lambda}{\lambda_c^2}
\]

where \(\lambda_c, \Delta \lambda\) are the center wavelength and span in wavelength, respectively. Then the FWHM is given by

\[
FWHM = \frac{\sqrt{2\ln 2}}{\pi} \frac{\lambda_c^2}{\Delta \lambda}
\]

(2.50)

2.3.5 Scanning for 2D and 3D data

Until now, SS-OCT has been described for generating a depth resolved measurement of reflectivity at a single location on a sample. In practical SS-OCT systems, the laser beam is focused by a lens down to a single spot on or near the surface of the sample. This yields a one-dimensional data set (1-D image) of the depth-dependent reflectance of the sample known as an A-scan. By scanning the spot in a line across the surface of the sample, a two-dimensional data set (cross-sectional image) can be created. This is known as a B-scan. Scanning an area will yield a three-dimensional data set (volumetric image). This is known as a C-scan.

Two-dimensional data sets (B-scans) provide cross-sectional information about sample reflectivity and are displayed as (2D) cross-sectional gray scale images, where the intensity of each pixel corresponds to the reflectivity at a particular depth and lateral position in the sample. Three-dimensional data sets (C-scans) can be displayed as volumetric renderings where the intensity of each voxel corresponds to the reflectivity at a particular depth and x/y position in the sample. The digital nature of the volumetric data provides SS-OCT with arbitrary sectioning capabilities, enabling slicing (and viewing) of any plane through the volume. For example, three-dimensional data sets can also be displayed with sections taken by slicing through the volume at an arbitrary plane and creating a video fly-through of each (2D) section while moving in the orthogonal direction (e.g. flying through the z dimension for sections taken in the x-y dimensions).

The implementation of scanning and introduction of a focusing lens introduces additional complexity to the system that will be analyzed in a later chapter.

2.3.6 Coherence Length
Recall from Section 2.2.3 that the coherence length is the propagation distance over which an electromagnetic wave maintains the degree of coherence necessary for interference. In that section, it was shown that the use of a broadband (i.e. low coherence) light source for interferometry results in coherence gating, which only allows interference of light from a very short path length mismatch between the sample and reference arms. Light outside of this coherence gate is incoherent and does not interfere.

This coherence gating is one of the limiting factors on the depth of tissue that can be imaged with OCT. Certain implementations of OCT (e.g. time-domain OCT and spectral-domain OCT) rely on broadband light sources that simultaneously emit a wide band of wavelengths. This drastically reduces the coherence length of the output light and sets the axial resolution of the OCT system, as seen in Section 2.2.3. In SS-OCT, however, the coherence length sets the imaging depth of the system rather than the axial resolution. This is because the swept source light source (as we assumed in the above analysis) is monochromatic at any single point in time. In reality, the instantaneous light output from a swept source laser actually spans a narrow range of $k$ values (i.e. the instantaneous spectrum of the laser has finite width). However, this linewidth is still much narrower than the broadband light sources used in spectral-domain OCT and allows for a much greater coherence length. The improved coherence length enables SS-OCT to image much deeper into tissue, as light reflected from deeper layers in tissue is still coherent enough for interference with light from the reference arm.

2.3.7 Detector Bandwidth and CMRR

The bandwidth of the balanced detectors is another limiting factor on the depth of tissue that can be imaged with SS-OCT. As seen in Figure 2-6, a standard dual balanced detector has a relatively flat frequency response up to a rated bandwidth. This bandwidth is typically given as the -3 dB point, the frequency at which the detector gain has fallen by 3 dB relative to the passband and above which the detector gain rapidly decays. The rate at which the detector gain decays beyond the -3 dB point depends on the design and number of amplifier stage(s) within the detector. The common-mode rejection ratio (CMRR) describes the ability of the balanced detector to reject common-mode signals (signals that appear in-phase and simultaneously at both inputs).
Recall from Section 2.3.2 that in SS-OCT, the photocurrent at each of the photodiodes in the balanced detector consists of a sinusoid in wavenumber \( k \). Section 2.3.4 also showed that the interference signal from deeper layers/depths in the sample are encoded as sinusoids of higher frequencies in \( k \). Since SS-OCT uses a swept source laser (laser output sweeps through different wavenumbers in time), the resultant photocurrent is a signal that varies in time (i.e. \( I_{\text{det}}(k(t)) \)). Reflections from deeper layers of the sample thus have very high frequencies in time and a high detector bandwidth is critical for imaging deep into the sample. Without sufficient bandwidth, high frequency signals (i.e. signals from deep in the tissue) will be far beyond the -3 dB point and signal levels will be indistinguishable from noise.

The requirement for detector bandwidth will depend on the desired depth of tissue imaging, but it is also important to consider the magnitude of the detector gain itself. Balanced detectors use operational amplifiers to amplify the photodetector current and convert it into an output voltage. However, all operational amplifiers exhibit a fixed gain-bandwidth product equal to the bandwidth at which the gain is equal to unity. That is, amplifiers have a fundamental tradeoff between gain and bandwidth, where the gain is inversely proportional to bandwidth. In order to perform high-speed SS-OCT imaging, the sweep frequency (the rate at which a swept source laser sweeps through the entire band of output wavelengths) must be very high. Doing so will require balanced detectors with bandwidth at the hundreds of megahertz to gigahertz level. However, the gain-bandwidth tradeoff means bandwidth requirements necessary for high-speed imaging must be balanced with the gain requirements necessary for adequate signal-to-noise ratio (SNR) performance. This SNR issue will be discussed further in Sections 2.4 and 2.5.
In SS-OCT, strong common-mode rejection is also necessary to achieve high dynamic range through suppression of the DC component of the interference signal. The SS-OCT analysis above has assumed uniform performance of beamsplitters and photodiodes, allowing the autocorrelation terms described by Equation (2.36) to be perfectly canceled by a dual balanced detection scheme. In reality, these autocorrelation terms remain in the output interference signal due to imperfections in the dual balanced detector. Ideally, a balanced detector outputs only the amplified difference of the input signals

\[ V_{\text{ideal}} = A_d (I_+ - I_-) \]  

(2.51)

where \( V_{\text{ideal}} \) is the output voltage, \( A_d \) is the differential gain, and \( I_+, I_- \) are the two inputs. In reality, the output is better described by

\[ V_{\text{actual}} = A_d (I_+ - I_-) + \frac{1}{2} A_{cm} (I_+ + I_-) \]  

(2.52)

where \( A_{cm} \) is the common-mode gain. The common-mode rejection ratio is defined as the ratio of the power of the differential gain over the power of the common-mode gain:

\[ CMRR = 20 \log_{10} \left( \frac{A_d}{A_{cm}} \right) \text{ dB} \]  

(2.53)

In SS-OCT, the common-mode signal in Equation (2.52) will be the sum of the autocorrelation signals from the two photodiodes, since the out-of-phase AC components will be canceled by the addition operation. If the CMRR is low, then the common-mode signal will introduce a strong DC component into the output SS-OCT interference signal and the dynamic range of the SS-OCT system will suffer. This dynamic range issue will be discussed further in Section 2.3.8.

### 2.3.8 Analog to Digital Sampling and Dynamic Range

The interferometric signal from the balanced detector is an analog voltage that must be digitized for computational processing and interpretation. This is performed with a computer A/D (analog to digital) acquisition card that converts the analog signal from the detector (continuous in time and amplitude) to a digital signal (discrete in time and amplitude). In order to obtain images of weak reflectors in deep layers of the sample, the A/D card must have a high sample rate and high bit-depth.

Until now, the analysis has considered a continuous time Fourier transform of the interference signal to recover the reflectivity and depth of a layer in the sample. This cannot be done in practice, as computers store data in discrete sequences with finite length. Instead, a finite number of samples \( N \) is taken of the interference signal at a finite rate \( f_s \) for each sweep of the
laser and a discrete Fourier transform (DFT) of length $N$ is computed. The magnitude of the DFT is then plotted with frequencies between $-f_s / 2$ and $f_s / 2$ as dictated by the Nyquist sampling theorem. This is a depth image and commonly referred to as an A-scan, where the frequency corresponds to depth in the sample (relative to the zero delay position) and the amplitude corresponds to the sample reflectivity. This also establishes the upper limit in depth that can be seen with SS-OCT, as any frequency above the Nyquist sampling frequency will be aliased down to lower frequencies, producing artifacts in the depth image. Since the DFT was of length $N$, the depth image has $N$ samples with spacing $f_s / N$ and this sets the spacing in depth per DFT bin (i.e. the real length of each DFT bin). That is, the A-scan image is an $N \times 1$ pixel image where each pixel has a real length determined by $f_s / N$ and the intensity of each pixel corresponds to the sample reflectivity at that depth. It is possible to achieve denser sampling of the DFT by zero-padding the sampled interference fringe, but recall from discrete Fourier theory that this does not improve the frequency resolution of the DFT, which is fundamentally determined by $f_s / N$.

However, it is still important to perform dense sampling of the DFT to take advantage of the high (optical) axial resolution provided by SS-OCT. Recall from Section 2.3.3 and 2.3.4 that the axial resolution of the system is set by the point spread function of the system (which in turn is set by the shape and spread of the laser power spectrum). For good imaging results, the sampling of the DFT must be dense enough that the real length of each A-scan pixel (i.e. each DFT bin) does not exceed the width of the point spread function. Recall also from Section 2.3.4 that the Fourier transform of the interference signal is Hermitian symmetric, producing redundant information between the negative and positive frequencies. As a result, only $N / 2$ values in the DFT (i.e. only half the original A-scan image) provides useful data since half of the image is simply a mirror copy of the other half.

Another factor to consider is the dynamic range of the system and the dynamic range of the A/D card in particular. The A/D card can only digitize input signals within a certain range of voltages (usually a range of several hundred millivolts centered around zero) and this is done by subdividing the entire range into a number of equal intervals. Each sample of the input signal is quantized by representing the sample as a sequence of bits encoding the input voltage as belonging to one of the intervals within the range. The number of available intervals is determined by the number of bits used by the A/D card for each sample (i.e. the bit depth). If fewer bits are used, the quality of the sampled data is poorer since each interval is wider and there is greater rounding of the input signal. For example, a 1-bit A/D card has only two intervals in its dynamic range and a sine wave input spanning the entire input dynamic range would be quantized as either 0 or 1 (i.e. the lower interval or the upper interval). The resulting sampled signal would look like a square wave – clearly a poor reproduction of an input known to be a sine wave. If the common-mode rejection of the balanced detector is poor, then the SS-OCT interference signal will also have a strong DC component that may cause the interference signal
to become partially outside the dynamic range of the A/D card. To avoid saturating the A/D card, the power to the reference arm must be reduced in order to reduce the amplitude of the AC interference fringes now riding on top of the DC component. This is not ideal because for any given bit-depth, the amplitude of the AC fringes will now be smaller relative to the size of the quantization intervals. This reduces the signal power relative to the quantization noise (rounding error introduced by quantization). This is especially problematic when imaging a weak reflector, as the amplitude of the interference fringe might now be very close to the size of the quantization intervals, making it indistinguishable from quantization noise.

### 2.3.9 Imaging Range

The imaging range of an SS-OCT system is often given as the depth where the signal from a sample mirror becomes unusable. There are various definitions reported in the literature, but common definitions are the sample depth where the interference signal has decayed by -3, -6, -10, or -20 dB. In SS-OCT, the usable imaging range is affected by several factors including the laser coherence length, detector bandwidth, and A/D card sampling rate as described in the sections above. Figure 2-7 considers a variety of different configurations to illustrate the effect that each of these components has on the usable imaging range. Note that this specification describes an ideal sample (i.e. a mirror with strong, uniform reflectivity). In reality, biological tissue can be highly scattering and reflections from deeper layers can be very weak because most light has been scattered or absorbed.
**Figure 2-7** Analysis of SS-OCT imaging range in different configurations. (A) Sample arm imaging setup consisting of three equally spaced layers with equal reflectivity. (B) Configuration with low coherence length. Note the reduction in signal intensity at deeper layers due to the limited coherence length. (C) Configuration with low bandwidth detector with long coherence length. Note the signal intensity in deeper layers suffers beyond the detector bandwidth cutoff. (D) Configuration with low A/D sampling rate. Note the reduced Nyquist frequency (350 MHz instead of 500 MHz in other configurations). This results in a shorter range of viewable frequencies/depths and causes the signal from the layer at 2.4 mm to alias down to 1.8 mm.

### 2.3.10 Dispersion Compensation

The analysis of the SS-OCT signal in Section 2.3 has thus far assumed light from both sample and reference arms have propagated through the same non-dispersive materials. In reality, the propagation velocity of light in a material is wavelength dependent and optical design differences between the sample and reference arms result in a dispersion mismatch between the two paths. This results in a wavelength dependent phase delay that was analyzed in Sections 2.2.4 and 2.2.5. These sections showed that the dispersion mismatch results in a broadening of
the interferometric envelope and chirping of the interferometric signal itself. This ultimately distorts the SS-OCT point spread function and results in poor image quality.

To visualize the effect of dispersion mismatch on the point spread function, consider the phase mismatch given by Equation (2.25) and the interference signal given by Equation (2.26). Note that the dispersion mismatch introduces a dispersion phase term on the power spectrum of the light source. Recall from Section 2.3.3 that the point spread function is given by the Fourier transform of the light source power spectrum. Thus, the effect of the dispersion mismatch can be seen by convolving the (non-dispersed) point spread function with the Fourier transform of the dispersion phase term. Although the analysis in Section 2.2.4 considered only a second-order (analogous to group velocity dispersion) dispersion mismatch, the analysis is the same for higher-order dispersion mismatch. The mismatch always manifests in the interference signal as a dispersion phase term on the power spectrum of the light source. The effect on the point spread function of different orders of dispersion is visualized in Figure 2-8.

![Figure 2-8](image_url)

Figure 2-8 Distortion of point spread functions due to dispersion mismatch. (A) Point spread function with no dispersion. (B) First-order dispersion shifts the point spread function but does not affect its shape. (C) Second-order dispersion symmetrically broadens the point spread function. (D) Third-order dispersion asymmetrically distorts the point spread function.

The physical significance of different orders of dispersion were discussed in the Taylor expansion of the propagation constant in Sections 2.2.4 and 2.2.5. The first-order term corresponds to a simple group delay. The second-order dispersion term corresponds to group velocity dispersion (GVD). The third-order dispersion term corresponds to a variation of GVD with wavelength. In SS-OCT, the second- and third-order terms are dominant because optical differences between the sample and reference arms are physically dispersion matched with
compensation glass. Higher-order terms (fourth-order and above) are thus generally not considered.

Physical dispersion matching requires placing compensation glass in the reference arm to match the dispersion introduced by the scanning optics typically used in the sample arm. Good matching is difficult to achieve as this requires the use of precise lengths of compensation glass. Additionally, the tissue sample itself can introduce dispersion and perfectly matching this in the reference arm is extremely difficult to achieve. In this case, numerical dispersion compensation can be implemented to improve image quality. This works by assuming that within the limited imaging range of SS-OCT, the dispersion mismatch introduced by the different layers of the tissue is roughly uniform. Under this assumption, the dispersion mismatch phase term on the power spectrum of the light source in Equation (2.26) can be corrected for by numerically introducing a compensating complex phase factor [1]. As discussed above, the second- and third-order dispersion mismatch terms are dominant in SS-OCT, so the compensating phase factor can be given by

\[ \Phi_c = \exp\left[j\left( a_2(\omega - \omega_0)^2 + a_3(\omega - \omega_0)^3 \right)\right] \] (2.54)

Multiplying the compensating phase factor onto the SS-OCT interference signal will correct for dispersion in the positive frequencies but amplify dispersion in the negative frequencies. However, recall that SS-OCT images are created from the Fourier transform of the interference signal from the detector and this is Hermitian symmetric because the detector signal is purely real. Thus, no depth information is lost if only the dispersion compensated positive frequencies are retained for the SS-OCT image. Additionally, since the compensating phase term is digitally introduced to the recorded interference signal, the values of \( a_2, a_3 \) can be found experimentally to provide the best image quality.

2.3.11 Wavenumber Calibration and Optical Clocking

The analysis of the SS-OCT signal in Section 2.3 has thus far assumed that the wavenumber \( k = \frac{2\pi}{\lambda} \) of the laser output sweeps perfectly linearly in time. In reality, this is not the case and many swept source lasers sweep in a resonance mode, producing sinusoidal sweeps in time. Recall from the above analysis that the SS-OCT interference signal fundamentally consists of the Fourier transform of sinusoids oscillating in \( k \). If the interference signal at the detector is sampled at a fixed rate in the case of nonlinear sweeps, a nonlinear phase shift is introduced at each \( k \) value and the point spread function suffers. This is illustrated in Figure 2.9.
Figure 2-9 (A) The $k$ values from a sinusoidally swept laser. (B) The result of constant-rate sampling of the interference signal from a single sample reflector. With a nonlinear sweep, the interference fringe is chirped instead of oscillating at a single frequency. (C) The Fourier transform of (B) shows a degraded point spread function.

In order to obtain the optimal point spread function, the interference signal must be sampled linearly in $k$. In SS-OCT, this is often done with one of two different methods.

The first method entails recalibrating interference fringes sampled at a fixed rate in time such that the resultant sample points are equally spaced in $k$. This requires recording a calibration fringe and finding the specific points in time that are equally spaced in $k$. The calibration fringe is typically a recording of the interference signal from a single reflector near the middle of the imaging range. The time points for resampling are found by using a Hilbert transform to analyze the analytic representation of the calibration fringe

$$I_{\text{analytic}}(t) = I_{\text{det}}(t) + j\mathcal{H}\{I_{\text{det}}(t)\}$$

where the Hilbert transform is defined by

$$\mathcal{H}\{I_{\text{det}}(t)\} = I_{\text{det}}(t) \otimes \frac{1}{\pi t} \int_{-\infty}^{\infty} \frac{I_{\text{det}}(\tau)}{t-\tau} d\tau$$

Substituting Equation (2.37) into Equation (2.55) and utilizing Euler's formula, the analytic representation of the calibration fringe is a phasor given by
The shape of the $k$ sweep can be recovered by observing the unwrapped phase of the analytic signal and this is seen in Figure 2-10.

\[ I_{\text{analytic}}(t) \propto \exp\left[ j2k(t)\Delta L \right] \] (2.57)

Figure 2-10 (A) The unwrapped phase values from the analytic representation of the calibration fringe from Figure 2-9B. Red lines indicate equally spaced phase values and the corresponding time points. (B) Resampling the calibration fringe from Figure 2-9B to the time points in Figure 2-10A produces the true sinusoid in $k$ without nonlinear phase shifts. Note the interference fringe is oscillating at a single frequency, as expected for a single reflector. (C) The Fourier transform of (B) shows the point spread function of the resampled fringe is not degraded.

Note the unwrapped phase of the analytic signal has the same shape as the $k$ sweep. Thus, the time points that correspond to equally spaced values of the unwrapped phase also correspond to equally spaced values of $k$. If the SS-OCT system resamples interference fringes to these points in time (obtained from the calibration fringe), the resulting fringes will be linear in wavenumber and the degradation of the point spread function can be eliminated. These time points can be used for resampling even when imaging biological tissue.

The above recalibration method assumes that every single sweep of the laser is identical (i.e. each sweep covers the same values of $k$). If this is not true, the system will require recalibration for every (different) sweep. In many SS-OCT systems, successive sweeps of the laser are different enough that every sweep will require a different recalibration to avoid significant degradation of the point spread function. To perform this recalibration for every sweep, a calibration signal must be simultaneously recorded alongside each recording of the
tissue/sample interference signal. This can be done by splitting off a small fraction of the laser output to a second path consisting of a Mach-Zehnder interferometer (MZI), as seen in Figure 2-11.

![Figure 2-11](A) Bulk optics setup of SS-OCT interferometer with balanced detection and MZI for linear-k calibration. (B) Bulk-optics setup of MZI. Geometry has been simplified for illustration purposes.

Only a small fraction of the total laser output is coupled into the MZI, typically with a 90/10 or similar beamsplitter. The MZI functions almost identically to a Michelson interferometer except each of the light paths is traversed only once. Note the difference in
distance traveled by light between the two paths (MZI geometry has been simplified for illustration purposes). With balanced detection, the MZI produces an interference fringe identical to that obtained from a single reflector as analyzed in Section 2.3.2, where the fringe frequency is set by $\Delta L_{\text{MZI}}$. By enabling simultaneous recording of a calibration fringe for every interference fringe from the tissue/sample, the setup depicted in Figure 2-11 can be used to obtain the optimal point spread function even when successive $k$ sweeps are not perfectly reproducible.

The second method for obtaining the optimal point spread function entails creating an optical clocking signal for non-uniform sampling of the interference fringes (in time) such that the sampled fringes are equally spaced in $k$. This can be achieved by looking at Equation (2.37) and noting that no matter the shape of the $k$ sweep, the interference fringe of a single reflector always has zeros that are equally spaced in $k$. Using the configuration in Figure 2-11, uniform sampling (in $k$) can be achieved by sampling the tissue/sample interference fringes only at times corresponding to the zero-crossings of each MZI fringe. Thus, a clock signal derived from the zero-crossings of each MZI fringe will achieve uniform sampling (in $k$) of each tissue/sample interference fringe. To create an optical clock signal, electronics are added to the balanced detector in Figure 2-11B to digitize the MZI fringe. The resulting clock signal is used by the A/D card as an external clocking signal to achieve uniform-in-$k$ sampling of tissue/sample interference fringes. This is known as optical clocking and the method is illustrated in Figure 2-12.

![Optical Clock](image)

**Figure 2-12** Optical clock signal derived from zero-crossings of MZI fringe. This figure assumes the same $k$ sweep as in Figure 2-9.
Recall from Section 2.3.9 that the imaging range of an SS-OCT system is limited by the A/D sampling rate and the associated Nyquist frequency. The A/D sampling rate is non-uniform with optical clocking, so the Nyquist frequency is set by the highest sample frequency within the range of frequencies present in the optical clock. As seen in Figure 2-12, the optical clock frequency is itself set by the MZI fringe frequency. Thus, when using optical clocking, the maximum viewable imaging range of an SS-OCT system is determined by the MZI fringe frequency (set by modifying $\Delta L_{MZI}$).

2.4 Noise Sources

This section reviews the dominant noise sources in SS-OCT. Knowledge of these noise sources will inform analysis of the signal-to-noise ratio (SNR) and minimum detectable reflectivity of the SS-OCT system.

The noise sources considered in the following sections are described by wide-sense stationary (WSS) stochastic processes. A WSS stochastic process $p(t)$ has a mean $\mathbb{E}\{p(t)\}$ and statistical autocorrelation $R_p(t_1, t_2)$ given by

$$\mathbb{E}\{p(t)\} = \langle p(t) \rangle = m_p$$

and

$$R_p(t_1, t_2) = \mathbb{E}\{p(t_1)p(t_2)\} = \langle p(t_1)p(t_2) \rangle$$

For a WSS stochastic process, the mean $m_p$ is constant and $R_p$ is a function of the time lag $\tau = t_2 - t_1$ alone. The frequency content of a WSS stochastic process is described by the power spectral density $S_p(\omega)$, given by the Fourier transform of the statistical autocorrelation

$$S_p(\omega) = \int_{-\infty}^{\infty} R_p(\tau)e^{-j\omega\tau}d\tau$$

The WSS stochastic processes describing the SS-OCT noise sources are all real-valued, so the power spectral density of these processes are real and even functions of $\omega$. In reality, only the positive frequencies are observed. For convenience, the single-sided power spectral density is defined as

$$S^+_p(\omega) = S_p(\omega) + S_p(-\omega) = 2S_p(\omega)$$

Note this is only valid for non-negative frequencies $\omega \geq 0$. 

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2.4.1 Thermal Noise

Thermal noise is the result of random particle motion due to thermal energy in a system. Resistors in the receivers used for SS-OCT are the only passive electrical elements that exchange energy with the environment. The transfer of energy between a resistor and its surroundings results in a temperature equilibrium describing the thermal noise. This can be modeled by the parallel combination of an ideal resistor of resistance \( R \) and a noisy current source \( I_{\text{noisy}} \) representing thermal noise/energy provided by the environment [2]–[4]. The noise current can be approximated by zero-mean white noise such that the single-sided power spectral density is given by

\[
S_{I_n}^+(\omega) = \frac{4k_B T}{R}
\]  

(2.62)

where \( T, k_B \) are the temperature and Boltzmann constant, respectively. In an SS-OCT system with limited electrical bandwidth \( B \), the mean square current noise is thus given by

\[
\langle I_{\text{thermal}}^2 \rangle = \frac{4k_B T}{R} B
\]  

(2.63)

Thermal noise is a property of the detector design and it is used to model electronic noise in the SS-OCT receiver [5].

2.4.2 Shot Noise

Shot noise is the result of current fluctuations due to quantization of light and charge incident on the photodetector. This is understood by considering that a photodetector emits charge proportional to a mean rate given by the photocurrent, but the time between specific charge emissions is random. In fact, the photon arrival and electron emission times are described by a random variable with a Poisson distribution. The shot noise associated with a mean detector photocurrent \( \langle I_{\text{det}} \rangle \) can be shown to be a white noise process with mean \( \langle I_{\text{det}} \rangle \) and single-sided power spectral density

\[
S_{I_{\text{c}}}^+(\omega) = 2q \langle I_{\text{det}} \rangle
\]

(2.64)

where \( q \) is the electrical charge constant. In an SS-OCT system with limited electrical bandwidth \( B \), the mean square current noise is thus given by

\[
\langle I_{\text{shot}}^2 \rangle = 2q B \langle I_{\text{det}} \rangle
\]

(2.65)

2.4.3 Excess Intensity Noise and Amplified Spontaneous Emission
Excess intensity noise consists of noise from any source where the power spectral density scales linearly with the mean photocurrent power $\langle I_{\text{det}}^2 \rangle$. This can include fluctuations in optical power from the source, mechanical motion of optical mounts, and self-beating of broadband light waves [6]. In broadband light sources, amplified spontaneous emission (ASE) also produces noise that scales linearly with photocurrent power. The excess intensity noise and ASE can be modeled as a white noise process with single-sided power spectral density given by

$$S_{I_n}^+(\omega) = \left(1 + \Pi^2 \right) \langle I_{\text{det}}^2 \rangle \frac{1}{\Delta \nu_{\text{eff}}}$$

(2.66)

where $\Pi, \Delta \nu_{\text{eff}}$ correspond to the degree of source polarization and the effective optical line width of the light source, respectively. In an SS-OCT system with limited electrical bandwidth $B$, the mean square current noise is thus given by

$$\langle I_{\text{ex}}^2 \rangle = \left(1 + \Pi^2 \right) \langle I_{\text{det}}^2 \rangle \frac{B}{\Delta \nu_{\text{eff}}}$$

(2.67)

### 2.5 Sensitivity and Noise

This section reviews the signal-to-noise ratio (SNR) and minimum detectable reflectivity of the SS-OCT system by considering the noise sources described in Section 2.4.

#### 2.5.1 Theoretical OCT Sensitivity

The sensitivity of the SS-OCT system is a measure of the minimum detectable sample reflectivity. This metric describes the ability of the SS-OCT system to distinguish signal from noise and incorporates many aspects of the system, including the light source, input power level, optical alignment, and detector choice. The sensitivity is also known as the signal-to-noise ratio (SNR) and is defined as the ratio of the signal power to the noise process variance. If the noise process is zero-mean WSS, then the noise process variance is equal to the mean noise power, given by the integral of the noise power spectral density over all frequencies such that

$$\text{SNR} = \frac{P_{\text{signal}}}{\text{var}\{n(t)\}} = \frac{P_{\text{signal}}}{P_{\text{noise}}} = \frac{P_{\text{signal}}}{\int_{-\infty}^{\infty} S_n(\omega) d\omega}$$

(2.68)

The mean photocurrent signal power is generated by the signal photocurrent from Equation (2.37):

$$54$$
\[ P_{\text{signal}} = \left\langle I_{\text{det}}^2 \right\rangle \]
\[ = \left\langle 2qB I_{\text{det}} + \frac{1}{\eta_0} A_R A_S \cos(2k(t)\Delta L) \right\rangle^2 \]
\[ = \frac{1}{2} \left( \frac{\eta q}{h\nu} \frac{1}{\eta_0} A_R A_S \right)^2 \tag{2.69} \]

Section 2.4 described the multiple noise sources in SS-OCT systems. Since these noise sources are uncorrelated, their noise powers are additive and the mean photocurrent noise power is given by

\[ P_{\text{noise}} = \left\langle I_{\text{noise}}^2 \right\rangle \]
\[ = \left\langle I_{\text{thermal}}^2 \right\rangle + \left\langle I_{\text{shot}}^2 \right\rangle + \left\langle I_{\text{ex}}^2 \right\rangle \tag{2.70} \]
\[ = \left[ 4k_B T \frac{B}{R} \right] + \left[ 2qB \left\langle I_{\text{det}} \right\rangle \right] + \left[ \left( 1 + \Pi^2 \right) \frac{B}{\Delta V_{\text{eff}}} \left\langle I_{\text{det}} \right\rangle^2 \right] \]

Note that thermal noise dominates when the signal photocurrent is low and excess intensity noise dominates when the signal photocurrent is high. SS-OCT systems operate between these regimes, as live tissue (e.g. the retina) has power exposure limits that set the upper bound on \( I_{\text{det}} \) but the reference arm power must be high enough that \( I_{\text{det}} \) is large enough for detection. In this regime, shot noise is the dominant noise source and the mean photocurrent noise power is given by

\[ P_{\text{noise}} = 2qB \left\langle I_{\text{det}} \right\rangle \tag{2.71} \]

It is important to note that this noise is present at both detectors in the dual balanced detector schemes used for SS-OCT. Since the output SS-OCT signal is the difference signal between the two detectors and the noise between detectors is uncorrelated, the overall noise power is actually the sum of noise powers at each detector. This means that the noise power at each detector is defined by the photocurrent at each individual detector (without autocorrelation terms canceled by balanced detection). Thus the individual detector photocurrent is given by Equation (2.36), but this can be simplified by noting that the reference autocorrelation generally dominates [7] since the reference reflection is much stronger:
\[ P_{\text{noise}} = P_{\text{noise,1}} + P_{\text{noise,2}} = 2P_{\text{noise,1}} = 4qB \langle I_{\text{det,1}} \rangle \]

\[ = 4qB \left[ \frac{\eta q}{h
u} \cdot \frac{1}{\eta_0} \right] \frac{1}{2} A_R^2 \]  
\[ = 2qB \left[ \frac{\eta q}{h \nu} \cdot \frac{1}{\eta_0} \right] A_R^2 \]  

(2.72)

The sensitivity is thus given by

\[ \text{Sensitivity} = \text{SNR} = \frac{P_{\text{signal}}}{P_{\text{noise}}} = \frac{1}{4} \left( \frac{\eta q}{h \nu} \cdot \frac{1}{\eta_0} \right) A_R^2 \cdot \frac{1}{q} \cdot \frac{1}{B} \]  

(2.73)

Note that in the shot noise limited regime, the sensitivity is inversely proportional to the electronics bandwidth. Additionally, note that the sample reflection power \( A_R^2 \) is itself directly proportional to the light source power, showing that the system sensitivity has a linear relationship with the light source power.

2.5.2 Measuring OCT Sensitivity

The sensitivity of an SS-OCT instrument can be measured experimentally by placing a neutral density (ND) filter with a measured optical density (OD) in the sample arm between the beamsplitter and a perfectly reflecting mirror. The mirror reflectivity is flat (i.e. independent of wavelength) and the mirror is placed at a fixed position within the imaging range of the system. The ND filter is used to prevent the saturation of the balanced detector that normally occurs when all sample arm power is reflected back into the system. Following Fourier transform of the interference fringe, the power value \( P_s \) of the peak is compared to the mean power of the surrounding noise \( P_n \). The optical density of the ND filter is also added back in to compensate the fact that the ND filter blocks signal energy and artificially lowers the peak power value. The sensitivity in decibels (dB) is thus given by

\[ \text{Sensitivity}_{\text{dB}} = 10 \log_{10} \left( \frac{P_s}{P_n} \right) + 20 \cdot \text{OD} \]  
\[ = 10 \log_{10} \left( \frac{P_s \cdot 10^{2 \cdot \text{OD}}}{P_n} \right) \]  

(2.74)

Note the optical density is the base 10 logarithm of the energy blocked by the ND filter. The OD is multiplied by a factor of 20 (instead of 10) to account for the round trip attenuation of light through the ND filter.
2.5.3 Design for Shot Noise Limited Sensitivity

Quantum limited operation of an SS-OCT system is only attained when the shot noise dominates all other noise sources. This can be seen by repeating the analysis in Section 2.5.1 without simplifying the noise power. The sensitivity is thus

\[
\text{Sensitivity} = \frac{P_{\text{signal}}}{P_{\text{noise}}} = \frac{P_{\text{signal}}}{P_{\text{noise,1}} + P_{\text{noise,2}}} = \frac{P_{\text{signal}}}{2P_{\text{noise,1}}}
\]

\[
= \frac{1}{2} \left[ \frac{4k_B T}{R} B \right] + 2qB \langle I_{\text{det,1}} \rangle + \left( 1 + \Pi^2 \right) \frac{B}{\Delta v_{\text{eff}}} \langle I_{\text{det,1}} \rangle^2
\]  

(2.75)

Note that

\[
\frac{\langle I_{\text{det}}^2 \rangle}{\langle I_{\text{det,1}} \rangle} = \frac{1}{2} \left( \frac{\eta q}{h \nu} \cdot \frac{1}{\eta_0} \right) A_R^2 A_S^2 = A_S^2
\]  

(2.76)

where \(A_S^2 \ll 1\) for SS-OCT imaging of biological tissue samples. Equation (2.75) can be rewritten as

\[
\text{Sensitivity} = \frac{1}{2} \left[ \frac{4k_B T}{R} B \right] + 2qB \langle I_{\text{det,1}} \rangle + \left( 1 + \Pi^2 \right) \frac{B}{\Delta v_{\text{eff}}} \langle I_{\text{det,1}} \rangle^2
\]  

(2.77)

Note that the photocurrent at each detector \(I_{\text{det,1}}\) is directly proportional to the reference arm power such that \(I_{\text{det,1}} \propto A_R^2\). The sensitivity can thus be altered by modifying the reference arm power, producing the sensitivity curve seen in Figure 2-13.
As seen previously in Section 2.5.1, thermal noise dominates at low reference arm power and system sensitivity is low. Increasing reference arm power until shot noise dominates brings the system into a regime where sensitivity scales linearly with reference arm power. Beyond this regime, excess intensity noise dominates and sensitivity tails off. **Figure 2-13** shows that optimal sensitivity is achieved in the shot noise limited regime and this operating point can be found by measuring the sensitivity as a function of reference arm power.

**2.5.4 Speckle Noise**

Speckle noise is a type of granular noise that is intrinsic to imaging methods making use of coherent sources (such as OCT and ultrasound). Speckle is caused by the interference of multiple returning waves at the detector and arises from multiple scattering in the forward and backward propagation of the light beam through the tissue/sample. The finite resolution of the OCT system means that at any point in time, the detector is receiving light from an array of scatterers within the tissue/sample. The size of this array is set by the system resolution cell (in OCT this is set by the coherence length). Since the light is coherent, light from multiple scatterers within the resolution cell will add coherently and produce constructive and destructive interference patterns. These interference patterns will then show up as bright and dark spots in the image.

Speckle noise is very common in OCT because certain layers of organic tissue are highly scattering. As a result, it is very likely that several scatterers within a tissue are located close enough to produce the speckle interference patterns. Speckle noise is generally modeled as the sum of statistically independent phasors of random amplitude and phase [8]. The sum of phasors can be modeled as a random-walk phenomenon [9] with probability density given by

$$P(I_{det}) = \frac{1}{\langle I_{det} \rangle} \exp \left( -\frac{I_{det}}{\langle I_{det} \rangle} \right)$$  \hspace{1cm} (2.78)
Speckle noise is different from the noise sources discussed in Section 2.4 because speckle noise patterns are spatially dependent. Speckle noise is not temporally dependent and instead depends only on the position and complex reflectivity of multiple scatterers within the tissue sample. Consequently, the speckle pattern from a stationary piece of tissue will always be the same, even at different points in time, if the light source is unchanged and the sample is imaged at the same location. This has practical applications, as careful observation of speckle noise can allow measurement of changes in tissue over time. However, standard OCT imaging does not make use of this and speckle is treated as noise because it introduces artifacts and false layer information in images.

2.6 References


Chapter 3
Handheld Optical Coherence Tomography Sample Arm
Requirements
3.1 Overview

This chapter discusses the design parameters and requirements for the sample arm of a handheld OCT device. Several common scan patterns and optical scanning elements are considered. The fundamental performance limits of the sample arm are examined through theoretical analysis of the optical design. Requirements for alignment to achieve optimal imaging are also discussed.

3.2 Scanning Optics

The integration of optical scanning elements enables OCT systems to image in more than one dimension. Several different types of scans are possible and the nomenclature of these scans follows the conventions used in ultrasound imaging. An OCT beam incident on the sample tissue creates a single depth profile image in one dimension known as an A-scan. By using scanning mirrors, the OCT beam can be translated in a line along the surface of the tissue, producing a two-dimensional cross-sectional image known as a B-scan. Orthogonally translating the line scanned by the optical beam and stitching together the resulting B-scans will produce three-dimensional volumetric data. The volumetric data can be digitally sliced at different depths to produce two-dimensional images known as C-scans.

The performance of a scanning mirror is primarily determined by the mechanical scan angle, frequency response, and mirror size. The mechanical scan angle is defined by the maximum tilt angle that a scanning mirror can achieve. In OCT systems, the incident light beam is reflected off the surface of the scanning mirror so that the total optical angle scanned by the beam is actually twice the mechanical scan angle.

The frequency response of the mirror is chiefly defined by the resonance frequency of the entire scanning assembly. Scanning mirrors in OCT systems generally do not perform resonance scanning and instead perform scanning from one static point to another. With these scan patterns, the scanning frequency must be kept below the resonance frequency in order to prevent undesired ringing of the mirrors.

The size (and weight) of a mirror strongly affects the frequency response of the entire scanning assembly. More importantly, the size of the mirror limits the diameter of the laser beam incident on the sample arm optics. Generally, a wide laser beam incident on a focusing lens is necessary to produce a small beam spot on the tissue and achieve good transverse resolution. Together, the mirror size and mechanical scan angle set the fundamental limit on the number of resolvable spots that can be scanned by the OCT system.

3.2.1 Scan Patterns

In order to visualize all of the desired scan positions on the sample tissue, an appropriate scan pattern must be chosen to minimize scan time or distortion. The simplest scan pattern is for a cross-sectional B-scan, where the laser beam is scanned in a straight line across the surface of
the tissue sample. However, more complex scan patterns are necessary to scan a two-dimensional area on the surface of the tissue. This arises from the fact that each scanning mirror has finite inertia, preventing them from changing direction instantaneously. Sudden, sharp jumps in the scan pattern are equivalent to step functions that can excite resonance modes in the mirrors. Many scan patterns exist to steer the laser beam along the two-dimensional surface, each attempting to optimize on different parameters such as scan uniformity, density, or speed. Three of the most commonly used scan patterns are presented in Figure 2-2.

![Scan Patterns](image)

**Figure 3-1** (A) Linear raster scan pattern (B) Zigzag scan pattern (C) Sinusoidal scan pattern

Each scan pattern represents the path along which the laser beam is steered on the surface of the tissue pattern. A-scans can be acquired at each point along the path specified by the scan pattern. Some patterns, such as the linear and zigzag patterns, make use of flyback scans during which A-scans are not acquired. Instead, these flyback scans are incorporated to permit the scanning mirrors to smoothly reset position for the next segment of the scan pattern without exciting resonances in the mirrors. To achieve smooth flybacks, investigators have demonstrated a spline equation to construct a path that optimally achieves continuous position, velocity, and acceleration throughout the scan [1].

The linear raster scan is the standard scan pattern for volumetric OCT imaging and ensures that every B-scan is scanned along the tissue in the same direction.

The zigzag scan improves on the linear raster scan by alternating the scan direction of each B-scan between forwards and backwards. This reduces the flyback time and the time needed to scan the desired area. However, recall that A-scans are acquired sequentially in time as the beam is steered along the surface of the tissue sample. As a result, B-scans from backward sweeps must be reversed to match the forward sweeps. If the scan timing is imperfect, however, the A-scans in the backward scans will not match up exactly with the A-scans from the forward scans, resulting in images with a "zipper"-like alignment artifact.
The sinusoidal scan improves further on the zigzag scan by eliminating the need for flyback scans. This further reduces the time necessary to scan the desired area. Like the zigzag scan, the sinusoidal scan sweeps in both the forward and backward direction. Likewise, it potentially suffers from the same “zipper”-like alignment artifacts. The sinusoidal scan causes the scan mirror velocity (and thus the velocity of the beam across the tissue surface) to be maximal in the middle of a B-scan and minimal at the ends. Consequently, the spacing (on the surface of the tissue) between A-scans is uneven and B-scan images will appear distorted. Additionally, in contrast with the linear and zigzag patterns which produce straight sweeps for B-scans, the sinusoidal scan pattern produces slanted sweeps for B-scans due to linear motion in the y-direction. However, this problem can be mitigated by increasing the number of B-scans in the scanned area. With enough B-scans, the tilting of each B-scan is negligible.

3.2.2 Scanning Mirrors

Options for scanning mirrors in a handheld OCT device are limited, as they must be compact without sacrificing performance. OCT systems typically use galvanometer scanners due to their high performance. Galvanometer scanners have high resonance frequencies and support driving large mirrors (for large beam diameters) without sacrificing maximum acceleration or velocity. With the use of closed loop control systems to detect the galvanometer position, galvanometer scanners can achieve resonance frequencies on the order of several kHz [2]. This enables galvanometer scanners to perform linear raster scans with very fast flybacks while maintaining high point-to-point precision and accuracy. However, area scanning with galvanometer scanners requires two sets of actuators housed in an aluminum block with their mirrors displaced by a finite distance to prevent contact. Cambridge Technologies 6200H scanners are frequently used in this configuration for area scanning in a variety of OCT systems.

This setup is bulky compared to alternatives such as MEMS scanning mirrors and as seen in Figure 3-2, the mirror displacement \( \Delta d \) shifts one or both scanners out of the backfocal plane of the scan lens. In a typical pair of galvanometer scanners, the mirror displacement \( \Delta d \) is roughly 1 cm. At larger scan angles, this displacement can cause vignetting artifacts along one axis. Since the other mirror is still in the backfocal plane, there is no vignetting along the associated axis. To minimize overall vignetting between the two scan axes, a compromise is made by placing backfocal plane between the two mirrors such that \( \Delta d \) is roughly 0.5 cm.
MEMS scanners are more compact, but they also have lower resonance frequencies and generally use smaller mirrors, thus trading off scanning speed and beam diameter for overall size and weight. Just as in galvanometer scanners, the resonance frequency of MEMS scanners scales inversely with the area of the mirror. However, for the same mirror size, MEMS scanners generally have lower resonance frequencies than their galvanometer counterparts and this severely limits the types of scan patterns that can be performed. Many MEMS mirrors can only operate at resonance, but investigators have recently demonstrated MEMS mirrors that can perform point-to-point scanning outside of resonance [3]. MEMS scanners are also able to avoid the displacement issue intrinsic to galvanometers by using a single mirror that can be tilted in two dimensions.

3.3 Sample Arm Optical Design

The standard arrangement of optics for a sample arm imaging a piece of tissue can be seen in Figure 3-3.
Figure 3-3 Imaging parameters for standard scan configuration of optics for a sample arm imaging a flat tissue sample.

The sample arm consists of scanning mirrors and a scan lens that steer and focus the laser beam onto the tissue sample, respectively. The choice of scanning mirrors and scan lens ultimately determine the optical performance when imaging the tissue sample.

3.3.1 Transverse Resolution

In contrast to optical microscopy, the transverse resolution of an OCT system is decoupled from its axial resolution. The axial resolution of an OCT system was discussed in a previous chapter. The transverse resolution of an OCT system is determined by the size of the focused laser spot on the tissue specimen. If the laser beam incident on the scan lens is a Gaussian beam, then the spot size (1/\(e^2\) diameter) on the tissue 2\(w_t\) is given by

\[
2w_t = \frac{2\lambda_0 f_S}{\pi n_t w_i}
\]  

(1.1)

where \(\lambda_0\) is the vacuum wavelength of the light, \(f_S\) is the effective focal length of the scan lens, \(n_t\) is the refractive index of the tissue specimen, and \(w_i\) is the width (1/\(e^2\) radius) of the Gaussian laser beam. Transverse resolution can be improved by reducing the spot size. From Equation (1.1), it is clear that this can be achieved by using light with a shorter wavelength, a scan lens with a shorter effective focal length, or a larger incident beam diameter. However, lasers suitable for OCT only exist at certain wavelengths and the optimum wavelength for imaging depends on the absorptive and scattering properties of the tissue sample. In a practical
(non-ideal) lens design, using a scan lens with a short focal length generally requires trading off the field of view. Finally, recall that the beam diameter is limited by the scanning mirror diameter and increasing the mirror size will limit the scanning frequency.

3.3.2 Confocal Parameter and Depth of Field

The depth of field (also known as the confocal parameter) of an OCT system describes the range of depths on the tissue where the light is in focus. If the laser beam incident on the scan lens is a Gaussian beam, then the confocal parameter is given by twice the Rayleigh range \( z_R \)

\[
2z_R = \frac{2\pi n_i w_i^2}{\lambda_0}
\]

where \( n_i \) is the refractive index of the tissue specimen, \( w_i \) is the width (1/e radius) of the focused spot, and \( \lambda_0 \) is the vacuum wavelength of the light. OCT systems are designed so that the depth of focus is generally equal to or greater than the thickness of the region of interest in the tissue. This enables easier axial alignment of the OCT system and ensures that enough light is reflected by the region of interest for acceptable image quality.

3.3.3 Field of View

To first order, the maximum field of view of an OCT system is determined by the useable (clear) aperture of the scan optics. In the ideal case, the clear aperture is equivalent to the diameter of the scan lens. The laser beam incident on the scan lens must be kept within the clear aperture to avoid vignetting and since the beam has finite width, the maximum field of view will necessarily be smaller than the clear aperture. The maximum distance on the surface of the tissue sample that can be imaged without vignetting is thus given by

\[
FOV_{dist} = 2r_{lens} - 2w_i
\]

However, in a practical scan lens, imaging performance at the edge of the lens suffers due to optical aberrations that gradually increase the spot size beyond the diffraction limit. A more thorough calculation of the field of view can be done with an optical simulation of the scanned laser beam through the scan lens.

In practical scenarios, the field of view is defined as the maximum distance on the tissue sample where the focused spot is still diffraction limited. Generally, scan lenses with shorter effective focal lengths have smaller fields of view. This is because such lenses have stronger optical aberrations at the edges due to increased lens thickness and/or use of optically dense materials (materials with very high refractive indices). Consequently, a scan lens can only achieve diffraction limited spots for a laser beam scanned through a limited range of angles.
\( \theta_{\text{eff}} \) in Figure 3-3 be the maximum scan angle (in radians) that produces a diffraction limited spot. The field of view is thus

\[
FOV_{\text{dist}} = 2f_S \tan \theta_{\text{eff}}
\]  

(1.4)

In OCT systems, the scan lens is generally chosen such that the maximum scan angle is limited by the mechanical scan angle of the scanners. These high-speed, high-precision scanners can only scan relatively small angles and the small angle approximation can be used such that

\[
FOV_{\text{dist}} = 2f_S \theta_{\text{eff}}
\]  

(1.5)

3.3.4 Telescope Magnification

The use of the telescope configuration in Figure 3-4 can provide additional flexibility in the optical design of the sample arm.

![Figure 3-4 Imaging parameters for telescopic scan configuration of optics for a sample arm imaging a flat tissue sample.](image)

Note the introduction of two lenses in a telescope configuration (lens A and B) compared to the standard configuration in Figure 3-3. The telescope amplifies the scan angle of the scanning mirror, enabling a larger field of view at the tissue sample. However, this reduces the beam size at the scan lens, consequently increasing the focused spot size and reducing the transverse resolution. The magnification of the scan angle is determined by the choice of telescope lenses, where the magnification provided by the telescope is given by

\[
M = \frac{f_A}{f_B}
\]  

(1.6)
The magnification increases the scan angle on the scan lens such that

$$\theta_{mag} = M \theta_{eff}$$

(1.7)

The magnification also decreases the beam size at the scan lens such that

$$w_{mag} = \frac{w_i}{M}$$

(1.8)

### 3.3.5 Number of Resolvable Spots

From Section 3.3.4, it follows that the spot size and field of view are inversely proportional to each other based on the magnification of the system. As such, it is useful to consider a parameter that is invariant to magnification in order to easily compare system designs. One such parameter is the number of resolvable spots, defined by the number of unique scan points along the field of view. The number of resolvable spots \( NRS \) can be found by dividing the field of view by the spot size

$$NRS = \frac{FOV_{dist}}{2w_i} = \frac{2f_S \theta_{mag}}{2w_i} = \frac{2f_S M \theta_{eff}}{Mw_i}$$

(1.9)

As seen here and in Section 3.3.4, enlarging the field of view will proportionally enlarge spot sizes. Consequently, enlarging the field of view without changing the input beam diameter will prevent the system from detecting small features in the tissue. In order to continue detecting small features with an enlarged field of view, the number of resolvable spots must be increased. To do so, the initial beam diameter \( w_i \) must be increased proportionally to the magnification.

### 3.4 Handheld Device Alignment

The handheld OCT device must be easy to use in a clinical setting and its impact on existing clinical workflow must be minimized in order to achieve success. As such, it is critical that the handheld device can be easily aligned in order to reduce operator fatigue and improve clinical throughput. Aligning the handheld device requires several steps corresponding to the different axes of movement illustrated in Figure 3-5. During each of these steps, it is critical that the operator is able to receive real-time feedback in order to align the device and acquire optimal images.
Handheld device alignment steps.

1. Calibrate zero delay position to match scan lens focus depth.
2. Translate across tissue surface to find features or regions of interest.
3. Axial alignment in Z direction to place tissue within imaging range.

3.4.1 Focusing and Zero Delay Calibration

The scan lens of the handheld device will focus the OCT beam down to a spot at a fixed depth. In order to achieve high quality images, the focus depth must be placed within the imaging range of the OCT system. The zero delay position of the OCT system needs to be adjusted so that the focus depth and the entire depth of field are placed within the imaging range. Recall from the chapter on OCT theory that because the length of the sample arm is fixed, this can be done by increasing or decreasing the length of the reference arm. Furthermore, since the scan lens focuses the OCT beam to a fixed depth, this is a calibration that only needs to be done once per scan lens. Once the zero delay is calibrated for a scan lens, the operator can skip this in subsequent imaging sessions and proceed directly to the next step.

3.4.2 Feature Alignment

The next step in alignment is to orient the handheld device so that the scanned area on the tissue contains features of interest. These features may or may not be visible to the naked eye, but the compact nature of the handheld device allows it to be easily translated across or rotated around the sample until a region of interest is found.

3.4.3 Axial Adjustment

Once the handheld device has been positioned over an area of interest, the optical axis (i.e. the Z-axis) must be adjusted so that the imaged tissue is properly aligned within the imaging range of the OCT system. This can be done by pulling or pushing the handheld device away or towards the tissue sample. It is crucial that the handheld is positioned such that tissue is located entirely on one side of the zero delay depth/position. As discussed in the chapter on OCT theory,
if this is not performed correctly then the Hermitian symmetry of the Fourier transform will invert the image across the zero delay and introduce artifacts.

Since the handheld device is not stabilized, the ergonomics of the handheld device must be carefully considered to minimize operator motion during imaging. Tremors from the operator in the axial or transverse directions can displace the OCT beam during scanning and introduce motion artifacts in the images. To improve stability, the distal end of the handheld device can be designed to provide tissue contact. With a properly sized spacer placed on the end of the scan lens, tissue contact can be set to occur at the working distance of the scan lens. This would reduce the axial alignment step of the handheld device to simply making contact with the tissue.

3.4.4 Scan Alignment on the Sample

At this point, the handheld device is fully axially aligned. Depending on the tissue being imaged, the focus depth can be set to emphasize features deeper inside the tissue by bringing the handheld device closer to the sample (or applying pressure if imaging with tissue contact). The operator may also wish to look for other regions of interest by translating or rotating the handheld about the tissue surface. By maintaining tissue contact, the axial alignment can be preserved while searching for regions of interest.

3.5 References


Chapter 4
Swept Source Optical Coherence Tomography System Design
4.1 System Overview

This chapter discusses and characterizes the different modules of the SS-OCT system used to acquire images with the handheld device. The schematic for the constructed SS-OCT system is shown in Figure 4-1. This is the final design used in the system. Later in this chapter, a different configuration is discussed and evaluated against the configuration shown below.

![SS-OCT System Diagram](image)

**Figure 4-1** SS-OCT system layout. This system is implemented with a mixture of fiber optic and free space components. PC = polarization controller, LPF = low pass filter, A/D = analog to digital, RM = reference mirror, SM = scanning mirror. Note the presence of two scanning mirrors (one each for scanning the x- and y- axes).

This SS-OCT system makes ample use of fiber optics to minimize system size and reduce sensitivity to spurious vibrations that can cause optical misalignment. Note the use of fiber optic couplers with uneven split ratios instead of bulk-optics beam splitters. Five percent of light from the swept source laser is coupled into a Mach-Zehnder interferometer (MZI) for calibration of acquired OCT interference patterns. The remaining ninety-five percent of light is split between the sample and reference arm paths – ten percent is coupled into the reference arm path and ninety percent is coupled into the sample. Light reflected from the sample and reference arm paths pass through an optical circulator, a special fiber-optic component designed such that light entering a port exits from the next (clockwise in the schematic). The sample and reference arm light is interfered at the 50/50 fiber coupler and evenly split into two paths for the balanced
detectors. The balanced detectors convert the input light (optical signal) into electrical signals and measure the difference signal between the two inputs, eliminating the DC component (i.e. the constant term) and extracting the OCT interference pattern. Spectral information in the interference pattern is obtained by sampling the balanced detector with an A/D acquisition card from a computer. Low pass filters are used to prevent aliasing due to the finite sample rate of the A/D acquisition card. Acquisition is synchronized with the start of each sweep of the laser by a trigger signal produced by the swept source laser and a scan signal produced by the multifunction I/O card. The components used in the system are listed in Table 4-1.

<table>
<thead>
<tr>
<th>Function</th>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synch Circuit</td>
<td>Custom</td>
</tr>
<tr>
<td>Swept Source Laser</td>
<td>Thorlabs prototype VCSEL</td>
</tr>
<tr>
<td>Fiber Optic Couplers</td>
<td>AC Photonics, Inc. couplers with various coupling ratios</td>
</tr>
<tr>
<td>Fiber Optic Circulators</td>
<td>AC Photonics, Inc. fiber optic circulators</td>
</tr>
<tr>
<td>Scanning Mirror (SM)</td>
<td>Cambridge Technology 6200H</td>
</tr>
<tr>
<td>Scanning Mirror (SM) Drivers</td>
<td>Cambridge Technology MicroMax 671</td>
</tr>
<tr>
<td>Low Pass Filter (LPF)</td>
<td>Mini-Circuits SLP-1000+</td>
</tr>
<tr>
<td>Balanced Detectors</td>
<td>Thorlabs PDB-480C-AC</td>
</tr>
<tr>
<td>Multifunction I/O Card</td>
<td>NI PCIe-6323</td>
</tr>
<tr>
<td>A/D Card</td>
<td>Alazartech ATS9373</td>
</tr>
<tr>
<td>Lenses</td>
<td>Custom configuration of commercial Thorlabs lenses</td>
</tr>
</tbody>
</table>

Table 4-1 List of components used in the SS-OCT system depicted in Figure 1-1.

The design of the sample arm will be discussed at length in a later chapter. This chapter will focus on the remainder of the SS-OCT system.

4.2 Light Source

The system light source must be carefully chosen as this component ultimately defines the performance of the SS-OCT system. For an SS-OCT system, careful consideration of factors such as sweep speed, coherence length, and light bandwidth are crucial to creating a high-performance system suitable for handheld operation in a clinical setting.

The light source selected for this system is a prototype vertical cavity surface emitting laser (VCSEL) at 1310 nm produced by Thorlabs. This laser source is extremely compact and fully integrated, enabling turnkey operation and dramatically simplifying operation of the SS-OCT system. VCSEL light sources are well suited for SS-OCT operation and have been demonstrated in applications including ophthalmic and dermal imaging [1]–[4] with imaging speeds up to 1 million A-scans per second [2].

VCSEL light sources operate by actuating a vertically suspended MEMS mirror in the laser cavity with high voltage [1]. Light pumped into the laser cavity is amplified by a gain material, but only light at certain wavelengths exhibit sufficiently strong resonance within the cavity to
escape the device. By carefully controlling the mirror position, the laser cavity length and thus the output wavelength can be modulated. The laser sweep rate and output bandwidth can thus be controlled with the frequency and intensity of the mirror actuation.

Mirror actuation is typically sinusoidal at a fixed sweep frequency, producing forward sweeps where the output wavelength decreases over time and backward sweeps where the output wavelength increases over time. Note the inverse relationship between wavelength and wavenumber means that the output wavenumber increases over time for forward sweeps. By using active gain media in the cavity, the gain media can be switched off so that light from only forward or only backward sweeps are output from the device. If the gain media is kept on for both forward and backward sweeps, this effectively doubles the VCSEL sweep rate and enables two A-scans to be performed for every actuation of the MEMS mirror.

The VCSEL light source used in this system has a total measured output power of 32.94 mW and performs sweeps centered at 1310 nm at a rate of 400 kHz with 50% duty cycle. The duty cycle indicates that the VCSEL gain media is only on for half of each sweep period and thus the VCSEL scans unidirectionally. Laser output consists only of forward sweeps (increasing wavenumber), where each sweep occurs at 400 kHz. Additionally, this VCSEL light source has optimized actuation of the MEMS mirror so that forward sweeps are (close to) linear instead of sinusoidal. The measured spectrum of the light source is shown in Figure 4-2. The laser output power versus time is shown in Figure 4-3 alongside the corresponding Mach-Zehnder interferometer (MZI) signal. The MZI is discussed further in Section 4.3. During operation, the VCSEL light source also outputs a short electronic pulse/trigger signal at the beginning of each sweep. This trigger signal can be used as an aid in sweep-to-sweep calibration.
Figure 4-3 VCSEL output power over time and corresponding MZI fringe signal. Note that this VCSEL has a 50% duty cycle.

4.3 Interferometer Design

The fiber based interferometer used in the OCT system consists of several sets of commercially available 2x2 couplers from AC Photonics, Inc. The unused ports in each coupler in Figure 1-1 are not shown. Referring back to Figure 1-1, the first coupler after the light source is used to divert power into a Mach-Zehnder interferometer (MZI) to create calibration traces. The MZI generates a calibration trace consisting of an interference fringe at a fixed frequency in wavenumber (set by the path length mismatch between the two MZI paths) and requires only a small amount of power to provide enough signal. This coupler must be chosen carefully to maximize signal power to the rest of the system. A 95/5 coupler is used because five percent of the total output light from the source described in Section 4.2 was sufficient power to create high-quality calibration traces. The remaining ninety-five percent of light is sent to a second coupler for the OCT part of the system.

The second coupler acts as a beam splitter and splits incident power between the sample and reference arm paths of the OCT interferometer. Since biological tissue samples are generally much less reflective than the mirror in the reference arm, the signal power from the sample arm is much lower than that from the reference arm. System sensitivity can thus be improved by increasing the power delivered to the tissue sample. A 90/10 coupler is used where ninety percent of input light is coupled into the sample and the remaining ten percent is coupled into the reference arm path. This coupler was chosen because it increases the amount of light delivered to the tissue sample while also delivering enough light to the reference arm to keep the OCT system in the shot noise limited regime (recall the discussion of shot noise in the chapter on OCT theory). Light in the sample and reference arms then pass through optical circulators on their way
to the tissue sample and reference mirror, respectively. Optical circulators are special fiber-optic components designed such that light entering one port exits from the next (clockwise in the schematic in Figure 1-1). Light reflected by the tissue sample and reference mirror then pass through their respective circulators into a third and final coupler.

The last coupler is located immediately before the balanced detectors for the OCT signal. This coupler is required for interference of the reference and sample arm signals as well as splitting the interference fringe signal to the balanced detectors. Since the signal power between the balanced detectors must be equal in order for balanced detection to work, a 50/50 coupler is used. Note that polarization controllers are also placed on the inputs to this coupler to achieve maximum interference by matching the light polarization between the sample and reference arms.

Note that the optical path length of the sample and reference arms must be matched to observe the interference pattern. This requires matching the optical fiber lengths and the air gaps between the two arms. Additionally, the response of the optical circulators and the coupling ratio of all couplers in the system must be flat over the operating wavelengths for optimal OCT performance. Otherwise, fixed pattern noise is introduced to the final interference signal.

4.4 Reference Arm Design

The reference arm is a dual-pass design and consists of a fiber optic patch cord, a collimating lens, and a perfect reflector (i.e. mirror). Light from the fiber optic patch cord is collimated into a beam projected onto the reflector. This beam is subsequently reflected and focused back into the fiber optic patch cord. The reflector is mounted on a one-dimensional translation stage and aligned with the collimator so that movement of the reflector does not greatly affect the back-coupling of reference arm power. By translating the reflector, the reference arm length can be changed and the zero delay position can be adjusted relative to the sample arm.

Note the mismatch in optics between the sample and reference arms. As discussed in the chapter on OCT theory, this results in a dispersion mismatch that degrades the system point spread function. However, this dispersion mismatch can be compensated either physically or numerically and the compensation process is described in the chapter on OCT theory.

4.5 Image Acquisition and Processing

This section describes the electronic hardware and processing software used in the system to acquire raw data and process it into useful images of tissue.

4.5.1 Scan Synchronization

Synchronization between the swept source laser and all acquisition devices is critical for proper operation of an SS-OCT system. Since the laser has a 50% duty cycle, the laser output is only useable for a fraction of each sweep. To avoid generating large quantities of useless data,
the acquisition must be timed to occur only during the useable fraction of each sweep. Additionally, the multi-function I/O card in Figure 1-1 is responsible for commanding the scanning mirrors and directing the positioning of the beam on the tissue sample. To obtain useful data points for OCT, the mirror scanning must be carefully synchronized with data acquisition. Any fluctuations in timing will result in mismatched or lost data, so it is paramount that mirror scanning and data acquisition are synchronized with the useable portion of each laser sweep.

The laser used in this system outputs a short electronic pulse/trigger signal at the beginning of the useable portion of each sweep. The A/D acquisition card and the multifunction I/O card used in this system can be programmed to begin acquiring data and begin scanning, respectively, upon receiving a trigger signal. Ideally, the laser trigger signal can simply be connected to both the A/D and multifunction cards. However, the two cards run on independent internal clocks and it is possible for the acquisition card to react to an incomplete trigger (from the previous sweep) while the I/O card is initializing for each scan. This leads to possible scenarios where acquisition begins before mirror scanning has begun or vice versa. To synchronize the two cards, a digital deglitching (synchronization) circuit using CMOS logic was created to ensure that both the I/O card controlling the scanning mirrors and the A/D acquisition card are synchronized with the laser sweep trigger. The synchronization circuit is shown in Figure 4-4 and it makes use of a single delay flip-flop along with several logic gates to ensure the A/D acquisition card always receives a complete sweep trigger. A timing diagram demonstrating the function of the circuit is shown in Figure 4-5.

![Figure 4-4 Logic layout of synchronization circuit. The circuit consists of an inverter, delay flip-flop, and an AND gate. Circuit inputs are the Trig and Scan signals. Trig indicates the beginning of each useable sweep from the laser. Scan indicates the scanning mirrors are moving and data should be acquired. The Output signal is sent to the A/D acquisition card to trigger acquisition for each sweep.](image-url)
Figure 4-5 Timing diagram of the synchronization circuit. (1) The Scan signal is high, indicating that the mirrors are scanning and the acquisition card should sample/record data values. (2) On the rising edge of the next inverted Trig signal, the flip-flop stores the high value and the Q output is high. The Output signal is now a direct copy of the Trig signal due to the AND gate. (3) When the scanning mirrors stop moving, the Scan signal switches to low. (4) Only on the next rising edge of the inverted Trig signal does the Q output of the flip-flop go low. This ensures the Trigger waveform is not clipped in the Output signal.

The multifunction I/O card used in this system is an NI PCIe-6323 card. This card has four analog outputs running at up to 900 kilo-samples per second and 48 high-speed bidirectional digital input/output lines. This system requires at least three analog high-speed analog outputs - two for the mirror scanners (one each for the x- and y-axes) and one for the scan synchronization signal. This system also requires a digital input line for the synchronized trigger signal. This card was chosen for the quantity, speed, and versatility of its connections, as it was capable of providing all of the required analog outputs and bidirectional digital input/output lines.

4.5.2 Balanced Detection

Recall from the chapter on OCT theory that balanced detection enables removal of the autocorrelation terms from the interference signal. This is possible because the 50/50 coupler used immediately before the balanced detector will directly transmit half of the optical interference signal into one input and reflect the second half of the signal with a $\pi$ phase shift into the other input. The DC (autocorrelation) terms are unaffected while the AC (interference) terms are now out of phase. By subtracting the signals at the balanced detectors, the DC (autocorrelation) terms are canceled while the AC (interference) terms are combined due to the phase delay. This permits the interference terms (from tissue reflections) to have a higher dynamic range before saturating the detectors, enabling the use of more power in the reference arm to improve system sensitivity.

In reality, balanced detection is not able to perfectly remove the DC component from the interference signal. The coupling ratios offered by the 2x2 couplers in the system are not flat but
instead exhibit a wavelength dependence. For example, light input to a 50/50 coupler may be split evenly between the two output ports at $\lambda_1$ but it may be split 55/45 at $\lambda_2$. Consequently, the autocorrelation terms are not perfectly canceled and this leads to a residual DC component upon which the AC interference fringe rides. This limits the permissible dynamic range on the AC fringe. By extension, this limits the reference arm power that can be used and reduces the sensitivity of the system.

The detectors used in this system are Thorlabs PDB-480C-AC balanced detectors. These detectors were chosen for their high bandwidth (30 kHz to 1.6 GHz) enabling long imaging ranges. These detectors also exhibit outstanding noise characteristics and an excellent common mode rejection ratio (CMRR) without sacrificing gain.

4.5.3 Analog to Digital Acquisition Cards

Given the high sweep rates of swept source lasers, SS-OCT requires the use of A/D acquisition cards with incredibly high sample rates in order to record enough data points per sweep for a faithful reproduction of the frequency content of each interference fringe. These A/D cards must also have enough bit-depth to accurately reproduce the shape of each fringe and minimize quantization noise introduced by the digitization process. Together, this requires bit rates that can only be achieved with acquisition cards using the PCI-Express socket.

The acquisition card chosen for this handheld SS-OCT system is an AlazarTech ATS9373. This is a 12-bit waveform digitizer card that can sample one analog input at rates up to four giga-samples per second or two inputs at two giga-samples per second. The card can accept an external trigger signal and as well as a variable frequency external clock signal. The latter could prove extremely useful to achieve uniform-in-k sampling of fringes with optical clocking. The presence of two input channels is also useful as it enables acquisition of MZI calibration traces alongside OCT interference fringes.

Recall from the chapter on OCT theory that a high sample rate is necessary to achieve a long imaging range. It is thus crucial to use a high-speed acquisition card to achieve a long imaging range and take advantage of the long coherence lengths afforded by swept source lasers.

4.5.4 Wavenumber Calibration

Typical swept source lasers have a nonlinear wavenumber sweep in time and without correction, this will degrade the system point spread function. Although the VCSEL laser used in this system has been linearized, the sweep trajectories are still sufficiently nonlinear to require correction. Recall from the chapter on OCT theory that there are two commonly used methods to correct for these nonlinearities in the laser sweep trajectories. The first method entails a wavenumber calibration step with phase extraction and linear-k resampling. OCT interference fringes sampled uniformly in time are resampled to time points that are uniform in wavenumber. This requires acquiring an interference fringe from a single reflector and extracting its phase to
be used as a calibration trace. In reality, successive laser sweep trajectories are not perfectly identical due to dynamic instabilities in the tunable optical filter, so a calibration trace must be acquired for every sweep in order to achieve optimal resampling. This requires simultaneous acquisition on two data channels – one for the calibration traces (typically a Mach-Zehnder interferometer at a fixed interferometer delay) and one for the OCT interference fringes.

The second method involves optical clocking, where an optically derived variable frequency clock signal is used so that the A/D acquisition card only samples at time points that are uniform in wavenumber. This clock signal can be produced by noting that for any monotonic laser sweep trajectory, the zero crossings of the interference fringe produced from a single reflector are spaced uniformly in wavenumber. The desired optical clock signal is thus a clock signal with edges located at these zero crossings. This clock signal is typically produced using a Mach-Zehnder interferometer at a fixed interferometer delay and a clock box that conditions and digitizes the interference fringe to create the optical clock signal. Changing the interferometer delay will change the interference fringe frequency (in wavenumber) and thus change the optical clock frequency.

Both methods were analyzed using different configurations of this system. The wavenumber calibration method was analyzed using the configuration in Figure 1-1. The optical clock method was analyzed using the configuration in Figure 4-6. The performance of each configuration is discussed further in later sections.
Figure 4-6 SS-OCT system layout with optical clocking. Note this configuration has replaced balanced detectors B and its associated LPF from Figure 1-1 with a clock box. In this configuration, the MZI interference fringe is used by the clock box to generate an optical clock signal instead of being recorded in the second channel of the A/D card. PC = polarization controller, LPF = low pass filter, A/D = analog to digital, RM = reference mirror, SM = scanning mirror.

4.5.5 Phase Extraction and Linear-k Resampling

The system configuration in Figure 1-1 runs the A/D acquisition card at a fixed sample rate instead of using an optically derived external clock. In this configuration, the system records the OCT fringes in the first channel and a Mach-Zehnder interferometer calibration trace for every laser sweep in the second channel. As previously discussed, the recorded OCT interference fringes must be resampled in time to be linear (equally spaced) in wavenumber to optimize the system point spread function. Using the method described in the chapter on OCT theory, the phase of each calibration trace can be extracted and used to find the nonlinear time points where the laser is sweeping linearly in wavenumber. Both the calibration and OCT fringes can be interpolated to these time points such that the resulting fringe points are linear in wavenumber. This resampling step is performed for every sweep to account for sweep-to-sweep variations caused by dynamic instabilities in the tunable optical filter of the laser. This method is demonstrated for a representative calibration fringe in Figure 4-7 and Figure 4-8. The calibration fringe was acquired using a fixed frequency 2 GHz sampling rate and a Mach-Zehnder interferometer with a maximum fringe frequency of 250 MHz. Note that these fringes look nearly identical to the OCT fringes produced by placing a mirror in the sample arm.
Figure 4-7 (A) Unwrapped phase from a Mach-Zehnder interferometer (MZI) fringe used for calibration. Fringe (shown in Figure 4-8A) was acquired at fixed 2 GHz clock rate and delay between paths within the MZI was set so that maximum fringe frequency was 250 MHz. Note the nonlinearity. (B) Unwrapped phase of MZI fringe from (A) following linear-k resampling. Note the resampled fringe (shown in Figure 4-8B) now has linear phase. This is achieved using the resampling procedure described in the chapter on OCT theory. Once the time points corresponding to linear phase are found in the calibration fringe, the same resampling procedure is applied to the OCT fringe in the first acquisition channel.
**Figure 4-8** (A) MZI calibration fringe corresponding to the unwrapped phase from Figure 4-7A. Fringe was acquired at fixed 2 GHz clock rate and delay between paths within the MZI was set so that maximum fringe frequency was 250 MHz. (B) The result of phase extraction and linear-k resampling of the calibration MZI fringe from (A). This is the MZI calibration fringe corresponding to the unwrapped phase from Figure 4-7B.

### 4.5.6 Optical Clocking

The system configuration in Figure 4-6 uses an optically derived external clock instead of running the A/D acquisition card at a fixed sample rate. In this configuration, the optically derived variable frequency clock signal is used so that the A/D acquisition card only samples at
time points that are uniform in wavenumber. Provided that the optical clock is stable, this eliminates the need for acquiring calibration fringes on a second acquisition channel. This eliminates a substantial amount of fringe post-processing in addition to reducing the data transfer and storage requirements for raw fringe data. A representative OCT fringe of a mirror placed in the sample arm acquired using optical clocking is shown in Figure 4-9. This shows the calibrated sweep behavior of the system and is nearly identical to the resampled fringe shown in Figure 4-8B. The difference in fringe frequencies between Figure 4-8B and Figure 4-9 is due to the use of different interferometer delays between the MZI in Figure 4-8B and the OCT interferometer in Figure 4-9.

Figure 4-9 (A) OCT fringe of mirror placed in sample arm. Acquired using optical clocking with a maximum sample frequency of 1 GHz. (B) Unwrapped phase of fringe acquired in (A). Note that optical clocking enables sampling with linear phase (i.e. linear wavenumber) without the need for a resampling step in post-processing.
4.5.7 Imaging Range

The imaging range of the system is given as the depth where the signal from a sample mirror becomes unusable. There are various definitions reported in the literature, but common definitions are the sample depth where the interference signal has decayed by -3, -6, -10, or -20 dB. Recall from the chapter on OCT theory that the useable imaging range in SS-OCT is affected by several factors including the laser coherence length, detector bandwidth, and A/D card sampling rate.

To measure the sample rate limited imaging range, a mirror is placed in the sample arm while the system is imaging and the zero-delay position is adjusted by translating the reference mirror. Since the mirror in the sample arm is fixed, translating the reference mirror will adjust the location of the A-scan peak. The useable imaging range can thus be found by translating the mirror until the A-scan peak is at the top of the imaging range followed by translating the mirror until the peak is at the bottom. The distance between these mirror positions is the imaging range limited only by the sample rate. This is because the A-scan image is the DFT of the interference fringe, so the top and bottom of the imaging range thus correspond to DC and the Nyquist frequency, respectively. Translating the mirror beyond the bottom will result in aliasing, so this is the deepest point that can be imaged assuming ideal laser coherence and detector bandwidth. Note that this measurement is performed by imaging through air. When imaging through other materials (such as biological tissue), the refractive index is different from air. The optical path length through the material is thus different from the real length and this changes imaging range in this material. For example, a system with a 3 mm imaging range in air only has an imaging range of 2 mm in a piece of glass with a refractive index of 1.5.

The imaging range was measured for two different configurations of this system. Using the configuration in Figure 1-1, the interference fringes were sampled at the maximum fixed rate supported by the A/D card for two-channel acquisition: 2 GHz. This yielded an imaging range of 9.5 mm. Using the configuration in Figure 4-6, the MZI frequency was adjusted to produce an optical clock with a maximum sample frequency of 1 GHz. This is the maximum optical clock frequency that could be attained before instabilities in the clock box caused unstable optical clocking. This yielded an imaging range of 3.9 mm.

Note that the imaging range is directly proportional to the Nyquist rate. Since the Nyquist rate scales is directly proportional to the sample rate, the imaging range thus scales linearly with the sample rate. For example, halving the sample rate will halve the imaging range. Using the configuration in Figure 1-1 at a fixed sample rate of 2 GHz will yield an imaging range of 4.75 mm. Adjusting the MZI frequency in Figure 4-6 to produce an optical clock with a maximum sample frequency of 500 MHz will yield an imaging range of 1.95 mm.

4.5.8 Fixed Pattern Noise and Background Subtraction
SS-OCT images often suffer from fixed pattern noise artifacts which manifest as strong erroneous horizontal lines laid over B-scan images. This artifact is caused by a variety of phenomena, but the primary source is usually the non-flatness of the reference spectrum that is interfered with the signal light. Additionally, the laser spectrum itself may exhibit a fine spectral structure that creates a Fourier-transform conjugate in OCT images. Unintended internal reflections from the fiber optic components or the sample/reference arm optics can also introduce optical interferences in the middle of the optical pathway. These interferences will manifest in the images as a static noise pattern.

Because SS-OCT uses balanced detection, the OCT signal should nominally be exactly zero in the absence of a sample. In reality, this is not the case and fixed pattern noise shows up as time-invariant background noise that is always present in the OCT signal. When a sample is introduced to the system (i.e. when imaging tissue), the sample interference signal is superimposed on this background noise. Therefore, in order to optimize OCT signal and image quality, this background noise must be removed. Since this noise is additive, it can be compensated for nearly exactly by measuring the OCT signal in the absence of a sample and subtracting away this background signal. This is easily performed in the handheld system by scanning the mirrors to a background position where the laser beam does not reach the sample. Thus, every A-scan for an area scan of tissue can have the fixed pattern noise removed by steering the scanning mirrors away from the sample for a small portion of the mirror scan trajectory and acquiring background A-scans where.

4.5.9 Phase Stability

In a swept source laser, the mechanical nature of the wavelength tuning creates small variations in wavelength sweeps and trigger timing. This introduces an uncertainty in trigger timing such that the starting point of the acquisition for spectral interference fringes (in wavenumber) changes from cycle to cycle. Put another way, this means that each acquired interference fringe may not always start at the same wavenumber in the laser sweep. Furthermore, in systems with fixed rate sampling, this means that acquired interference fringes are not always sampled with the same wavenumber distributions. This adversely affects the reproducibility of interference fringes and reduces the effectiveness of subtractive fixed-pattern noise removal.

This shift in the digitized wavenumber range between fringes can be corrected for in post processing with the use of a recalibration interferometer [5] like the MZI used in Figure 1-1. Achieving phase stability with this method is not possible with the configuration in Figure 4-6 due to the lack of acquired calibration traces.
The alignment procedure to achieve phase stability is described with an exaggerated example in Figure 4-10. Two successive OCT interference fringes (A-lines) and their respective MZI calibration fringes are shown in Figure 4-10A. The wavenumber sweep for each A-line is shown with a color bar. Note the wavenumber shift (different starting color) and different wavenumber sampling (different color distribution). Recall that the wavenumber sampling can be found with a phase analysis consisting of unwrapping the phase from a Hilbert transform of the MZI fringe. The unwrapped phase is shown in Figure 4-10B and this can be used to resample the fringes to be linear in wavenumber as described in Section 4.5.5. This is visualized in Figure 4-10C where the MZI fringes are plotted against their unwrapped phase, resulting in linear (in wavenumber) MZI fringes. However, there is still a shift in the digitized wavenumber range, as seen in the shift in the color bars between the two MZI fringes. This can be corrected.
by measuring the cross-correlation between the resampled MZI fringes. Shifting the second MZI fringe to maximize the cross correlation will correct the unwrapped phase curve, as seen in Figure 4-10D where the red phase curve has been shifted down compared to its place in Figure 4-10B. The corrected phase curves are now used to exactly align and phase stabilize the two A-lines, as shown in Figure 4-10E where the MZI fringes and A-lines are plotted against the corrected phase curves. The A-lines can now be resampled as described in Section 4.5.5 such that they are now both phase stabilized and linearly sampled in wavenumber.

Note that the configuration in Figure 1-1 enables acquisition of a reference MZI signal for each and every acquired A-line. Therefore, this procedure allows phase-stabilization of large sets of A-lines through the use of a reference MZI signal with respect to which all other A-lines (and their respective MZI signals) are stabilized.

4.5.10 The Point Spread Function, Numeric Dispersion Compensation, and Windowing

The point spread function (PSF) is characterized for the configuration in Figure 1-1 (fixed rate sample clocking) and the configuration in Figure 4-6 (optical clocking). The point spread function results are shown in Figure 4-11 and Figure 4-12. The point spread function was measured roughly one third of the way into the imaging range of each configuration. This corresponds to an interferometer delay of 3.17 mm and 1.3 mm for the configuration in Figure 1-1 (fixed rate sample clocking) and the configuration in Figure 4-6 (optical clocking), respectively.
Figure 4-11 Point spread function results for the configuration in Figure 1-1 (fixed rate sample clocking) measured 3.17 mm into the imaging range. Note that applying certain optimizations to the interference fringes can reduce the height of side lobes at the expense of broadening the main lobe width.
Figure 4-12 Point spread function results for the configuration in Figure 4-6 (optical clocking) measured 1.3 mm into the imaging range. Note that applying certain optimizations to the interference fringes can reduce the height of side lobes at the expense of broadening the main lobe width.
In this system, there is a mismatch in optics between the sample and reference arms. As discussed in the chapter on OCT theory, this results in a dispersion mismatch that degrades the system point spread function. However, it is possible to compensate this dispersion mismatch either physically or numerically (this is described in the chapter on OCT theory). The dispersion compensation in this system is performed numerically.

Recall that the PSF is the Fourier conjugate of the OCT interference fringe of a single reflector. Therefore, in addition to the numeric dispersion compensation, more traditional discrete signal processing techniques can be applied to the OCT interference fringes to optimize the PSF. A window function can be applied to the fringes in order to reduce the spectral leakage in the PSF. Additionally, recall from the chapter on OCT theory that the shape of the PSF is given by the Fourier conjugate of the laser power spectrum. In an ideal system with perfect balanced detection, beamsplitters, etc. the Fourier conjugate of the laser power spectrum provides the transform limited PSF. This describes the PSF with the minimum possible width that can be achieved for a given laser spectrum.

As seen in Figure 4-2, the laser used in this system has a non-uniform, asymmetric spectrum and this will naturally produce a suboptimal PSF. To correct for this, a window can be synthesized to selectively emphasize power at certain wavenumbers and in a sense retroactively reshape the power spectrum. If performed correctly, this spectral shaping using the synthesized window can improve the PSF by reshaping acquired fringes in a fashion that causes the envelope to be symmetric in wavenumber.

Taking a closer look at the point spread function results in Figure 4-11 and Figure 4-12, all of the experimentally measured PSFs appear worse than the transform limited PSF. The raw PSF suffers from an asymmetric broadening due to a lack of dispersion compensation (DC). Once the numeric dispersion compensation is applied, the main lobe of the PSF appears much sharper but the side-lobes are still relatively high. Application of a Kaiser window can help suppress these side-lobes but this comes at the expense of broadening the main lobe. Different windowing functions exist to make tradeoffs between main lobe width and side lobe height, but a Kaiser window was chosen for its ability to maximize the main lobe energy relative to the side lobe energy. Spectral shaping is applied together with windowing to further optimize the PSF. This method broadens the main lobe just as much as simple windowing but provides superior side lobe suppression.

Numeric measurements of the PSF width (FWHM) are found in Table 4-2. The performance of the experimentally measured PSF nearly matches the theoretical maximum described by the transform limited PSF. However, the presence of nonlinearities in the system such as dispersion and imbalanced beamsplitters limit the PSF performance. Note that axial resolution (i.e. PSF width) can always be traded for side lobe suppression through the use of windowing.
Fixed rate sampling & Optical clocking \\
Transform limited & 10.36 \, \mu m & 10.36 \, \mu m \\
DC only & 12.9 \, \mu m & 12.0 \, \mu m \\
DC + spectral shaping & 16.1 \, \mu m & 14.4 \, \mu m \\

Table 4-2 PSF width (FWHM) of the system with various levels of processing. The configuration in Figure 1-1 (fixed rate sample clocking) and the configuration in Figure 4-6 (optical clocking) are considered. This corresponds to an interferometer delay of 3.17 mm and 1.3 mm for the fixed rate sample clocking and optical clocking configurations, respectively.

4.5.11 Sensitivity

Recall from the chapter on OCT theory that the sensitivity of the SS-OCT system is a measure of the minimum detectable sample reflectivity. This sensitivity is also known as the signal-to-noise ratio (SNR) and is defined as the ratio of the signal power to the noise process variance. The sensitivity of this SS-OCT instrument was measured experimentally by placing a neutral density (ND) filter with a measured optical density (OD) in the sample arm between the beamsplitter and a perfectly reflecting mirror. Following Fourier transform of the interference fringe, the power value \( P_S \) of the peak is compared to the mean power of the surrounding noise \( P_n \). The optical density of the ND filter is also added back in to compensate the fact that the ND filter blocks signal energy and artificially lowers the peak power value. The sensitivity in decibels (dB) is thus given by

\[
\text{Sensitivity}_{dB} = 10 \log_{10} \left( \frac{P_S}{P_n} \right) + 20 \cdot OD
\]

\[
= 10 \log_{10} \left( \frac{P_S \cdot 10^{2 \cdot OD}}{P_n} \right)
\]

(3.10)

Note the optical density is the base 10 logarithm of the energy blocked by the ND filter. The OD is multiplied by a factor of 20 (instead of 10) to account for the round trip attenuation of light through the ND filter.

The sensitivity was measured with a 2.5 OD ND filter for sample arm attenuation and 57 \( \mu W/17.91 \, mW \) (measured with/without attenuation) incident on the sample mirror. This ND filter was chosen because it closely approximates scattering losses typically seen in tissue samples. The back-coupled power incident on each of the balanced detectors was approximately 458 \( \mu W \). The power value \( P_S \) of the peak was given by the square of the A-scan peak height. The mean power of the noise \( P_n \) was given by the mean variance of the noise floor taken at the location of the A-scan peak by blocking the sample arm.
This measurement was repeated for several zero delay positions to characterize the system sensitivity roll-off with depth and the measurement results for the fixed rate sample clocking system configurations can be seen in Figure 4-13 and Figure 4-14. Note that this measurement also enables observation of the system point spread function over the imaging range.

**Figure 4-13** Point spread function vs depth for the configuration in Figure 1-1 (fixed rate sample clocking). Note the width of the point spread function remains roughly constant at all depths. At greater depths, the PSF height tapers off as the interference fringes approach the low pass filter cutoff frequency.
Figure 4-14 Sensitivity vs depth for the configuration in Figure 1-1 (fixed rate sample clocking). Note the long coherence length of the swept source laser enables high sensitivity throughout nearly the entire imaging range. Sensitivity begins to taper off at greater depths as the interference fringes approach the low pass filter cutoff frequency.

4.5.12 Software

Custom acquisition software was written in C++ and the front end GUI used the Windows Forms graphical API. Both the A/D acquisition card and the multifunction I/O card interfaced with the acquisition software through their own dynamic link library (DLL) files containing common function calls for sending and requesting data. This software has been contributed to by multiple previous and current members of the lab group.

The software has five different modes of operation illustrated in Figure 4-15, Figure 4-16, Figure 4-17, Figure 4-18, and Figure 4-19. The first mode allows for the definition of custom scan patterns which can be added to a scan library. The second mode is a scan preview mode which displays preview B-scans in real-time to aid in alignment of the handheld device. This mode also allows the user to trigger the acquisition of an image/dataset. The third mode is an adjustment mode that allows the user to select recently acquired datasets and adjust contrast or other processing parameters such as numeric dispersion correction. The fourth mode allows for the visualization of the processed datasets as B-scans sliced in the XY, XZ, and YZ planes. The fifth and final mode allows the selection of a previously acquired dataset for use as a calibration file to resample subsequently acquired datasets.
Figure 4-15 Screenshot of custom acquisition software for the SS-OCT system. This is the first mode of operation allowing for definition and selection of custom scan patterns.

Figure 4-16 Screenshot of custom acquisition software for the SS-OCT system. This is the second mode of operation displaying preview B-scans in real-time to aid in alignment of the handheld device. This mode also allows the user to trigger the acquisition of an image/dataset.
Figure 4-17 Screenshot of custom acquisition software for the SS-OCT system. This is the third mode of operation – an adjustment mode allowing the user to select recently acquired datasets and adjust contrast or other processing parameters such as numeric dispersion correction.

Figure 4-18 Screenshot of custom acquisition software for the SS-OCT system. This is the fourth mode of operation allowing for visualization of the processed datasets as B-scans sliced in the XY, XZ, and YZ planes.
**Figure 4-19** Screenshot of custom acquisition software for the SS-OCT system. This is the fifth mode of operation allowing for selection of a calibration dataset to be used for resampling subsequent data sets.

### 4.6 References


Chapter 5
Handheld Optical Coherence Tomography Sample Arm Design
5.1 Overview

Creating a handheld OCT device for point-of-care imaging requires careful consideration of optical, ergonomic, and clinical workflow requirements. This chapter describes the design of the handheld OCT device and characterizes its optical performance. The optical setup, physical design, and imaging results of the handheld device are analyzed and an analysis of its effectiveness and limitations is performed.

5.2 OCT Optical Setup

Optical components for the handheld device must be carefully selected to achieve acceptable imaging performance. The theory and design equations describing optical performance are discussed in detail in the previous chapter on handheld optical coherence tomography sample arm requirements. Generally, a wide laser beam incident on a focusing lens is necessary to produce a small beam spot on the tissue and improve transverse resolution. The laser beam diameter in an OCT system is often limited by the scanning mechanism. Galvanometer scanners offer high performance and support driving large mirrors (for large beam diameters) without sacrificing acceleration or velocity. However, these scanners require two sets of actuators housed in an aluminum block and are bulky compared to alternatives such as MEMS scanning mirrors. While MEMS scanners are more compact, they also have lower resonance frequencies and must use smaller mirrors, thus trading off scanning speed and transverse resolution for size and weight. An optical design must be created to obtain an acceptable spot size without sacrificing speed and imaging length/angles on the tissue. This is important, as the number of resolvable spots on the tissue is determined by the imaging length divided by the spot size and a high number of resolvable spots is necessary for detection of tissue features for diagnosis.

Several optical configurations are considered for analysis below. The completed system made use of the primary optical configuration.

5.2.1 Primary Optical Configuration (Configuration A)

The primary optical setup used for the handheld is a modified version of the standard table mounted sample arm used by other SS-OCT systems in the lab [1]. The optical path for the OCT beam at 1310 nm wavelength is given in Figure 5-1. The collimating lens focuses light from the SMF-28 optical fiber and produces a collimated beam 4.8 mm in diameter. A pair of 6 mm Cambridge Technology 6200H galvanometer scanning mirrors steer the beam in two dimensions. Galvanometer scanners were chosen due to the need for high speed scanning in the handheld without sacrificing laser beam diameter.
The scan lens design consists of two commercially available 1” diameter achromatic doublets paired to focus the beam down to a tight spot and provide telecentric scanning without introducing excessive aberrations. The detailed drawing can be seen in Figure 5-2. Thorlabs AC254-100-C and AC254-075-C achromatic doublets were used. These lenses have an anti-reflection coating effective from 1050 – 1700 nm and effective focal lengths of 100 mm and 75 mm, respectively. When assembled, this scan lens design has an effective focal length of 42 mm. The system was simulated with a maximum optical scanning angle of ±5 degrees corresponding to a telecentric scan on the sample with a total field of view of 7.2 mm.

Recall the design equations from the chapter on handheld optical coherence tomography sample arm requirements. The above design parameters suggest a nominal spot size of 14.6 μm,
providing 494 resolvable spots for a 7.2 mm field of view. The simulated spot size at various angles is given in Figure 5-3, showing that the focused beam is within the diffraction limited spot size diameter of 26.98 μm for all angles in the field of view. The inverse relationship between the spot size and depth of field enables this scan lens to offer a large depth of field of 1.02 mm. Finally, this scan lens has a designed working distance of 33.4 mm.

Figure 5-3 Analysis of the spot size on the tissue for various galvanometer angles using the primary optical configuration. The black circle outline represents the diffraction limited Airy disk size.

5.2.2 Secondary Optical Configuration (Configuration B)

A secondary optical setup for the handheld was evaluated to provide the system with the flexibility to trade field of view for a higher resolution compared to the previously considered primary optical setup. The secondary configuration is identical to the setup shown in Figure 5-1 with the exception of a different scan lens.

Here, the scan lens design consists of three commercially available 1" diameter achromatic doublets instead of the two used in the primary configuration. The detailed drawing can be seen in Figure 5-4. Thorlabs AC254-100-C achromatic doublets were used. These lenses have an anti-reflection coating effective from 1050 – 1700 nm and an effective focal length of 100 mm. When assembled, this scan lens design has an effective focal length of 38 mm. Again,
the system was simulated with illumination from a 4.8 mm diameter beam at 1310 nm wavelength. However, the maximum optical scanning angle was changed to ±4 degrees for a telecentric scan on the sample with a total field of view of 5.4 mm.

Figure 5-4 Detailed drawing of scan lens design used in secondary optical configuration (configuration B)

The above design parameters suggest a nominal spot size of 13.2 μm, providing 408 resolvable spots for a 5.4 mm field of view. The simulated spot size at various angles is given in Figure 5-5, showing that the focused beam is within the diffraction limited spot size diameter of 24.34 μm for all angles in the field of view. The inverse relationship between the spot size and depth of field means this scan lens offers a shallower depth of field of 0.84 mm. Finally, this scan lens has a designed working distance of 16.4 mm.
Figure 5-5 Analysis of the spot size on the tissue for various galvanometer angles using the secondary optical configuration. The black circle outline represents the diffraction limited Airy disk size.

5.2.3 Commercial Optical Configuration

In addition to the custom optical setups described in Sections 5.2.1 and 5.2.2, several commercial scan lens were considered to assess their suitability for use in a handheld OCT device. For example, Thorlabs offers the OCTH-LK20 and OCTH-LK30 scan lenses. The advertised performance of these lenses are compared to the custom optical setups in Table 4-2. Optical models for these commercial lenses were not available for simulation. Lateral resolution in the table is defined as the $1/e^2$ diameter of the focused spot. More clearly, the beam is assumed to be a Gaussian beam and the lateral resolution is given as twice the radius at which the intensity of the focused Gaussian beam has decreased to $1/e^2$ of its peak value.
Table 5-1 Optical performance comparison of available OCT handheld scan lenses.

<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Lateral resolution</td>
<td>14.6 µm</td>
<td>13.2 µm</td>
<td>16.0 µm</td>
<td>24.0 µm</td>
</tr>
<tr>
<td>Focal length</td>
<td>42 mm</td>
<td>38 mm</td>
<td>20 mm</td>
<td>30 mm</td>
</tr>
<tr>
<td>Working distance</td>
<td>33.4 mm</td>
<td>16.4 mm</td>
<td>12 mm</td>
<td>22 mm</td>
</tr>
<tr>
<td>Field of view (diameter)</td>
<td>7.2 mm</td>
<td>5.4 mm</td>
<td>8 mm</td>
<td>10 mm</td>
</tr>
<tr>
<td>Resolvable spots</td>
<td>494</td>
<td>409</td>
<td>500</td>
<td>417</td>
</tr>
</tbody>
</table>

Configuration A was ultimately selected for use in the handheld device as it offered acceptable lateral resolution, a long working distance, and a large field of view.

5.3 Device Design

There are multiple ways a handheld device could be used. For example, the handheld device could be held like a pen, grasped like a camcorder, or pointed at the tissue with a pistol style grip for imaging. The intended grip must be sufficiently balanced and stable to minimize operator motion without degrading imaging capability. Additionally, the handheld device must be made of durable materials that can be easily sterilized whilst remaining lightweight enough to prevent operator fatigue, especially when multiple imaging sessions are expected. While heavy, glass for optical elements cannot be avoided without sacrificing performance. However, commonly used optical mounts are made of aluminum and these can be substituted with rapid-prototyped plastic to reduce weight. The handheld device can be designed to provide tissue contact for stability but the handheld device is still subject to operator motion while imaging and this potentially introduces motion artifacts. To alleviate this, the OCT system can be designed with a higher imaging rate to reduce overall imaging time and prevent operator fatigue. Additionally, post processing techniques such as registration using orthogonal data sets have been demonstrated to correct motion [2].

With the primary optical design from Section 5.2, the most ergonomic design for the handheld device is a pistol grip similar to the shape of a power drill. The handheld probe can be seen in Figure 5-6 and Figure 2-1. The handheld probe consists of a two-piece rapid-prototyped 3D-printed plastic enclosure that mounts a laser collimator lens, galvanometer scanners, and a custom scanning lens. A clamshell design was chosen so that the design for the top cover is a simple mirror image of the bottom cover. This design also allows for easy insertion and removal of optical components. The housing features built-in strain relief for a single cord carrying electrical cables for the scanners and optical fiber for the imaging laser. The two-piece design is easily closed by snapping the two halves of the shell together and its compact, lightweight form factor allows it to be ergonomically gripped like a power drill. The scan lens is mounted to the probe via a threaded lens tube, enabling rapid swapping of scan lenses by simply attaching a different lens tube. This provides the imaging system with the flexibility to easily modify transverse resolution and field of view. Additionally, the lens tube contains an integrated spacer
that can be used to adjust the working distance between the scan lens and tissue. This spacer also
provides tissue contact for stability. To maintain sterility in surgical environments, the entire
probe is wrapped in a sterile ultrasound sleeve. A circular hole is cut in the sleeve and covered
with sterile, adhesive, transparent Tegaderm film (3M Health Care) with minimal effect to image
quality.

Figure 5-6 Solidworks 3D rendering of handheld probe at different angles. (A) Side view of probe. (B)
Side view of probe with top cover removed. Note the presence of two lens tubes. The smaller lens tube
contains the fiber collimating lens and the larger lens tube contains the scan lens. The large lens tube is
threaded onto a plate mounted inside the probe. Different scan lenses can be used with the probe by
swapping the lens tube for another containing the desired scan lens. (C) Angled view of probe. Note the
lens tube shroud is rotated to permit viewing the inside of the lens tube.
In addition to being ergonomic, the handheld device was designed to be easy to use in a clinical setting to minimize its impact on existing clinical workflow. During clinical use, alignment feedback is necessary to find regions of interest and target specific areas of the tissue for imaging. Potential solutions include using a visible optical path for direct or indirect viewing of the targeted area. A direct view would provide a visible optical path from the tissue to the operator’s eye, similar to a microscope. An indirect view would use a camera in this path and display the targeted area on a computer screen. However, both of these would require the introduction of a second (visible) optical pathway to the handheld device on top of the existing OCT pathway. To avoid the additional weight and complexity of a second pathway, OCT preview scans are displayed on a computer screen in real time to be used for alignment. During typical use, orthogonal cross sections are taken in real time to check for off axis alignment of the imaging plane. Additionally, enface previews of the entire imaging surface are acquired in real time for 2-D alignment data by taking a quick raster scan of the tissue and summing the data.

**5.4 Imaging Performance**

*5.4.1 Optical Testing and Characterization*

The performance of the primary optical setup used in the handheld was characterized by imaging a roll of Scotch tape, imaging a standard US Air Force resolution target, and by measuring the spot size with a beam profiling camera.

*Figure 5-8* shows images of a roll of Scotch tape acquired using the handheld OCT device with raster scans at a rate of 400,000 A-scans per second. Images were acquired using
scans of a 1 mm x 1 mm field of view. Each A-scan fringe is linear-k resampled, background-subtracted, dispersion corrected, and spectrally shaped prior to Fourier transform. Following Fourier transform, the logarithm of each voxel is taken and high/low intensity values are clamped to make optimal use of the dynamic range afforded by electronic displays. A representative B-scan illustrating the different layers of the roll of Scotch tape is taken from the resulting volume and shown below.

Figure 5-8 Handheld OCT image of a roll of Scotch tape. (A) Representative B-scan image of the tape. An imaging depth of 9.5 mm in air was obtained. (B) Magnified view of tape image. Layers of the tape were clearly visible.
Figure 5-9, Figure 5-10, Figure 5-11, Figure 5-12, and Figure 5-13 show images of a US Air Force resolution target acquired using the handheld OCT device with raster scans at a rate of 400,000 A-scans per second. Images were acquired using scans of different fields of view. Each image of the resolution target is found by taking a full depth projection of the computed OCT volume and taking the average intensity value at each scan position. Each OCT volume is computed in much the same way as it was for the Scotch tape described previously. However, the square root is taken of each voxel instead of the logarithm in order to enhance edge contrast in the final image.

In the smallest scan, the smallest bars resolved were those of group 6 element 4, indicating the transverse resolution is less than 5.52 μm. Note that the bars throughout the target are regularly spaced and the edges of each bar are straight, indicating that the scan lens (and associated scanning) is free of pincushion distortion and barrel distortion. This is verified by the scans of grid targets in Figure 5-14 and Figure 5-15.
Figure 5-10 Handheld OCT image of US Air Force resolution target with 3.0mm x 3.0mm field of view.

Figure 5-11 Handheld OCT image of US Air Force resolution target with 4.0mm x 4.0mm field of view.
Figure 5-12 Handheld OCT image of US Air Force resolution target with 5.0mm x 5.0mm field of view.

Figure 5-13 Handheld OCT image of US Air Force resolution target with 6.0mm x 6.0mm field of view.
Figure 5-14 Handheld OCT image of grid target verifying lack of distortion at different fields of view. (A) 1.0mm x 1.0m field of view (B) 1.5mm x 1.5mm field of view. (C) 2.0mm x 2.0mm field of view. (D) 3.0mm x 3.0mm field of view.
Figure 5-15 Handheld OCT image of grid target verifying lack of distortion at different fields of view. (A) 4.0mm x 4.0m field of view (B) 5.0mm x 5.0mm field of view. (C) 6.0mm x 6.0mm field of view.

The spot size of the handheld was measured with the use of a DataRay WinCamD-XHR CMOS beam profiler camera. The camera was placed at the focal plane of the handheld device and the spot size was measured as the galvanometer mirrors scanned the spot across the camera sensor. This enabled assessment of how the spot size (and thus the focal plane) varied across the field of view of the handheld device. The measured $1/e^2$ spot sizes are given in Figure 5-16.

![Figure 5-15](image)

**Figure 5-16** Spot size measurement of primary optical setup of handheld device using DataRay WinCamD-XHR beam profiler camera

Note that the measured spot sizes in Figure 5-16 are $1/e^2$ spot sizes. Using the camera to instead measure to the first null in the Airy disk diffraction pattern yields a spot size of 27.2 μm at the center of the field of view. This is consistent with the diffraction limited spot size predicted from the simulation in Section 5.2.1. Note also that the spot size increases as the beam is scanned away from the center of the scan lens. This is because the scan lens cannot focus the beam onto a perfectly flat imaging plane, an effect known as field curvature. Scanning the laser beam away
from the center of the scan lens thus causes the spot to be out of focus by the time it reaches the camera sensor for measurement.

The curvature of the actual focal plane can be assessed by using the measured spot sizes to calculate the defocus of an ideal Gaussian beam. This is found by noting that at a position $z$ measured from the focus of a Gaussian beam, the spot size parameter $w$ is given by

$$w(z) = w_0 \sqrt{1 + \left( \frac{z}{z_R} \right)^2}$$

where $w_0$ is the radius of the beam waist and $z_R$ is the Rayleigh range. As such, knowledge of the beam waist diameter can be used to compute the field curvature from the measured spot size as

$$z = z_R \sqrt{\left( \frac{w}{w_0} \right)^2 - 1}$$

The result is shown in Figure 5-17 and is consistent with the field curvature predicted by optical simulation.

![Field Curvature in FOV](image)

**Figure 5-17** Field curvature measurement of primary optical setup of handheld device calculated using spot sizes measured with DataRay WinCamD-XHR beam profiler camera.
5.4.2 Tissue Imaging Results

Tissue imaging experiments were conducted to perform proof of principle imaging with the handheld device and the resulting images can be seen in Figure 5-18, Figure 5-19, Figure 5-20, and Figure 5-21. In these experiments, the device scanned at a rate of 400,000 scans per second using a prototype VCSEL swept source laser. This is 4 to 20 times faster than current commercial systems. The handheld device was tested on fixed human kidney specimens to evaluate the image quality and ease of imaging, as seen in Figure 5-18. The images obtained are comparable to images obtained using standard tabletop OCT systems and they visualize common architectural morphology (such as proximal convoluted tubules) in renal tissue. The handheld device was also tested in vivo on skin, as seen in Figure 5-19, and live rat kidney specimens, as seen in Figure 5-20 and Figure 5-21. Image quality in the rat kidney was relatively poor due to the low transverse resolution of the system relative to feature size. The scan lens available at the time was designed for use in human kidney, where morphologic structures are significantly larger than in the rat kidney. However, the live rat kidneys provided a chance to utilize the ultrahigh imaging speed of the system to produce OCT angiography images. OCT angiography produces images of blood flow in tissue by comparing the decorrelation signal between sequential images taken at precisely the same location.

![Images from a 3 x 3 mm 1571 x 1571 pixel scan of a fixed human kidney specimen. (A) and (B) are horizontal cross sectional images taken from the yellow and green lines, respectively, of (C). (C) is a single en-face image of the entire imaged region taken the red line in (A) and (B). That is, (C) is a single slice in depth (denoted by the red line) of the entire imaged region.](image)
Figure 5-19 Images of skin acquired using the handheld OCT probe. (A) Cross sectional image of a human thumbpad. (B) Summed en-face image of thumbpad. Yellow arrow denotes the line taken to obtain the cross sectional image in (A). (C) Cross sectional image of a human nailbed. (D) Summed en-face image of a human nailbed. Yellow arrow denotes the line taken to obtain the cross sectional image in (C).

Figure 5-20 Images from a $3 \times 3 \text{ mm } 500 \times 500 \text{ pixel scan of a live rat kidney specimen imaged in vivo.}$ (A) and (B) are horizontal cross sectional images taken from the yellow and green lines, respectively, of
(C). (C) is a single en-face image of the entire imaged region taken the red line in (A) and (B). That is, (C) is a single slice in depth (denoted by the red line) of the entire imaged region.

Figure 5-21 Image of a 3 x 3 mm 500 x 500 pixel OCT angiography scan of a live rat kidney specimen imaged in vivo. Structural information of the kidney is shown in grayscale as a summed en-face image. Angiography information is overlaid in red. Note the left half of the image, where (red) blood vessels correlate strongly with the location of (grayscale) tubule structures in the kidney.

5.4.3 Discussion

The SS-OCT images obtained using the handheld device demonstrate the feasibility of non-invasive, three-dimensional imaging and diagnostics of a range of biological tissues at the point of care. Through rapid prototyping and the use of printed plastic, a lightweight and compact OCT handheld device was constructed to meet clinical requirements for speed and ease-of-use without sacrificing alignment requirements for OCT image quality. High-speed imaging and an ergonomic, one-handed design enabled stabilized, motion-free volumetric scans of tissue with a large field of view. The large field of view provides the operator with some tolerance for scan alignment so that the scan does not have to be perfectly placed to acquire useable volumetric data sets. Additionally, the motion-free volumetric data sets allow for arbitrary cross-sections at regions of interest.

Future studies can be performed to fully assess the imaging performance and clinical value of the system following deployment to clinical settings. The combination of the wide scanning angle in the handheld and the high imaging speed of SS-OCT could allow for screening of pathology with a single volumetric data set spanning the areas of interest on the patient. The compact, easy-to-use form factor could enable the adoption of SS-OCT in settings like primary
care clinics or the surgical theater where space is limited. Emergent applications can include intraoperative assessment of kidney transplant viability, as many donor kidneys suffer ischemic insult while awaiting transplant and there is a critical clinical need for a reliable, real-time assay to evaluate donor kidney viability and predict post-transplant outcome.

5.5 References
