High Speed Handheld Instrument for Ophthalmic Optical Coherence Tomography

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Abstract

Optical coherence tomography (OCT) is a non-contact, high resolution biomedical imaging technique that uses low coherence interferometry to generate cross-sectional images of tissue. OCT has become a standard tool in ophthalmology for imaging the retina to detect or monitor pathologies. Recent research advances in swept source lasers have allowed swept source OCT (SS-OCT) to have 5-50x faster imaging speeds when compared to SD-OCT commercial systems.

This thesis describes the design of a handheld SS-OCT instrument to screen for retinal diseases. Many retinal diseases are asymptomatic in their early stages and remain undetected until they advance to cause irreversible vision loss. Early detection and treatment of these diseases can prevent permanent damage to the retina. While OCT has been proven effective at diagnosing retinal pathology, most commercial systems are bulky and table mounted, limiting their screening capabilities. The compact and easy to use handheld device can be used to quickly screen patients outside of the ophthalmology clinic in primary care, pediatrics applications, or in the field in developing countries. A custom motion registration algorithm corrects for the additional operator motion in the images. The wide scanning angle combined with the high imaging speeds used in SS-OCT allows screening of pathology with a single volumetric data set spanning the areas of interest on the retina.

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1.1 Introduction

Optical coherence tomography (OCT) allows for non-invasive and non-contact depth imaging through the use of low coherent light. Our group at MIT and collaborators developed OCT as a novel non-invasive imaging modality in 1991[1]. OCT functions analogously to ultrasound except that OCT generates depth resolved images by measuring the backscattered light instead of sound. The interference between light backscattered or back-reflected from a sample and a reference path can be detected interferometrically and processed to reconstruct the 1-D depth profile along a single axis in the sample, known as an A-scan. By sweeping the light in one transverse direction, a 2-D cross sectional image or a B-scan can be acquired. Sweeping the B-scan sweeps in a raster scan allows a 3-D volumetric data set to be acquired.

Recent advances in OCT research have greatly improved the imaging speed and resolution of OCT. The first generation of OCT was known as time domain OCT (TD-OCT) because it physically changed the reference length and detected the interference signal in the time domain to sample the interference fringe. In recent years, spectral domain OCT (SD-OCT) utilizing fixed spectrometers to sample the fringe directly have largely replaced TDOCT systems due to its higher speed and sensitivity [2, 3]. Another type of OCT system, swept source OCT (SS-OCT) samples a laser sweeping through wavelengths or frequencies in time. Both methods detect light in the Fourier domain by measuring the interference spectrum and then Fourier transforming to extract the A-scan information. SS-OCT has greater imaging range than SD-OCT because the linewidth of the laser is narrower than the resolution of a spectrometer[4]. Spectrometers utilizing line scan cameras also suffer from higher roll-off in sensitivity at higher frequencies due to a finite pixel size averaging higher spatial frequencies[5, 6]. Recent advances in swept source lasers have allowed systems to have much higher imaging speeds in the
hundreds of kilohertz to megahertz[7-10]. These advances allowed SS-OCT to be an ideal system to construct a high speed system.

OCT can be incorporated in a great variety of instruments from the standard ophthalmoscope down to endoscopes, catheters, and needle probes. The objective of this thesis is to construct a handheld OCT device as an alternative to current tabletop ophthalmic imaging systems for use in screening for retinal pathologies. Although a handheld device will also have additional operator and patient motion, our collaborators at Erlangen University have developed a custom registration software that corrects motion by acquiring multiple scan patterns[11]. In addition, recent developments in high speed SS-OCT imaging using swept lasers can dramatically reduce image acquisition times. By designing and validating a portable and easy to use system, OCT retinal imaging can be used beyond the ophthalmology clinic to primary care or pediatrics applications for detection and monitoring of retinal diseases.

1.2 Background

Undetected Retinal Diseases

With the increasing life expectancy in the past decades, the rates of eye diseases will also rise with a larger elderly population[12]. Early detection is essential for treatment and prevention of the diseases and will reduce the rate of blindness[13]. A Canadian study of 133 optometrist practices with 24,570 patients of all ages showed that 14.4% of those had asymptomatic eye disease even though 66.8% of the people with disease had a best-corrected visual acuity of 20/25 or better[14]. Undiagnosed eye diseases are more severe in minority communities that do not have as extensive access to medical services. In East Baltimore, a 1994 study with 405 general medicine patients over the age of 40 of whom 94% were black showed that 50.6% of the examined patients had clinically important ocular pathology and one third of those were unaware of the disease[15]. A study of 6,357 Latinos showed 53% of subjects had eye disease and of those, 63% had undetected eye disease[16]. Clearly, detection of these diseases is necessary to inform the patients and enable early treatment to prevent the disease from causing blindness.

The three leading causes of blindness that affect the retina are age related macular degeneration (AMD), glaucoma, and diabetic retinopathy[17-21]. AMD is diagnosed by the
appearance of yellow or white spots known as drusen in the retina. In the western world, it is the leading cause of blindness in the elderly[19]. Although the prevalence of AMD is 1.47% among persons over 40 years old in the United States, the prevalence is greatly correlated with age, increasing to 3.24% for ages 75-79 and 11.77% for ages 80 and higher. [17]. Because early AMD is often asymptomatic, screening of elderly patients will allow for detection and early treatment of AMD before irreversible vision loss.

Glaucoma is a chronic eye disease characterized by atrophy of the nerve fiber layer around the optic nerve head. In the United States, glaucoma is the second leading cause of blindness, but is the number one cause of blindness in black Americans[22]. Studies have shown that fewer than half of the people suffering with glaucoma are aware of their disease and this number only decreases in developing countries[23]. Because the prevalence of open angle glaucoma in Caucasians above 40 years of age is 1.1% - 3%[24-29], the low prevalence requires a screening method for glaucoma with high specificity to prevent false positives[30]. Like AMD, the prevalence of glaucoma increases with age, but the prevalence is much higher in certain ethnic groups. A prevalence model of open angle glaucoma based on multiple studies demonstrated that African people have a higher prevalence compared to Europeans: 10% versus 4% in ages 70-79 and 17% versus 7% in ages 80-89, respectively. [31] Portable screening devices with high sensitivity will be useful in developing countries to detect glaucoma before it causes serious vision loss.

Diabetic retinopathy is characterized by vascular damage of the retinal vessels due to diabetes. Affecting 347 million people in the world, diabetes is a chronic disease that is caused by an insufficient production or use of insulin, a blood sugar regulator, in the body[32]. In the United States, the prevalence of diabetes differs among ethnicities: 7.1% in non-Hispanic whites, 8.4% in Asian Americans, 12.6% in non-Hispanic blacks, and 11.8% in Hispanics[33]. There is a high prevalence of diabetic retinopathy in diabetic patients. Among patients diagnosed with diabetes after the age of 30, those who have had diabetes for 15 or more years have a 77.8% prevalence of diabetic retinopathy[34]. In a study of 271 patients without retinopathy who were diagnosed with diabetes before the age of 30, 59% developed diabetic retinopathy when reexamined four years later[35]. Regular eye examinations of diabetic patients are crucial as the early stages of diabetic retinopathy are usually asymptomatic and early treatment can greatly decrease the chances of severe vision loss[36].
**OCT in Ophthalmology**

Optical coherence tomography (OCT) is an imaging technique commonly used in ophthalmology for diagnosing and monitoring diseases of the eye [37-40]. OCT allows for the diagnosis and monitoring of retinal diseases mentioned in the previous section. The cross sectional imaging allows for identification of choroidal neovascularization and scar formation in the retina, one of the symptoms of exudative (wet) AMD. OCT scans have also been used to monitor treatment of wet AMD with vascular endothelial growth factor (VEGF) inhibiting applications[41, 42]. OCT can also detect the precursors of nonexudative (dry) AMD by imaging the drusen accumulation and atrophy in the retinal pigment epithelium[43-46]. Glaucoma detection by analyzing the retinal nerve fiber layer (NFL) thickness, optic nerve head morphology and ganglion cell layer atrophy[47-49]. In diabetic retinopathy, OCT can detect the swelling or leakage within the layers of the retina before symptoms of the diseases are apparent to the patient[50, 51]. OCT offers the ability to monitor other morphological changes in the various layers of the retina caused by other diseases as well. Commercial devices are now standard in ophthalmology clinics with ~9 million OCT procedures performed in the US in 2010 as reported by Medicare reimbursements[52].

Recent studies have shown that OCT can be used to screen for undetected eye diseases. In 500 randomly selected eyes from 500 normal and asymptomatic individuals imaged with commercial systems, three eyes showed vitreal-macula syndrome, three eyes had suspected posterior staphyloma, and two eyes had retinoschisis[53]. Commercial companies have also focused efforts on OCT screening. A study with 111 normal subjects and 108 patients with retinal disease were examined with the iWellnessExam screening protocol by Optovue, a commercial OCT company, to show 99% specificity and 93% and 90% sensitivity for retinal and optic nerve pathology detection, respectively[54]. Furthermore, OCT has proven effective for monitoring diabetic retinopathy without time consuming eye dilation, and the resulting OCT images can be analyzed with web based databases or with off-site diagnosis[55, 56].

**Portable/Handheld OCT**

Miniaturizing OCT devices for medical imaging is currently a popular research area in multiple fields including ophthalmology. Probe and handheld OCT devices allow for portability and flexibility, allowing for applications such as OCT use during surgery. The literature has
many different designs while utilizing unique methods to direct and steer the optical beam onto tissue.

Because an OCT beam images along a single axis, these miniaturized OCT devices use unique scanning mechanisms to steer the beam along tissue as well as reduce the size of the instrument. The scanning mechanisms have tradeoffs between speed, scan angle, and size. Rotating right angle probe devices are used for a circumferential scan or translated for a linear scan parallel to tissue for endoscopic or cardiovascular applications. Their performance is limited by the ability of rotary actuation at the proximal end of the device to transmit rotation through torque cables to the distal end of the device. Forward scanning probes often use high voltage PZT cantilevers attached to the optic fiber. The small PZT cantilevers offer fast scanning speeds of kHz and only scan sinusoidal in one direction. While these cantilevers require high voltages to operate, low voltage cantilevers using 10 volts peak to peak have been shown to scan at 480 Hz for fiber based endoscopes. Two rotating angle cleaved grin lenses have been used for linear large scan angles in needle probes but require double or single motors which result in probe vibration. Lastly, fabricated microelectromechanical system (MEMS) scanning mirrors have been used in miniaturized devices to scan in 1-D or 2-D. While MEMS devices are compact, their resonance frequency inversely scales with the scanning mirror area.

Larger gripped handheld devices using galvanometers are another group of portable OCT for imaging the eye. Galvanometers are the standard magnetically actuated scanning mirrors employed in most tabletop OCT systems. The gripped handhelds include corneal imaging at 1310 nm and retinal imaging at 830 nm wavelength. Bioptigen and Optovue, two commercial OCT makers, also sell SD-OCT handheld imaging devices: the Spectral Domain Ophthalmic Imaging System (SDOIS) and the iVue, respectively. The handheld grips on the larger systems allow for more stability while imaging the eye and most devices contain alignment feedback to the operator with an iris camera. The grip designs also allow for imaging of patients in both sitting and supine positions.

Many clinical studies have been performed given the advantages of handheld OCT devices over standard table mounted setups. OCT handhelds allow for imaging of premature infants or children who otherwise could not be imaged using standard OCT systems. The studies
examined the anatomy of retinopathy of prematurity using a Bioptigen handheld[73, 74] or a converted commercial Spectralis system[75]. Other studies on premature neonates have examined cystoid macular edema [76]. Children with or without retinal pathology have also been examined with a custom OCT device[77]. Lastly, ophthalmic intraoperative procedures can be monitored with OCT handheld devices to visualize the removal of layers in the retina during surgery with a Bioptigen device [78].

1.3 Scope of Thesis

This thesis focuses on the development of a handheld OCT device that utilizes the high speed of swept source lasers for screening of retinal pathologies. Conventional ophthalmic OCT devices are bulky and table mounted which limit their flexibility for screening individuals. Due to the strict standards for alignment in OCT, a portable OCT device must be developed to be easy to use for the operator. With the use of printed plastic and MEMS scanning mirrors, a lightweight and compact OCT device can be constructed. The combination of the high speed of swept source systems and motion correction registration software will allow for acquisition of large, motion-free volumetric scans. A single wide field volumetric scan can be used to detect various types of retina pathology in different parts of the retina.

Chapter 2 introduces OCT theory by describing the Michelson interferometer and how it can detect displacement through interference. The role of axial resolution to distinguish two separate layers is also analyzed. Next, swept source OCT is defined along with the parameters that affect the imaging depth of a system. The signal processing to compensate dispersion and calibrate the OCT device is described. Lastly, an analysis of the sensitivity of the instrument and the noise sources is presented.

Chapter 3 describes the specifications for a retinal imaging OCT handheld sample arm. The different types of scanning lenses along with their limitations are specified. The equations for the imaging parameters of the device such as the transverse resolution and field of view on the retina are derived and analyzed. In addition, the necessary alignment steps to acquire an OCT image are described.
Chapter 4 outlines the swept source OCT system used for testing and acquisition of retinal data. The laser source, interferometer, reference arm, and the acquisition unit are specified. The various iterations of the sample arm are described in the next chapter.

Chapter 5 shows the evolution of the OCT handheld device. Starting from the galvanometer scanning device to the later 3-D printed plastic handholds using MEMS scanning mirrors, every version is analyzed in terms of its optical setup, physical design, and results. A discussion of the effectiveness and limitations is also included.

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Chapter 2

Swept Source OCT Theory

2.1 Overview

This chapter reviews the theoretical background information on swept source OCT. The Michelson interferometer is described as the functional unit to obtain interference fringes used to detect depths in OCT. A section on the details of swept source OCT analyzes many of the parameters that determine how much signal can be recovered from varying depths. Lastly, the sensitivity and sources of noise in a system are defined and characterized.

2.2 The Michelson Interferometer

OCT images are generated by processing the interference fringes that result from two optical paths combining in a Michelson interferometer. A basic bulk optics Michelson interferometer consisting of a light source, beam splitter, two mirrors and a detector is shown in Figure 2-1.

![Michelson interferometer diagram](image)

**Figure 2-1.** Michelson interferometer constructed with bulk optics in free space. The reference and sample arms are indicated. Mirrors M1 and M2 are indicated.
The complex vector for the initial electric field $E_i$ entering the interferometer from the light source at a fixed point in time can be represented as an amplitude $A_i$ and phase $\phi$ shown in equation (2.2.1) as a function of the wavenumber $k = \frac{2\pi}{\lambda}$. In this chapter, the boldface of a variable indicates a complex number.

$$E_i(k) = A_i(k)e^{j\phi(k)}$$ (2.2.1)

After this field is initially split by the beam splitter, both beams are reflected back by mirrors M1 and M2. The beam splitter recombines the two beams and a portion of the combined beams are detected at the detector. The field at the detector can be written as the sum of the fields from the reference and sample arms.

$$E_{\text{det}}(k) = E_R(k) + E_S(k)$$ (2.2.2)

For simplicity, assume that the beam splitter equally splits power between the two arms for all wavelengths. This results in the round trip of both the reference and sample arms generating a $\frac{1}{2}$ factor in the resulting fields. Adding in the terms for round trip propagation of the beams and the complex field reflectivities $r_R(k)$ and $r_S(k)$ of the mirrors in both arms, the reference and sample arm fields can be written as

$$E_R(k) = \frac{1}{2} A_i(k)e^{j\phi(k)}r_R(k)e^{-j2kL_R}$$
$$E_S(k) = \frac{1}{2} A_i(k)e^{j\phi(k)}r_S(k)e^{-j2kL_S}$$ (2.2.3)

In the detector, the photodiode can only sense the intensity of the beam and produces the current

$$i_{\text{det}}(k) = \frac{\eta q}{\hbar \nu} |E_{\text{det}}(k)|^2$$ (2.2.4)

Where $\eta$ is the detector sensitivity, $q$ is the quantum of electric charge, and $\hbar \nu$ is the single photon energy. Equation (2.2.3) can be substituted to expand (2.2.4) to

$$i_{\text{det}}(k) = \frac{\eta q}{4\hbar \nu} A_i^2(k) \left[ \frac{R_R(k) + R_S(k)}{\text{autocorrelation}} + 2 \text{Re} \left\{ r_R^*(k)r_S(k)e^{-j2k\Delta z} \right\} \right]$$ (2.2.5)

Where $R_R = r_R r_R^*$ and $R_S = r_S r_S^*$ are the power reflectivity of the mirrors. The variable $\Delta z = L_S - L_R$ represents for the difference between the sample and reference arms. The
autocorrelation terms given by the power reflectivities of each arm are also known as the DC terms because they produce a constant value. The cross-correlation term with a magnitude equal to the multiplication between the field reflectivities of both arms is known as the AC component because it produces a sinusoid in the k domain with frequency proportional to the displacement between the arms.

This can be demonstrated in the simple case that \( r_R = r_S = 1 \) Equation (2.1.4) simplifies to

\[
  i_{\text{det}}(k) = \frac{1}{4} \eta q A_i^2(k) [1 + 2\cos(2k\Delta z)]
\]  

(2.2.6)

Notice that there is a constant component from the autocorrelation terms \( R_R \) and \( R_S \). The intensity detected has a sinusoidal frequency depending on the difference in the distance between the sample and reference lengths with a magnitude determined by the cross correlation of the reflection between the reference and sample arms. To recover the frequency, a Fourier transform must be taken of equation (2.1.5) with respect to \( k \). We define the Fourier transform of a function as

\[
  \mathcal{F}(\omega) = \mathcal{F} \{ f(x) \} = \int_{-\infty}^{\infty} f(x)e^{-j\omega x} dx
\]  

(2.2.7)

Assume that the source has a constant magnitude for all wavenumbers \( A_i(k) = 1 \). The Fourier transform of equation (2.2.6) is therefore

\[
  F \{ i_{\text{det}}(k) \} \propto \delta(z) + \delta(z \pm 2\Delta z)
\]  

(2.2.8)

Where \( \delta(z) \) is the Dirac delta function. The inverse of the wavenumber \( k \) is position in space given by the variable \( z \). The Dirac delta peaks are at a distance proportional to the displacement between the two arms relative to \( z = 0 \) or the zero delay position. Figure 2-2 illustrates the original sinusoidal single and the resulting position of the reflector given by the Fourier transform.
Figure 2-2. (A) The fringe signal as a function of wavenumber. (B) The Fourier transform of the fringe signal with a DC peak and two peaks spaced from the DC based on the difference in distance between sample and reference arm.

Thus, with a single reflector, there is a single sinusoidal waveform which encodes the position of the reference arm relative to the sample arm.

Multiple Reflectors in Biological Tissue

Figure 2-3. Modified Michelson interferometer with the sample arm mirror replaced with a biological tissue with several layers.

Due to the multiple layers and types of cells in a biological specimen, multiple reflections must be considered when imaging biological tissue. Figure 2.3 shows a Michelson interferometer
with the sample mirror replaced by a section of tissue. A lens in the sample arm focuses the beam to a point on the tissue. Assume that the tissue is within the depth of field of the lens. In addition, an identical lens is placed in the reference arm to match the lens in the sample arm.

The field from the sample arm can now be written as the summation of all the complex field reflectivities \( r_n(k) \) at differing depths \( z_n \) relative to the reference arm depth.

\[
E_S(k) = \frac{1}{2} A_t(k) e^{i \phi(k)} \sum_{n=1}^{\infty} r_n(k) e^{-jk^2(z_n+L_R)}
\]  

(2.2.9)

The field from the reference arm is the same as in the case of the single reflector. With multiple reflectors, the current at the detector specified in equation (2.2.4) can now be written as

\[
i_{\text{det}}(k) = \frac{1}{4 \hbar \nu} A_t^2(k) \left[ R_R(k) + \sum_{n=1}^{\infty} R_n(k) + \sum_{n=1}^{\infty} 2 \text{Re}\left\{ r_R^*(k) r_n(k) e^{-j2kz_n} \right\} \right]
\]

\[
+ \left[ \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} \text{Re}\left\{ r_m^*(k) r_n(k) e^{-j2k(z_n-z_m)} \right\} \right]
\]

(2.2.10)

Equation (2.2.9) has many similarities with equation (2.2.5) in the previous section. However, in the case of multiple reflectors, each tissue layer will have an autocorrelation and cross-correlation term with the reference arm as well as a cross-correlation with every other tissue layer.

In standard OCT operation, much more light is reflected from the reference arm than from the tissue layers. Therefore, using relation \( r_R(k) \gg r_n(k) \) for all values \( n \). This simplifies equation (2.2.10) to

\[
i_{\text{det}}(k) = \frac{1}{4 \hbar \nu} A_t^2(k) \left[ R_R(k) + \sum_{n=1}^{\infty} 2 \text{Re}\left\{ r_R^*(k) r_n(k) e^{-j2kz_n} \right\} \right]
\]

(2.2.11)
The phase term \( \theta_n(k) = \angle r_R(k) - \angle r_n(k) \) is the difference in phase between the phase of the reflectivities of the sample layers and reference layers. Comparing this equation with (2.2.6), once again there is a DC term based on the power reflectivity of the reference arm and multiple AC sinusoids that with magnitudes depending on the layer reflectivity and the frequency based on the displacement from the reference arm.

Similar to the single reflector case, a Fourier transform is taken of equation (2.2.10) with respect to \( k \) to isolate the depth information encoded in frequency. We assume that the tissue complex reflectivities \( r_n(k) = r_n \) and phase differences \( \theta_n(k) = \theta_n \) are independent to \( k \) to simplify this calculation.

\[
F\{i_{\text{det}}(k)\} = \frac{\pi n q}{2 hv} F\{A_n^2(k)\} \otimes \left[ R_R(k)\delta(z) + \sum_{n=1}^{\infty} \sqrt{R_R(k)} \sqrt{R_n(k)} e^{\pm j \theta_n(k)} \delta(z \pm 2z_n) \right] \tag{2.2.12}
\]

Similar to the analysis of the single reflector, there is a DC component that is the result of the power reflection from the reference signal. The amplitude of each layer is equal to the multiplication between the square root of the reference and sample layer power reflectivities. Each layer is represented by two Dirac deltas located away from DC in the positive and negative direction directly proportional to the displacement of each layer relative to the sample arm. The Fourier transform of the power spectrum \( F\{A_n^2(k)\} \), known as the point spread function, is convoluted with the DC and every other Dirac delta representing the layers in the tissue.

Further examining equation (2.2.12), the Fourier transform of the detector current is Hermitian symmetric. This can be explained by noticing that the detector senses the real-valued intensity and converts it to current. Due to this symmetry, there is an ambiguity between positive and negative distances of the layers from the reference arm. Thus, it is important to properly position the sample so that all the layers are positive or negative distances from the reference arm position to avoid overlapping artifacts.

**Axial Resolution**

In our previous analysis of the interferometric signal at the detector, we assumed a laser source that encompassed all bandwidths. After Fourier transform, this produces infinitesimally...
narrow Dirac delta for each reflected layer. In reality, laser sources have limited optical bandwidth and thus, the resolution between two layers after a Fourier transform is finite. The axial resolution limits how finely OCT can distinguish two layers in depth.

This resolution value is defined as the axial resolution of the system. To illustrate the relationship between optical bandwidth and axial resolution in OCT, assume that the input laser power follows a Gaussian distribution as a function of $k$

$$A^2_f(k) = \exp\left(-\frac{4 \ln(2)(k - \bar{k})^2}{\Delta k^2}\right)$$  \hspace{1cm} (2.2.13)

where $\bar{k}$ is the mean wavenumber and $\Delta k$ is the full width half maximum (FWHM) of the Gaussian. A Fourier transform of a Gaussian remains a Gaussian function but the transform’s FWHM is inversely proportional of the original FWHM. In this case, the Fourier transform of (2.2.11) is given by

$$F\{A^2_f(k)\} = \Delta k \sqrt{\frac{1}{\pi 4 \ln(2)}} \exp\left(jkz\right) \exp\left(-\frac{z^2 \Delta k^2}{4 \ln(2)}\right)$$ \hspace{1cm} Gaussian \hspace{1cm} (2.2.14)

This is known as the point spread function. The axial resolution is given by the FWHM of the point spread function.

$$FWHM_z = \frac{4 \ln(2)}{\Delta k}$$ \hspace{1cm} (2.2.15)

This can also be written in terms of wavelength by noting the relationship $\Delta k = 2\pi \frac{\Delta \lambda}{\bar{\lambda}^2}$ where $\bar{\lambda}$ is the mean wavelength and $\Delta \lambda$ is the FWHM span of the wavelength. The axial resolution can then be written as

$$FWHM_z = \frac{2 \ln(2)}{\pi} \frac{\bar{\lambda}^2}{\Delta \lambda}$$ \hspace{1cm} (2.2.16)

Figure 2-4 illustrates how the shape and spread of the power envelope $A^2_f(k)$ determines the point spread function $F\{A^2_f(k)\}$ which is then convolved with the Dirac delta functions.
representing each layer seen in equation (2.2.12). This convolution determines the ability to resolve two distinct layers.

![Figure 2-4. The result of the point spread function convoluted with the Dirac deltas representing the layers. (A). Well-spaced layers are clearly distinguishable (B). The two closely spaced layers cannot be distinguished when convoluted with this point spread function.]

### 2.3 Swept Source OCT

In a swept source OCT system, the laser light source in the system sweeps a band of wavelengths over a period of time $T$. For simplicity, assume that the wavenumber $k$ of the monochromatic laser sweeps linearly in time with the following relation

$$k(t) = k_0 + k't$$  \hspace{2cm} (2.3.1)

where $k_0$ is the initial wavenumber and $k'$ is the change in wavenumber over time. Substituting this relation into equation (2.2.11), the intensity at the detector can now be written as a function of time rather than of $k$.

$$i_{\text{det}}(t) = \frac{1}{4} \frac{\eta q}{\hbar \nu} A_i^2 (t) \left[ R_R (t) + 2 \sqrt{R_R (t)} \sum_{n=1}^{\infty} \sqrt{R_n (t)} \cos \left( 2k_0 z_n + 2k't z_n - \theta_n (t) \right) \right]$$  \hspace{2cm} (2.3.2)

Notice how there is an additional phase in the cosine that depends on the initial wavenumber and the depth of the layer relative to the reference arm. With the wavenumber encoded in time, it is
possible to sample in time with a detector to sample a span of wavenumbers. Taking the Fourier transform of (2.3.2) with respect to time will generate the encoded depth information.

Coherence Length

The coherence length is the distance an electromagnetic wave can travel and still maintain a specific level of coherence necessary for interference. This is one of the limiting factors on the depth of interference possible in an OCT system. For time-domain and spectral-domain OCT systems which rely on a broadband light source, the coherence length is equal to the axial resolution of the system. This is due to coherence gating only allowing interference of a very narrow depth of tissue with the reference beam. All the other reflected light outside of the coherence gate is incoherent and does not interfere with the reference beam.

In a swept source system, the coherence length of the laser affects the imaging depth of the device rather than the axial resolution. We assumed above that at a single point in time, the light is monochromatic at one value of \( k \). In reality, the spectrum or linewidth at a point in time from the swept source laser spans a narrow range of \( k \) values inversely proportional to the number of output modes of the laser. A narrow spectrum or linewidth will allow for a higher coherence length so that deeper layers in depth can interfere with the reference signal at each swept wavenumber.

Detector Bandwidth

The detector bandwidth also provides a limiting factor on the depth of layers that can be detected in swept source OCT. Shown in Figure 2-5, a standard detector has a relatively flat frequency response up to the specified bandwidth. The specified bandwidth indicates the -3 dB point when the gain of the detector begins to rapidly decay. After the -3 dB point, the detector gain decays rapidly depending on the number of amplifier stages.
Figure 2-5. Measured frequency response each input on a Thorlabs PDB130C 350 MHz bandwidth balanced detector.

Because a swept source system sweeps the wavenumber in time, each individual layer depth is encoded as a frequency in time that is directly proportional to the difference in reference and sample arm length and sweep rate of the laser. Detecting depths further away from the zero delay position requires higher detector bandwidths than detecting shallower depths. After a certain depth, the signal level will drastically decrease until it cannot be discerned from noise.

In addition, with the same photodiodes, the gain of the amplifiers in a detector is inversely proportional to the bandwidth. The operational amplifier in the amplifier circuit has a fixed gain-bandwidth product equal to the bandwidth where the gain is equal to unity. Increasing the gain linearly decreases the bandwidth of the amplifier. As swept source lasers increase in sweep frequency, the sweep rate increases and there is an increasing need for detectors with bandwidths above hundreds of megahertz to gigahertz. However, the gain must be balanced with the bandwidth to generate enough signal to noise (SNR) for clear OCT images. This SNR issue will be explored in more detail in section 2.4.

Analog to Digital Sampling

The interferometric signal from the detector must be digitized so that it can be processed and interpreted. High sample rate A/D converters are essential to SS-OCT to resolve the depths encoded in high frequency. Before, we have assumed that the Fourier transform that we take of the detector current is a continuous time Fourier transform over all time. In reality, a discrete
Fourier transform (DFT) is taken because of the limited sampling rate $f_s$ and number of samples per sweep $M$. The properties of the DFT create limits on the viewable depths as well as the sampling between depths a swept source system.

The depth profile acquired depends on relationship between the sampling rate in time and the number of samples acquired during the sweep. This relationship is listed in Table 2-1.

<table>
<thead>
<tr>
<th>Time (k) Domain</th>
<th>Frequency (z) Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling rate $f_s$</td>
<td>Total depth span $-f_s/2$ to $f_s/2$</td>
</tr>
<tr>
<td>Number of samples $M$</td>
<td>Spacing between depths $f_s/M$</td>
</tr>
</tbody>
</table>

Table 2-1. Relationships between the time domain and frequency domain due to the properties of the Fourier transform.

After taking a DTFT of the sampled detector current, the frequencies are plotted on the scale of $-f_s/2$ to $f_s/2$ according to the Nyquist sampling theorem. This establishes the limit of depths encoded in frequency. Any higher frequencies above the Nyquist sampling frequencies will be mapped to lower frequencies, creating artifacts in the depth image. Between $-f_s/2$ to $f_s/2$, there are $M$ samples with spacing $f_s/M$ which provide the spacing in depth per sample. While it is possible to have denser sampling by zero padding the sample, the sampling resolution is still limited by $f_s/M$. The sampling resolution must also be precise enough to take advantage of the high axial resolution provided by OCT.

As mentioned in the previous section, because the Fourier transform of the detector current is Hermitian symmetric, there is a redundancy between the negative and positive frequencies. In standard OCT processing, only $M/2$ sample values provide useable data. There has been research in techniques to shift the data so that the entire Fourier domain can be used to encode depth information[1-4].

Imaging Depth

There are some differences in over the definition of imaging depth which is defined as how deep a swept source system can image. Some published papers measure the depths when the signal from a reflecting mirror decays -3, -6, -10, or -20 dB to indicate the depth when the signal
is unusable. In a swept source system, the coherence length, detector bandwidth, and A/D sampling rate all affect the total imaging depth ability of a swept source system. Figure 2-6 illustrates how several different arrangements of coherence length, detector bandwidth, and A/D sampling rate affect the total imaging range. These components must be carefully chosen based on the intended function of the swept source OCT system.

**Figure 2-6.** Analysis of the imaging depth of SS-OCT. (A) Imaging setup of three equally spaced layers that generate the same magnitude response at separate depths. (B) A configuration with low coherence length causes a gradual decrease in signal. (C) Using a lower bandwidth detector with long coherence length generates a dramatic decrease in signal after the bandwidth cutoff. (D) A reduced A/D sampling rate reduces the Nyquist limited sampling window. This causes the signal from the layer at 1.5 mm to alias down to 1.1 mm.
2.3 Signal Processing

Dispersion

In the previous analysis of OCT theory, the light from both sample and reference arms is assumed to propagate through the same materials and optics. In reality, there are distinct optical design differences between the sample and reference arms that can create dispersion mismatch between the two arms. Dispersion occurs because the propagation velocity depends on the wavelength or frequency of light passing through the material. This produces a wavelength dependent phase delay determined by the type and length of material. Excessive dispersion in OCT can cause a broadening of the point spread function, reducing axial resolution and image quality.

To illustrate the effects of dispersion, a phase delay $\Phi(k)$ dependent on the wavenumber in vacuum $k = 2\pi c / \lambda_0$ where $c$ is the speed of light in vacuum and $\lambda_0$ is the wavelength in vacuum is added to both the sample and reference arms fields.

$$
E_R(k) = \frac{1}{2} A_i(k) e^{j\phi(k)} r_R(k) e^{-j[k2L_R + \Phi_R(k)]} \\
E_S(k) = \frac{1}{2} A_i(k) e^{j\phi(k)} \sum_{n=1}^{\infty} r_n(k) e^{-j[k2(z_n + L_R) + \Phi_S(k)]} \quad (2.3.1)
$$

The detector current can now be written with a phase difference $\Delta \Phi(k) = \Phi_R(k) - \Phi_S(k)$ equal to the dispersion mismatch.

$$
i_{det}(k) = \frac{1}{4 \ h_v} A_i^2(k) \left[ R_R(k) + 2\sqrt{R_R(k) \sum_{n=1}^{\infty} R_n(k) \cos \left( 2kz_n + \theta_n(k) + \Delta \Phi(k) \right) \right] \quad (2.3.2)
$$

To simplify the analysis, only the signal component of one layer is considered. By Euler's formula, the cosine can be written as the sum of two complex exponentials.

$$
i_{sig}(k) = 2\sqrt{R_R(k)R_0(k)} \cos \left( 2kz_0 + \theta_0(k) + \Delta \Phi(k) \right) \\
= \sqrt{R_R(k)R_0(k)} \left[ e^{j[2kz_0 + \theta_0(k) + \Delta \Phi(k)]} + e^{-j[2kz_0 + \theta_0(k) + \Delta \Phi(k)]} \right] \quad (2.3.3) \\
= \sqrt{R_R(k)R_0(k)} \left[ e^{j[2kz_0 + \theta_0(k)]} e^{j\Delta \Phi(k)} + e^{-j[2kz_0 + \theta_0(k)]} e^{-j\Delta \Phi(k)} \right]
$$

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Taking the Fourier transform and assuming that $\theta_0(k)$ does not depend on $k$ the depth information encoded in frequency can be recovered.

$$F\{i_{\text{sig}}(k)\} \propto e^{i\theta(k)} \delta(z - 2z_0) \otimes F\{e^{j\Delta\Phi(k)}\} + e^{-i\theta(k)} \delta(z + 2z_0) \otimes F\{e^{-j\Delta\Phi(k)}\}$$ \hspace{1cm} (2.3.4)

The dispersion mismatch phase term is convoluted with the Dirac delta of the depth signal. The phase difference from dispersion $\Delta\Phi(k)$ has a strong dependence on the wavenumber in vacuum. A Taylor expansion of $\Delta\Phi(k)$ separates the higher order terms of dispersion about the mean wavenumber $\bar{k}$.

$$\Delta\Phi(k) = \Delta\Phi(\bar{k}) + \Delta\Phi'(\bar{k})(k - \bar{k}) + \frac{\Delta\Phi''(\bar{k})}{2}(k - \bar{k})^2 + \frac{\Delta\Phi'''(\bar{k})}{6}(k - \bar{k})^3 + ...$$ \hspace{1cm} (2.3.5)

The first term in the Taylor expansion $\Delta\Phi(\bar{k})$ only contributes a constant phase delay. The next term $\Delta\Phi'(\bar{k})$ provides a linear phase delay dependent on $k$ that shifts the Fourier spectrum but does not affect the shape of the Dirac delta. This is analogous to group velocity. The second and third order dispersion terms have a $k$ dependence that can affect the shape of the spectrum as seen in Figure 2-7.

**Figure 2-7.** Broadening of point spread functions due to distortion. (A) Point spread function with no dispersion. (B) Second order dispersion broadens the function symmetrically. (C) Third order dispersion distorts the point spread function asymmetrically.

The second order term is analogous to group velocity dispersion (GVD) while the third order is analogous to cubic dispersion or variation of GVD with wavelength/frequency. The fourth and
higher order dispersions are generally not considered because the two arms are initially physically dispersion matched with compensation glass and the second and third order terms are dominant.

Note that $\Delta \Phi(k)$ is assumed to not depend on $z_n$ because dispersion caused by the difference in layers at different depths is negligible because the limited imaging depth of OCT. This is useful because it is possible to numerically correct for dispersion when processing the images[5]. The received detector current received can be multiplied with a complex compensating phase factor given by

$$\Phi_C(k) = -a_2(k - \bar{k})^2 - a_3(k - \bar{k})^3$$ (2.3.6)

The dispersion in the positive frequencies is corrected for but the dispersion in the negative frequencies is amplified. Since the Fourier transform of the detector current is Hermitian symmetric, no depth information is lost if only the dispersion compensated positive frequencies are used to generate the OCT image. The values of $a_2$ and $a_3$ are determined experimentally to produce the highest image quality.

Calibration

Figure 2-8. (A) The $k$ values from a sinusoidal swept laser. (B) The resulting interference fringes from a single reflector sampling at a constant rate. (C) The Fourier transform of B showing a degraded point spread function.

A swept laser source does not perfectly sweep the wavenumber $k$ linearly in time. Some swept source lasers sweep in a resonance mode, producing a sinusoidal sweep over time. If the interference fringes of these nonlinear sweeping lasers are sampled with a fixed sampling rate,
the phase shifts from the nonlinear k values degrade the point spread function shown in Figure 2-8. To remedy this, an A/D card can be calibrated to sample at specific points so that the resulting sample points are equally spaced in k.

The swept source OCT system calibrates the sampling points by recording the fringe signal from a single reflector near the middle of the imaging range with equally spaced samples in time. The data \( i_{\text{det}} \) is processed to obtain the analytical signal equation:

\[
i_{\text{analytic}}(t) = i_{\text{det}}(t) + jH\{i_{\text{det}}(t)\}
\]

(2.3.7)

Where \( H\{i_{\text{det}}\} \) is the Hilbert transform of \( i_{\text{det}} \) defined by

\[
H\{i_{\text{det}}(t)\} = i_{\text{det}}(t) \otimes \frac{1}{\pi t} = \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{i_{\text{det}}(\tau)}{t-\tau} d\tau
\]

(2.3.8)

In contrast to the real detected signal \( i_{\text{det}} \), the analytical signal equation \( i_{\text{analytic}} \) is complex so the phase can be determined. Shown in Figure 2-9A, the phase of the analytical signal directly corresponds to the shape of the wavenumber sweep in Figure 2-8A.

**Figure 2-9.** (A) The unwrapped phase values of the analytical signal fringe from Figure 2-8B. The red lines indicate equally spaced phases and the resulting time sampling points. (B) The resulting resampled fringe is a sinusoid without phase shifts. (C) The point spread function of the resampled fringe.

The phase curve can now be interpolated to determine sampling points in time so that the phase representing the wavenumber is linearly sampled. If the system samples at these calibrated sampling points in time, the resulting fringe will be linear in wavenumber, eliminating the
degraded point spread function. Note that any changes in the system that affect the sweep timing will require the system to be recalibrated.

2.4 Sensitivity and Noise

OCT Sensitivity

One of the important metrics for an OCT system is the sensitivity of system to differentiate signal versus noise. The sensitivity metric takes into account many aspects of the system such as the light source, input power, proper alignment, detector choice, and signal acquisition. One definition of sensitivity $S$ is based on the minimum sample reflectivity $R_{s,\text{min}}$ that generates a signal power equal to the noise power. The signal power from a perfectly reflecting sample mirror is compared to the minimum sample reflectivity in the sensitivity definition. Since the signal powers are directly proportional to the sample arm reflectivities, the sensitivity equation simplifies to

$$S = \frac{1}{R_{S,\text{min}}} \bigg|_{\text{SNR}=1}$$  \hspace{1cm} (2.4.1)

Often times, this measurement is difficult because the noise level can fluctuate and the exact sample arm reflectivity is difficult to determine. Another method of measuring sensitivity is to place a neutral density (ND) filter with a measured OD value between a perfectly reflecting sample arm $R_s = 1$. The mirror is placed within the imaging range of the system with flat gain and depth scans are acquired. The ND filter prevents saturation of the detector that would occur if all the sample arm power is back-coupled into the system. After the Fourier transform of the signal, the peak power value representing the mirror $P_s$ is compared to the average surrounding noise power $P_n$. The OD value is then added for the complete sensitivity value. The sensitivity in decibels (dB) is given by:

$$S = 10 \log \left( \frac{P_{\text{signal}}}{P_{\text{noise}}} \right) + 20 \cdot OD$$  \hspace{1cm} (2.4.2)
Where \( OD \) is the base 10 logarithm of the power attenuations of the ND filter. The factor of 20 multiplied with \( OD \) represents the round trip through the ND filter.

Sources of Noise

The theoretical determination of OCT system sensitivity requires analysis of the signal photocurrent and noise generated by the detector. For this analysis, assume the light source spectral density \( A_2(k) \) provides uniform power over all optical wavenumbers and the reflectivity from the sample and reference arm are not dependent on the wavenumber. Only the amplitude of a signal reflector signal from the AC component containing the depth information is considered. From equation (2.3.11), the peak amplitude of the signal component in \( M \) samples is

\[
\sum_{m=1}^{M} S[k_m]
\]

\[
= \frac{1}{2} \frac{\eta q}{\hbar \omega} \sqrt{R_{R} R_{S}} \sum_{m=1}^{M} S[k_m]
\]

\[
= \frac{1}{2} \frac{\eta q}{\hbar \omega} \sqrt{R_{R} R_{S}} S_{SSOCT}
\]

The dominant sources of noise in an OCT system are shot noise, excessive intensity noise, and receiver noise. Shot noise is due to the discrete nature of charge moving in the photodetector. Excessive intensity noise is caused by the self-beating in a broadband light wave. Lastly, receiver noise, usually modeled as thermal noise, is a property of the detector design[6, 7]. Since the noise sources are uncorrelated, their mean squared values are additive. The mean square photocurrent noise can be written as

\[
\langle i_{\text{noise}}^2 \rangle = \langle i_{\text{sh}}^2 \rangle + \langle i_{\text{ex}}^2 \rangle + \langle i_{\text{re}}^2 \rangle
\]

\[
= 2qB \langle i_d \rangle + \left(1 + \Pi^2 \right) \langle i_d \rangle^2 \frac{B}{\Delta \nu_{\text{eff}}} + 4k_B T \frac{B}{\rho_L}
\]

where \( B \) is equal to the electrical bandwidth of the system, \( \langle i_d \rangle \) the mean detector photocurrent, \( \Pi \) the degree of source polarization, \( \Delta \nu_{\text{eff}} \) the effective optical linewidth of the light source, \( k_B \) is the Boltzmann's constant, \( T \) the absolute temperature, and \( \rho_L \) the load resistor of the detector. In general, the current generated by the autocorrelation of the reference arm reflection dominates so the mean detector photocurrent can be written as[8]
\[ \langle i_d \rangle = \frac{1}{4} \frac{\eta q}{\hbar \nu} S_{SSOCT} R_R \]  \hspace{1cm} (2.4.5)

At high levels of \( S_{SSOCT} \), the excessive noise intensity dominates. On the other hand, at low levels of \( S_{SSOCT} \), the receiver noise dominates. OCT operates between these regimes because there is a safety limit on the intensity of light on the eye but \( S_{SSOCT} \) and \( R_R \) need to be high enough so that the signal current is visible. In this regime, the shot noise is the dominate source of noise. The sensitivity is given by the ratio of the signal current over the dominant shot noise current.

\[ S = \frac{1}{4} \frac{\eta q}{\hbar \nu} S_{SSOCT} \frac{1}{q B} \]  \hspace{1cm} (2.4.6)

In the shot noise limited regime, the sensitivity has a linear relationship between the source spectral density and an inverse relationship between the electrical bandwidth of the detector.

**Speckle Noise**

Speckle noise is another form of noise common to imaging methods that require coherent sources such as ultrasound. Because OCT is sensitive to the phase of the light entering the detector, phase differences in the wavefront at the detector can cause constructive or destructive interference which result in speckle. These phase changes are generally caused by multiple scatterers in the forward and backward propagation of the light beam through tissue. The light from two scatterers only needs to arrive with a delay at the detector within the coherence time of the laser. One way this could occur is if two scatterers in a tissue are separated by a distance close to a quarter of a wavelength.

Statistically, this has a high chance of occurring as certain layers of organic tissue are highly scattering. Speckle noise can be modeled as the sum of statistically independent phasors with random amplitudes and phases[9]. The sum of the phasors can be considered a random-walk phenomenon with the following probability density versus intensity show in equation (2.4.6)[10].

\[ p(I) = \frac{1}{\langle I \rangle} \exp \left( -\frac{I}{\langle I \rangle} \right) \]  \hspace{1cm} (2.4.7)
One difference between speckle noise and the previous noise sources discussed is that the speckle noise pattern is spatially dependent and not temporally dependent. Assuming no changes in the light source and a stationary sample, the speckle pattern at one spot will be the same if measured in the same way at a different point of time. This has many advantages as speckle noise can be used to measure changes in a tissue over time. However, in standard intensity imaging, speckle noise is treated as noise because it can cause artifacts and false layer information.

References

Chapter 3

Handheld OCT Sample Arm Requirements

3.1 Overview

This chapter outlines many of the design parameters that must be carefully considered for
the sample arm of a handheld OCT. The first section describes the scanning optics and scan
patterns for a sample arm. The next section develops the physical equations that govern the
performance of the sample arm. Finally, the last section lists the essential alignment steps to
position the beam and acquire the correct area on the retina.

3.2 Scanning Optics

The scanning optics on an OCT system allow for imaging in more than one dimension.
The vocabulary for the types of scans follows ultrasound conventions. A single depth profile in
one dimension is called an A-scan. Translation of the beam along a tissue produces a two
dimensional cross sectional image known as a B-scan. Movement of the beam in the orthogonal
direction allows for acquisition of three dimensional data. In the volumetric data set, slices at
different depths or axial ranges produce two dimensional images called C-scans.

The main properties of the scanning mirrors are the mechanical scan angle, frequency
response, and mirror size. The mechanical scan angle determines the maximum tilt a scanning
mirror can accomplish. The total optical angle of travel is equal to twice the mechanical angle
due to the reflection off the surface of the mirror. The frequency response of the mirror is
generally dependent on the resonance frequency of the device. Since most mirrors operate in
static point to point scanning rather than resonance scanning, the scanning frequencies must be
lower than the resonance frequency to prevent unwanted ringing. Lastly, the mirror size on the
scanning mirror is generally the limiting diameter for the beam size into the system. The
combination of mirror size and scan angle determine the number of resolvable spots that can be
scanned.
Scan Patterns

The appropriate scan pattern must correctly address all the desired scan positions on the retina. In the simple case, a cross sectional B-scan can be performed by moving the beam in a straight line transverse to sample the surface. However, scanning different transverse positions along a square two dimensional surface area of tissue is more complex. The scanning mirrors have their own inertia and cannot change directions instantaneously. In addition, any sudden jumps in the scan pattern will be interpreted as step functions that can excite resonance frequencies in the scanning mirrors. Three different methods of steering a beam along a square surface are presented in Figure 3-1.

![Scan Patterns Diagram](image)

Figure 3-1. (A) Linear raster scan. (B) Zigzag or back and forth scanning. (C) Sinusoidal scanning.

The first two scanning methods utilize portions of the scan known as the flyback scans that allow the scanning mirrors to smoothly move to another starting point to perform another straight scan. The flyback scan patterns used in the handheld follow a spline equation that is optimized to ensure continuous position, velocity, and acceleration at all points in the scan[1].

The raster scan ensures that every B-scan sweeps in the same direction. This is the standard scan pattern for most volumetric OCT data sets. The zigzag scan alternates the direction of the scan from forwards to backwards between two scans which results in a shorter flyback time. Because data is acquired in time, the backward scans must be reversed to match the forward scans. The downside of zigzag scans is that there may be a mismatch in the timing of the scans resulting in an alignment artifact that creates a "zipper" appearance in the image. Lastly,
the sinusoidal scan is similar to the zigzag scan in that it sweeps forwards and backwards but requires no flyback. Nevertheless, in a sinusoidal scan the velocity of the scan mirror is highest at the middle of the B-scan and slowest at the ends which results in uneven sampling. Although the sinusoidal scan has a slanted sweep due to the linear motion in the \( y \) direction, with a large enough number of B scans, this tilt is negligible.

**Scanning Mirror Choices**

The two types of scanning mirrors used in the OCT handheld instruments are a pair of galvanometer mirrors and a MEMS 2-D scanning mirror. Galvanometers are most commonly used scanning mirrors in OCT systems due to their high resonance frequencies in the tens of kHz and closed loop control systems that detect the position of the galvanometer\[2\]. This means that they have can scan linear raster scans with a very fast flyback with high point to point precision and accuracy. The pair of galvanometers used in one of the handheld iterations is shown in Figure 3-2.

![Figure 3-2. Pair of Cambridge Technologies 6215H galvanometers in an aluminum mount.](image)

While a single galvanometer scanning mirror is very effective at scanning in one axis, area scanning requires a pair of galvanometers with their mirrors displaced by a finite distance so that the mirrors do not physically contact. This finite separation results in one or both scanners not placed at the posterior focus of the telescope shown in Figure 3-3. This displacement shifts
the pupil plane away from the pupil position which can cause magnification and curvature errors in that scanning direction.

**Figure 3-3.** The offset in the pupil plane caused by the finite displacement between two scanning galvanometers shifting the posterior focus.

To analyze how much pupil plane displacement this creates, let $\Delta d_{post}$ be the displacement of one of the scanning mirrors relative to the focal position in the direction of light propagation. $\Delta d_{pupil}$ is the displacement of the pupil plane. The equivalent displacement can be calculated using geometric optics by:

$$\Delta d_{post} = \left( \frac{f_C}{f_F} \right)^2 \Delta d_{pupil} \quad (3.2.1)$$

In the standard pair of galvanometers, the displacement between the mirrors is roughly 1 cm. In the ideal case, the galvanometer was aligned so that the posterior focus is between the mirrors so that $\Delta d_{post} = 0.5 \text{ cm}$. With $f_C / f_F = 0.5$, $\Delta d_{pupil} = 1.25 \text{ mm}$. As seen in Figure 3-2, the displacement along the pupil can cause larger scan angles of one axis to be clipped by the iris, causing vignetting artifacts along one axis.

In contrast to the large galvanometer mirrors, the MEMS scanning mirrors from Mirrorcle Technologies, Inc. are much smaller and more compact as shown in Figure 3-4. However, MEMS mirrors have lower resonance frequencies for the same mirror size than galvanometers and operate in an open loop without any knowledge of their current position. Unlike some MEMS mirrors that only operate at resonance, these MEMS mirrors used can scan
point to point based on the input voltage\cite{3}. Since the entire mirror is tilted in two dimensions, the MEMS scanning mirrors do not have the displacement issues found in galvanometers. The resonance frequency of the MEMS is scales inversely with the area of the scanning mirror which limit the types of scan patterns it can perform.

![Figure 3-4](image)

**Figure 3-4.** Size of the DIP-24 packaged MEMS scanning mirrors next to a reference ruler. From the left, the mirror diameters are 1.2 mm and 1.7 mm.

The frequency response $H(s)$ of the MEMS devices used can be modeled with a damping equation given by

$$H(s) = \frac{\omega_0^2}{s^2 + \frac{\omega_0}{Q} s + \omega_0^2}$$

Where $\omega_0$ is the frequency response in radians and $Q$ is the quality factor of the device. By applying this frequency response to scan patterns, it is possible to simulate the output scan trajectories of the MEMS device. Because of the speed of the scan and flyback, only the B-scan direction is considered. Figure 3-5 shows examples of different scan patterns and the ringing that result from the low resonance frequency.
From these simulations, the ideal scan pattern for the MEMS device would be sinusoidal scans because they do not excite frequencies higher than the scan frequency. The disadvantage was the low sampling density near the middle of the scans and the need to align the forward and backwards scans. To get the same sampling density as a raster scan, the sinusoidal scan must have three times the number of A-scans per B-scan.

### 3.3 Sample Arm Optical Design

![Image of imaging parameters for the standard telescope arrangement of optics](image_url)

**Figure 3-6.** Imaging parameters for the standard telescope arrangement of optics for a sample arm imaging the retina. The distances between the elements are listed above.
The sample arm contains a telescope arrangement of lenses that steer the beam into the eye. The choice of lenses will determine the performance of the system in imaging the eye. The general sample arm design can be seen in Figure 3-5.

**Telescope Magnification**

The telescope configuration of two sets of lenses allows a collimated beam to enter the eye. The scan of the beam provides a pivot point on the iris. The scan angle of the scanning mirror can be amplified to allow for a larger field of view of the retina at the cost of the beam size at the cornea. The choice of lenses in the telescope determines the overall magnification of the scan angle. The magnification $M$ in this telescope system is given by

$$M = \frac{f_C}{f_F} \quad (3.3.1)$$

The effective scan angle is limited either by the maximum optical scan angle of the scanning mirrors or by the diameter of the focusing lens.

$$\theta_{\text{eff}} = \min \left( \theta_{\text{scan}}, \arctan \left( \frac{\eta_{\text{lens}} - w_i}{f_F} \right) \right) \quad (3.3.2)$$

The angle on the cornea can be found by dividing the magnification by the effective scan angle.

$$\theta_{\text{eye}} = \frac{\theta_{\text{eff}}}{M} \quad (3.3.3)$$

Likewise, the beam size at the cornea is directly proportional to the magnification.

$$2w_{\text{eye}} = M \cdot 2w_i \quad (3.3.4)$$

**Transverse Resolution**

Unlike optical microscopy, the transverse resolution is uncoupled from the axial resolution in OCT. Assuming a Gaussian beam, the transverse resolution or spot size $2w_R$ on the retina is dependent on the diameter of the beam entering the eye.

$$2w_R = \frac{2\lambda_0 f_{\text{eye}}}{\pi n_{\text{eye}} M w_i} \quad (3.3.5)$$
Where $\lambda_0$ is the wavelength of light in vacuum, $n_{\text{eye}} = 1.336$ is the refractive index of the eye, and $f_{\text{eye}} = 16.6$ mm is the effective focal length of the cornea and crystalline lens of the eye. The spot size can be made smaller by decreasing the magnification in the telescope elements. However, the beam diameter is limited by the scanning mirror diameter and by the angle magnification required.

**Depth of Field**

The depth of field or confocal parameter in the OCT system determines a range of depths where the system is in focus. The depth of field can be calculated Assuming the laser outputs a Gaussian beam, the depth of field is equal to twice the confocal parameter $2b_R$

$$2b_R = \frac{2\pi n_{\text{eye}} w_R^2}{\lambda_0}$$

(3.3.6)

The depth of focus is generally longer than the thickness of the retina which allows for easier axial alignment and for retinal pathologies to be in the focal range of the OCT system.

**Field of View**

The maximum field of view of an OCT system allows for more visual information to be taken of the retina. With a large enough field of view, both the macula and the optic nerve head can be imaged at once instead of separately, reducing patient visit time and improving workflow for clinicians. Since the pivot point of the OCT beam is at the middle lens of the eye, the refractive power of the lens does not affect the beam angle but the cornea bends the beam angle because it is not a flat surface. For first order calculations, the equation for the field of view angle on the retina can be approximated by

$$\theta_R \approx \frac{\theta_{\text{eye}}}{n_{\text{eye}}}$$

(3.3.7)

A more thorough calculation for the angle on the retina can be done with an optical simulation of the OCT beam into a model eye. The field of view in length can be calculated by determining the total arc of the scan on the retina and assuming the pivot position is at the pupil.
\[ FOV_{\text{length}} = \frac{2\theta_R}{360^\circ} \cdot 2\pi \cdot l_{\text{post}} \]  \hfill (3.3.8)

Where \( l_{\text{post}} \approx 20 \text{ mm} \) is the posterior eye distance equal to the distance between the pupil of the eye and the retina.

**Number of Resolvable Spots**

Due to the inversely proportional relationship between spot size and field of view based on the magnification of the system, an invariant parameter describing the imaging performance is useful to compare system designs. The number of resolvable spot sizes determines the number of unique scan points along the entire field of view. The number of resolvable spot sizes \( NRS \) can be determined by dividing the length of the field of view by the spot size.

\[ NRS = \frac{FOV_{\text{length}}}{2\omega_R} \]  \hfill (3.3.9)

We can see that increasing the field of view will proportionally generate larger spot sizes. This means that without modifications to the initial beam diameter, a larger field of view will not be able to detect small areas on the retina.

**3.4 OCT Device Alignment**

The ease of alignment for a handheld device is critical in a clinical setting to reduce both patient and operator fatigue as well as improve the throughput of the clinic. Alignment of an OCT instrument to scan the eye occurs in several steps corresponding to different axes of movement shown in Figure 3-7. In each of the steps, operator feedback is critical to obtain the best possible image for screening.
Figure 3-7. OCT device alignment steps. (1) Pupil alignment in the X and Y directions. (2) Axial alignment in the Z direction. (3) Adjustment of zero delay. (4) Focus adjustment to correct for refractive error. (5) Scan alignment on the retina by pivoting the beam about the pupil.

Pupil Alignment

The first step in alignment is to orient the device so that the OCT beam aligns directly into the pupil of the eye. The X and Y directions are the key axes of movement for this step to position the beam correctly. In the majority of OCT scan sessions, the pupil is undilated which results in a ~4 mm pupil diameter. Thus, stability for the patient and operator is essential to ensure that the device does not move enough to displace the beam from the pupil during the scan session. Moving the beam into the iris will vignette a portion of the image.

Axial Adjustment

Once the beam is within the pupil, the next adjustment is along the Z or optical axis to ensure that the position of the retina is properly aligned within the imaging range of the device. This is done by pulling or pushing the device towards or away from the eye of the patient. As discussed from the previous theory section, the retina must lie on the correct side of the zero delay. If the retina is before the zero delay, the symmetry of the Fourier transform inverts the image. A proper retina image gives the operator feedback for the subsequent adjustments to optimize the image.
**Zero Delay Adjustment**

If the subject's eye is longer or shorter than the set zero delay distance, the image of the retina will vignette along the higher angle portions of the OCT scan after axial alignment. This is due to the pivot point of the OCT beam is not at the center of the pupil. The iris will then clip the higher angle scans which will result in the darkening of the edges. The zero delay adjustment is typically located on the reference arm because the sample arm length is fixed. By adjusting the zero delay, distance between the pivot point and retina can be lengthened or shortened so that all of the beams can enter the posterior eye and that the retina is correctly positioned in the imaging range.

**Focusing**

The refractive error on the eye of the subject will have detrimental effects on the spot size of the beam on the retina which will result in blurring and signal loss. This is especially true in elderly patients who are generally highly myopic. This error can be corrected for in the OCT beam by translating the sample arm optics to narrow or spread the beam before it enters the eye. This adjustment must be convenient so that the operator can change the focus while the device is aligned.

**Scan Alignment on the Retina**

The last step in alignment is to position the beam to area of interest on the retina. This involves angling the beam relative to the pivot position at the pupil. The two main landmarks on the eye are the foveal dip located at the macula of the eye and the optic nerve head located about 10 degrees away from the macula towards the middle of the head. Most commercial devices scan each area separately with specific patterns. Scanning with a wider angle can cover both landmarks in a single scan. The scan also does not need to be fully centered to capture the data required. Operator feedback is most necessary in this step to make sure that the image acquired is of interest.
References


Chapter 4

OCT System Design

4.1 Overview

This chapter describes the various modules of the OCT system used to acquire retinal data. Figure 4-1 shows the standard layout for a balanced detection swept source system. The various modules are indicated. The various iterations of the sample arm are documented in the next chapter.

Figure 4-1. Swept Source OCT system layout for balanced detection. Individual modules are indicated. PC = polarization controller, DC = dispersion compensation, A/D = analog to digital.

4.2 Light Sources

The swept source light sources will be discussed in this section. Each light source has advantages and disadvantages that impact the performance of the handheld OCT system if it is
deployed in a clinical setting. Although the sweep speed is a key factor in deciding which light source to use for handheld operation, many other factors such as convenient operation, coherence length, and light bandwidth must also be considered.

One light source used in the OCT handheld the commercial Axsun light source that sweeps at a rate of 100 kHz with 50-60% duty cycle single sweep at 1060 nm wavelength. The turnkey operation of the laser source allows great accessibility in its use in the laboratory. Within the source, a translating MEMs device translates laser light though a Fabry-Perot etalon to sweep through multiple wavelengths[1]. Figure 4-2 shows the spectrum of the Axsun light source. The laser also outputs an electronic sweep trigger that generates a high signal at the beginning of each sweep to aid in sweep calibration. Our lab has used the Axsun swept source laser in many applications of SS-OCT [2-5].

![Axsun Spectrum](image)

**Figure 4-2.** 110 nm bandwidth Axsun wavelength spectrum.

The other swept source system used is the prototype vertical cavity surface emitting laser (VCSEL) light source at 1050 nm which has shown to have imaging speeds of up to 1 million A-scans per second[6]. The VCSEL light source operates using a vertically suspended mirror that is actuated with high voltages[7]. Control over the actuation frequency and intensity controls the sweep speed and bandwidth respectively. The light pumped into the device excites the gain material and only the wavelength of light that can resonate in the laser cavity exits the device. The device can be controlled to operate with a single sweep or dual sweep where there is a forwards and backwards sweep in wavenumbers which allow two A-scans for every actuation of
the MEMS device. Although the VCSEL can sweep faster than the Axsun base rate, the system is not turnkey because it is a research prototype. During operation, the VCSEL requires adjustments to the voltages to the MEMS and booster stages while monitoring the sweep. Figure 4-3 shows the spectrum of the VCSEL system sweeping at 290 kHz.

![VCSEL Spectrum](image)

**Figure 4-3.** 75 nm bandwidth VCSEL wavelength spectrum.

### 4.3 Interferometer Design

The fiber based interferometer used in the OCT system consists of two sets of 2x2 couplers. The first coupler after the light source must be chosen carefully to limit power on the eye to 1.9 mW at 1050 nm wavelength due to ANSI standards[8] and maximize the signal return from the eye. In the previous chapter on OCT theory, the beam splitter was assumed to evenly split power between the reference arm and sample arm which equates to a 50/50 coupler. However, in this arrangement, only 50% of the signal power returning from the sample arm is collected at the detector while the remaining signal is lost in the other arm to the light source. A higher coupling ratio such as 80/20 requires more light source power to match the sample arm power in the 50/50 coupler but 80% of the signal power is recovered, increasing the sensitivity of the device. The second coupler before the detector is required for interference of the reference and sample arm signals. The coupler then splits the interference fringe signal to the balance detector. The response of this coupler must be flat over the operating wavelengths to prevent DC saturation of the balanced detector.
4.4 Reference Arm Design

The reference arm consists of the single path reflector, dispersion compensation glass, an optic fiber patch cord, and a polarization controller. The single path reference arm design is necessary so that the light from the reference arm and sample arm interfere at the second coupler and split the light evenly for balanced detection. The main components of the single path reflector are a pair of collimators projecting and collecting light from a retro-reflector. The retro-reflector is mounted on a one dimensional translation stage and the collimators are aligned so that movement of the retro reflector does not greatly affect the collection of the reference power. The translation of the reflector allows for adjustment of the zero delay relative to the sample arm.

Due to the mismatch in optics in the reference and sample arms, pieces of glass with dispersion equal to twice that of the sample arm optics are placed in the reference arm beam path to compensate for the round trip of light through the sample arm. A patch cord with length equal to the twice the distance between the first coupler and the sample arm is also placed in the reference arm to match for the round trip propagation of light in the fibers of the two arms. Lastly, to achieve maximum interference, polarization control paddles match the polarization in the reference arm to the polarization in the sample arm.

4.6 Image Acquisition and Processing

Balanced Detection

The use of balanced detection negates the autocorrelation from the reference arm. The 50/50 coupler before the detector transmits half of the interference power and reflects the other half with a \( \pi \) phase delay. At the balanced detector, the signals are subtracted which cancels the DC terms while the AC terms combine due to the phase delay. Without the DC signal, the sinusoidal signals from the tissue layers have higher dynamic range so more reference power can be put into the interferometer. However, the non-flat response of the 50/50 coupler over all frequencies leads to a residual DC component which limits the amount of reference power that can be supplied to the detector. The choice of a detector with an appropriate gain and bandwidth is critical for imaging applications.
Analog to Digital Acquisition Cards

Swept source OCT requires rapidly sampling A/D acquisition cards to generate enough samples per sweep especially when the light source is sweeping at high speeds. The bit rates for the devices also have to be high enough to accurately reproduce the signal waveform without data loss through digitalization. The acquisition cards used in the handheld swept source OCT system are all PCI-Express socket cards with an external trigger and the ability to sample non-uniformly to allow for proper calibration to sample in k-space. Table 3-1 lists the cards and the various parameters of operation.

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Model</th>
<th>Sampling Rate (MSPS)</th>
<th>Number of Bits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innovative Integrations</td>
<td>X5-400M</td>
<td>400</td>
<td>14</td>
</tr>
<tr>
<td>AlazarTech</td>
<td>ATS9350</td>
<td>500</td>
<td>12</td>
</tr>
<tr>
<td>AlazarTech</td>
<td>ATS9870</td>
<td>1000</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 4-1. Listing of the various acquisition cards used in the studies along with their specifications. MSPS = mega-samples per second

Trigger Synchronization Circuit

Communication among all the acquisition devices is critical for swept source OCT. All the devices must know the beginning of each sweep to accurately direct the positioning of the beam in the scanning mirrors and the timing of the acquisitions. Any fluctuations in the timing could result in mismatched or lost data. In addition, the data acquisition must occur only for useful data points. If the data was acquired for all sweeps while the system is on, a large amount of useless data would be generated.

To account for this mismatch, a digital circuit was constructed to ensure that both the digital to analog (D/A) card controlling the scanning mirrors and the data acquisition card were synchronized with the sweep trigger. The circuit uses a D flip-flop logic unit with logic gates to ensure that only a complete sweep trigger is ever sent to the acquisition card. Figure 4-4 shows the logic gate layout of the circuit. Figure 4-5 demonstrates the de-glitching capabilities.
Figure 4-4. Logic gate layout of the digital deglitching circuit consisting of an inverter, D-flip flop, and an AND gate. The two inputs are the Trig signal indicating the beginning of a sweep, and Scan signal indicating that the scanners are moving and data should be acquired. The Output signal triggers the acquisition for each sweep.

Figure 4-5. Timing diagram of the deglitching circuit assuming negligible delays. (1) The Scan signal is high which indicates that the system is sweeping and that the acquisition card should sample data values. (2) On the rising edge of the next inverted Trig signal, the flip-flop will store the high value and Q will be high. The Output signal is now a direct copy of the Trig signal due to the AND gate. (3) When the scanners stop moving, the Scan signal switches to low. (4) Only on the
next rising edge of the inverted Trig signal does the flip flop Q go low. This ensures the Trigger waveform is preserved in the Output signal and never clipped.

Software

Custom software was written in C++ and used Windows Forms graphical API for the front end GUI. Each data acquisition card interfaced with the software through its own dynamic-link library (DLL) file that has common function calls for setting and performing data acquisitions.

The software has four different modes of operation. The first mode allows for the custom definitions of scan patterns listed in a scan library. The second mode is the scan preview which displays OCT preview scans for alignment aid and can trigger the acquisition of images. In the third mode, the acquired images can be processed for dispersion correction and contrast adjustment. The last mode allows for visualization of the processed modes as slices in the XY, XZ, and YZ directions.

Orthogonal Registration

Motion artifacts have been a major problem in many of the applications of OCT. In table mounted OCT systems for ophthalmology, the subject's head is fixated using a chinrest. However, the human eye can still move rapidly in the form of saccades. These saccades can cause abrupt changes known as motion artifacts especially in volumetric data sets. From the previous section on scan patterns, movement of the beam along a square surface requires multiple repeated B-scans. The time between each point in a B-scan is equal to the period of the laser sweep while two points in two adjacent B-scans differ by the time it takes to perform the B-scan. Therefore, we can define the scan in the B-scan direction as the fast scanning direction while the direction of the B-scan steps as the slow scanning direction. Motion artifacts appear much more prominently in the slow direction as a displacement or cleaving of adjacent B-scans shown in Figure 4-6. Motion is a larger problem in handheld OCT systems because the acquired OCT data has both subject motion and operator motion.
Figure 4-6. Illustration of motion artifacts in retina OCT scanning. (A) Transverse motion can be seen as a discontinuity on the vessels of the eye in the slow scanning direction. (B) A cross section along the slow scanning axis shows axial motion at multiple points. (C) A fast B scan of the same cross section does not show axial motion.

One method of correcting this motion is image registration by transforming portions of the image to correct for motion. However, this requires a priori knowledge of the appearance of a motion free data set in both translational and axial directions.

The handheld OCT system mentioned in this thesis uses a custom registration software that corrects for motion by using information from two or more orthogonal scans[9]. Each set of orthogonal scans contains one standard scan called the X-fast scan where the transverse scans are in the X direction and a Y-fast scan where the transverse scan is along the Y axis. Since there is little motion in the fast scanning direction, the X-fast scans generally have motion free data in the X direction while the Y-fast scans have motion free data in the Y direction as illustrated in Figure 4-6B, C. The displacement fields of each scan are calculated and processed based on the time dependence of each scan and the direction of the scans. Using this information, it is possible to transform the images to correct for motion. The motion corrected volumes can now be overlaid and averaged for better signal quality. This technique also works to register and average multiple orthogonal volume sets to further increase signal quality.
References


2. B. Potsaid, B. Baumann, D. Huang, S. Barry, A. E. Cable, J. S. Schuman, J. S. Duker, and J. G. Fujimoto, "Ultrahigh speed 1050nm swept source / Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second," Optics Express 18, 20029-20048 (2010).


Chapter 5
Handheld OCT Sample Arm Designs

5.1 Overview

This chapter describes the evolution of the handheld OCT device through multiple iterations from the large galvanometer instrument to the current compact MEMS camcorder-style handheld. The optical and physical designs are outlined and described. The imaging results are also presented. Lastly, each handheld iteration section has a discussion subsection that analyzes the advantages and drawbacks of the system for screening purposes.

5.2 Galvanometer Based Handheld

The first iteration of the handheld device was a modified version of our standard prototype table mounted sample arms[1]. The main objective was to test if orthogonal registration was possible with the additional operator motion generated by using a handheld device. OCT data was taken with both the Axsun and VCSEL swept source lasers. Although registerable data was taken, the ergonomics and ease of alignment suffered because the device used standard aluminum and steel optical mounts and a large set of galvanometers. These issues provided valuable information for future iterations of OCT handheld devices.

OCT Optical Setup

The optical path for the OCT beam at 1 μm wavelength is given in Figure 5-1. The collimating lens focused the light from the HI 1060 optical fiber and produced a collimated beam of 3.4 mm in diameter. A pair of 5 mm galvanometer scanning lenses steered the beam in two dimensions. The telescope arrangement of the focusing and condensing lenses resulted in a 2.5 magnification factor. This reduced the beam size at the eye to 1.36 mm. The system was simulated with a maximum optical scanning angle of ±8° which corresponds to an angle of ±20° at the cornea and ±15.5° on the retina. The angle span on the retina was equal to a FOV span of 11 mm.
Figure 5-1. ZEMAX simulated OCT beam path for the galvanometer based handheld with the beam directed into a model eye. The condensing lens is adjustable to adjust for the refractive error of the eye.

Figure 5-2. Analysis of the spot size on the retina for various galvanometer angles. The black outline circle represents the diffraction limited airy disk size.

A model human eye was used to determine the simulated imaging parameters on the retina. The simulated spot size at various angles is given in Figure 5-2. The figure shows that for most angles, the beam was within the diffraction limited spot size diameter of 31.42 μm. Due to
the inverse relationship between depth of field and the spot size, this system had a large depth of field of 1.47 mm which allowed the region of focus to span most of the retina. The number of resolvable spot sizes for this system was 704.

Device Design

Figure 5-3 shows the design schematic of the handheld device created using Microsoft Visio. The 1 inch optics were placed in lens tubes and screwed onto a cage mount system to ensure that lenses can be placed in series with each other. The cage mounts were attached to steel rods mounted on a custom machined plate located on the aluminum galvanometer block. The rods located below the mount serve as a grip to hold the device. Figure 5-4 shows the instrument in operation when scanning a subject.

Figure 5-3. Microsoft Visio layout of the galvanometer showing the cage mount system attached to a custom aluminum adaptor placed on the galvanometer mount. The condensing lens mount has an axial translation micrometer to adjust the focus for the system.
Figure 5-4. Handheld device in operation. (A) Device viewed from the side. (B) Top view of the device. A rubber eye cup was added to the end of the condensing lens to set the working distance of the instrument.

Results

Two orthogonal 300 x 300 linear raster scans over an area of 5 x 5 mm on the optic nerve head were performed using the handheld device. For the Axsun sweeping at 100 kHz, each scan was completed in about 1 second including the flyback time. The scans with the 110 nm bandwidth Axsun light source used the Thorlabs PDB130C 200 MHz detector with the Innovative Integration X5-400M data acquisition card. With this light source, the axial resolution was 6 μm. With the 70 nm bandwidth VCSEL sweeping at 290 kHz, the resolution was 7 μm. The same scan was completed in 0.4 seconds while using a prototype Thorlabs PDB480C-SP1 1 GHz detector with the AlazarTech ATS9870 A/D card.

During the scan the operator held the handheld device up to the seated normal subject and aligned the instrument with the pupil of the eye. Once the macula could be seen, the operator tilted the instrument until the optic nerve head could be seen in the alignment preview OCT scans. The operator told the subject to blink a few times and then the scan was performed. The subject was fixated upon one spot in the background during the entire session.

After the images were acquired, the images were numerically dispersion compensated for the sharpest quality image and the orthogonal scans were registered to compensate for motion and to increase the signal quality through averaging. The resulting motion-free registered 3D
volume could be sliced in any direction using interpolation to generate any arbitrary cross section so that a single data set could be used for multiple measurements.

The registered images of the optic nerve head using the two different swept source lasers are shown in Figures 5-5 and 5-6[2].

**Figure 5-5.** Axsun results (A) Summed OCT fundus of the data set. (B) 300 pixel arbitrary tilted cross section produced through interpolation of the data cube as indicated on the fundus image for use in measuring radial disk size. (C) – (E) Single horizontal cross sections indicated in the fundus image. Scale bars are 0.5 mm.

**Figure 5-6.** VCSEL results (A) Summed OCT fundus of the data set. (B) 300 A-scan 3.4 mm diameter circular cross section centered at the nerve head generated by interpolation. (C) – (E) Single horizontal cross sections indicated in the fundus image. Scale bars are 0.5 mm.
Discussion

The images obtained with the handheld device are very similar in quality to the images taken by our prototype table mounted system. The additional motion from the operator can be corrected using our custom registration technique with two orthogonal scans. The images from the VCSEL system clearly have a lower signal to noise ratio when compared to the Axsun images. This can be explained by analyzing the different detectors and acquisition cards used due to the higher sweep speed of the VCSEL laser source. In the faster sweeping VCSEL, the detector used has a higher bandwidth and thus, lower gain. In addition, the AlazarTech ATS9870 acquisition card runs at 1 GSPS but only records 8 bit data values. The Innovative Integrations card bit rate of 14 bits at a slower speed of 400 MSPS which results in more precise values, reducing the overall noise.

Although high quality images were obtained, usage of the system revealed many alignment and ergonomic issues unique to handheld operation. The use of aluminum mounts with steel rods connecting the cage components resulted in a heavy handheld device. In addition, the galvanometer mount is a machined block of aluminum which holds the scanners stable but adds considerable weight. In addition to the weight of the device, the distribution of weight is not centered on the hand grip of the device due to the optical components extending forward from the galvanometer. This weight distribution puts strain on the wrist as the operator must counteract the torque caused by the displaced center of gravity. Because of these issues, the operator using the device will quickly feel fatigued while aligning and holding the device for acquisition.

The system also had issues with several alignment requirements for a handheld device illustrated in Chapter 3. One of the limiting aspects of the handheld was that the system only had the OCT preview as a feedback for the operator. For the pupil alignment, the OCT preview only provided feedback when the beam enters the pupil and the zero delay was close to the retina. This made the initial step of aiming the beam into the pupil very difficult and time consuming because it was not possible to see the direction of the OCT beam. Another factor was the focus adjustment method. The focus was controlled by a micrometer adjusting the position of the condensing lens on the bottom of the device. Due to the fact that the micrometer's rotation axis was the same as the optical axis, the focus could not be easily adjusted while the device was
pointed at the eye. Coupled with the weight of the device and the lack of pupil alignment, it was difficult to receive real time feedback while adjusting the focus while at the same time aiming the beam into the eye. Another factor hindering alignment was that the subject did not have a set position to fixate their eye. This requires that the device must be tilted to image specific areas of the retina, which could risk moving the beam away from the pupil. If the subject's gaze wanders, the imaged region could also be in the wrong position. All of these alignment issues provided great insight on improvements needed for handheld OCT imaging in future iterations.

5.3 Direct View 3-D Printed MEMS Handheld

The next iteration of the handheld device used a MEMS scanning mirror and a 3-D printed plastic enclosure to greatly reduce the weight of the device. The OCT optical path was modified to accommodate the smaller size of the printed device. In addition, this device tested a direct view visible optic path to image the iris for pupil alignment.

OCT Optical Setup

The OCT layout was optimized for the smaller 2.4 mm MEMS scanning mirror as well as the constraints of a smaller printed system. Figure 5-7 shows the optical simulation for the MEMS handheld device. The collimator produced a much smaller beam diameter of 2.4 mm limited by the diameter of the scanning mirror. This beam was incident on the MEMS scanner where it generates an optical scan of ±9° degrees. The focusing lens was chosen to be a 0.5 inch diameter lens so that it can be housed inside of a helical translation mount for focus adjustment. The condensing lens was 1 inch in diameter to allow the beam to focus down into the pupil. These two combined lenses generated a magnification factor of 2. After the condensing lens, the beam has an angle of ±18° on the cornea of the eye and an angle of ±13.5° on the retina. The span of the field of view on the retina is 9.7 mm. This design used shorter focal lengths in both the focusing and condensing lenses to shorten the optical path in order to generate a compact instrument.
Figure 5-7. ZEMAX simulation of OCT optical path of the direct view OCT handheld using MEMS scanning mirrors.

Figure 5-8. Simulated spot sizes at various angles showing diffraction limited performance. The black outline circle indicates the diffraction limited airy disk.

The beam after the telescope stage had a diameter of 1.2 mm on the cornea. This produced the spot diagram on a model eye shown in Figure 5-8. All the simulated scan angles in
the system generated a diffraction limited spot. The diffraction limited airy disk diameter was 31.67 μm. With this spot size, the number of resolvable spots on the retina was 597 and the depth of field of the device was 1.53 mm.

Direct View Optical Setup

Combined with the OCT optical path was a direct view visible optic path shown in Figure 5-9. A dichroic mirror between the focusing and condensing lenses split the visible and near infrared OCT light reflected from the eye. The visible light path included the condensing lenses from the OCT optical path in the setup. Once the light from the iris passed through the dichroic mirror, a lens focused the light onto a beam splitter that reflects the light upwards to shorten the optical path in the horizontal direction. The beam splitter was placed so that future iterations could include a fixation target in the visible path of the device. The light then enters another lens, a roof prism, and then the eye piece lens into the operator's eye. The operator's visual field of view was 30°. This visual field of view covered a span of 11 mm on the iris which is enough to visualize the edge of the cornea and the pupil position.

![Figure 5-9](image)

**Figure 5-9.** ZEMAX simulation of the direct view optical path of light from the subject’s iris to the operator’s eye next to the eyepiece.

Device Design

The 3-D printed enclosure for the OCT device was designed in SolidWorks. Figure 5-10 shows the rendering of the device from different views. A clamshell design was chosen so that the design for the top cover could just be a mirror version of the bottom cover. The clamshell design also allows for easy insertion and removal of optical parts. The angle of the handle was
chosen to point towards the subject because the device was designed to be placed up to the operator’s eye shown in Figure 5-11[3]. In contrast to the front heavy design in the galvanometer system, this handheld was designed so that the optical components in the direct view path way balance out the weight of the components in the OCT telescope. This enables the center of gravity to be located near the grip of the device.

Figure 5-10. SolidWorks exterior model for the 3-D printed direct view MEMS handheld. (A) Isometric view. (B) Back view showing the operator eyepiece. (C) Front view (D) Side View (E) Cross section showing the optical mounts.

Figure 5-11. Operator usage of the direct view MEMS handheld. The forward pointing handle is designed to match the angle of the hand grip when the arm is held close to the operator’s body.
For the interior of the device, the optical elements were housed in aluminum lens tubes and modified cage mounts for easy insertion of devices. The OCT pathway was greatly folded to reduce the volume and to have a large angle of incidence onto the MEMS device. With the focusing lens inside, the helical translation focus adjustment takes up most of the space between the MEMS device and the dichroic mirror. Two LEDs were inserted in the front of the device to provide illumination on the iris for the direct view. The direct view optical path is placed behind the OCT pathway on a detachable enclosure so that it could be swapped in future iterations.

Results

The first registerable MEMS scanning OCT images were taken using this system with the Axsun light source with 110 nm bandwidth giving 6 μm axial resolution. Two orthogonal 768 x 256 4 mm x 4 mm A-scan sinusoidal images were taken of the macula, resampled to a 256 x 256 image, and then registered. Each scan took about 2 seconds. A 200 MHz Thorlabs PDB360C detector was used to convert the interference signal to a voltage. The AlazarTech ATS9350 was used to have a sampling rate of 500 MSPS. An example of the data acquired is shown in Figure 5-12. The stretching of the image due to the low velocity at the ends of the sinusoidal scans can be seen in Figure 5-12A on the left and right of the X-fast en-face and the top and bottom of the Y-fast en-face.
**Figure 5-12.** (A) En-face fundus projection of the two 768 x 256 4 x 4 mm sinusoidal scans with indicated B-scan directions. (B) En-face fundus 256 x 256 image after linear resampling and registration of the two data sets. (C) Slices of the volumetric data set indicated by the line color.

**Discussion**

The images acquired by this device clearly show that the MEMS scanning mirror has comparable scanning ability to the galvanometer scanning mirrors while scanning sinusoidally instead of scanning in a raster pattern. The OCT scanning specifications are also similar to the original galvanometer despite the smaller scan mirrors. The reduced weight of the device through the use of printed plastic aided in making the instrument easier to hold when compared to the previous device. However, there were issues with acquiring large field scans because of the difficulty of using the direct view optics.

The direct view while aligning to the iris was less useful than intended. Because of the short focal distance from the front of the instrument to the pupil, the direct view did not have a large depth of field. This resulted in the view of the pupil blurring too quickly when the device was not in the correct axial position. While blurred, it was difficult to distinguish the middle of the pupil to align the OCT beam into it. Furthermore, the combined motion of the operator’s head looking into the eyepiece, the held device, and the subject’s eye made it difficult to pinpoint the OCT beam to the pupil. Another difficulty in alignment was that the focusing wheel was not located in a position that can be easily adjusted while aligned to the pupil. The focusing wheel required two hands to operate and the rotation of the wheel displaced the pupil alignment of the device. In addition, there was a lack of a trigger button on the device for the operator to take an acquisition when aligned. Also, like the previous design, it lacked a fixation target so the patient must fixate at an arbitrary point in the background and the device must be pivoted to scan different points on the retina. Although this device had many hardware advances, the ergonomics for operating the device were not ideal.
5.4 Indirect View MEMS Handheld

Because of the limitations of the direct view device, an indirect view utilizing a camera to image the iris was designed. The indirect view MEMS handheld included an LCD screen on the back of the device for to display the view of the iris and the OCT preview scans. In addition, a fixation target was included in the visible optical paths to aid in scan positioning. Although the OCT optical design remains the same as the previous MEMS handheld, there were several changes in the physical design to account for the different method of alignment.

OCT Optical Setup

The OCT optical setup was slightly modified from the direct view handheld device. Shown in Figure 5-13, the optical fiber and collimating lens were swapped to the other side and pointed at a steeper angle to the scanning mirror. This is possible because the focus adjustment was moved to the condensing lens. Some distances between the focusing lens, the dichroic mirror, and the condensing lens were also changed but the OCT sample arm specification remain the same as the ones listed for the direct view device.

![Figure 5-13. Modified OCT beam path for the indirect view MEMS handheld simulated in ZEMAX.](image-url)
Iris Camera Optical Setup

The iris camera optical setup uses the same lenses and beam splitter from the previous MEMS device as shown in Figure 5-14. Instead of focusing upwards to an eyepiece, it focuses into the lens of a Microsoft Studio webcam. The webcam has the ability to auto focus so that if the iris is not in the depth of focus, the focus automatically adjusts so that the pupil is in focus again. The camera has a $30^\circ$ field of view of a 1.2 mm diameter circle on the iris. Several of the distances between the lenses were also modified to compact the device. Because the image from the webcam could be flipped before being displayed, the orientation of the iris on the camera was not as essential.

![Diagram of iris camera optical setup](image)

**Figure 5-14.** ZEMAX simulation of the indirect view path of light from the subject’s iris to the lens of a webcam.

Fixation Target Optical Setup

The fixation target pathway was added behind the beam splitter in the indirect view pathway. The fixation target must allow a point source on the illumination target to focus onto the retina. The illumination target can be a dynamically adjusted by displaying an adjustable image on a screen or manually adjusted by mechanically moving a single point source. Due to the size constraints of the handheld device, a manual illumination device was used. Figure 5-15 shows the optical setup for the LED target and the location of the illumination on the retina when the target is translated manually. A translation of 4 mm on the LED fixation target and lens angled the light on the retina by $10^\circ$. With the eye fixated at this angle, it was possible for the middle of the OCT scan path to be between the macula and the optic nerve head.
**Figure 5-15.** ZEMAX simulation of the visible light path for the manual LED fixation target. (A) The side view of the fixation target. (B) Top of the fixation target translated 4 mm to the side to focus the light at an angle on the retina.

**Device Design**

Like the previous handheld, the plastic 3-D printed enclosure was designed in SolidWorks. Figure 5-16 shows the rendering of the handheld device. The LCD screen was enclosed on the back of the device for the operator to view during imaging. The hole in the front housed a finger triggered push button on the device that allowed acquisitions to be triggered from the device. Instead of the grip pointed towards the subject, the grip on this device was a pistol grip that points toward the operator. Figure 5-17 shows how the device was operated with an outstretched arm and that the resulting angle of the hand grip required that the handle is tilted towards the operator.

The location of the helical focus had been moved to the front of the device to translate the condensing lenses rather than the focusing lens. This focus adjustment compensated both the fixation target and the OCT beam to the refractive error of the patient's eye. A sliding switch on the top of the device allowed for manual operation of the fixation target.

Unlike the previous printed handheld, this design had the optical elements directly placed in the printed plastic so the heavy aluminum mounts were not needed. The indirect view camera was folded downwards so that the camera can be housed in the body of the device. The fixation target was located right on top of the camera with a manually adjustable slider. Two LEDs were fixed to the front of the translating condensing lenses to provide illumination for the iris camera.
Figure 5-16. SolidWorks rendering of the indirect view 3-D printed device. (A) Isometric view. (B) Back view showing the LCD mount. (C) Front view. (D) Side view. (E) Cross section of the optical mounts and wiring pathways in the device.

Figure 5-17. Usage of the indirect view handheld. The pistol grip style handle allowed for a forward pointing OCT beam when the device is held at arm's length away from the operator.
Results

Due to the addition of the iris camera and fixation target, the device was much better for alignment than the direct view handheld device. This enabled alignment of wider field scans while using the same imaging configuration as the direct view device. Figure 5-18 shows an example of a single 786 x 256 A-scan 7 x 7 mm sinusoidal scan focused on the optic nerve head using the Axsun light source.

![Image](image.png)

**Figure 5-18.** 768 x 256 A scan 7 x 7 mm sinusoidal images obtained by the indirect view handheld. (A) Enface view centered at the optic nerve head. (B) Cross section indicated through the optic nerve head.

Discussion

The addition of many of the features not found on the direct view handheld greatly aided in alignment of the device. The indirect view camera was more effective than directly looking through the device because there was no additional motion from the operator’s eye. The operator only needed to align the center of the camera to the pupil and move axially to obtain OCT signal from the retina. The low depth of field due to the short focus was compensated by the auto focus capabilities of the webcam. In addition, the fixation target improved the scan alignment of the OCT beam on the retina. The patient’s eye could be moved instead of tilting the entire device, speeding up the scan alignment step. Finally, the trigger button gave the operator control of the image acquisition when fully aligned. All these changes made the alignment of wider angle OCT images possible.

However, there were still some operational issues with this device. The first issue is that the device required two hands to operate due to the location of the fixation target and the focus
adjustment far from the hand grip. This could unnecessarily slow the screening procedure because of the unique settings for each individual eye. The other concern is the coupling of operator motion to the OCT beam. This movement can be represented as a lever from the OCT beam to the pivot on the operator wrist. Any motion in the operator’s wrist is greatly magnified at the output beam to the patient’s eye. After many imaging sessions, operator fatigue could generate more motion than patient motion. These issues must be tested before deployment in a clinical setting.

5.5 Camcorder Grip MEMS Handheld

After considering the issues of a handle grip system, the next iteration took inspiration from consumer electronics. Handheld camcorders are designed to be held stable by an operator for long periods of time. In addition, the camcorders allowed for one handed adjustment during operation. This design matched the requirements for an OCT handheld, and the printed plastic enclosure was redesigned to be similar to a camcorder. All the optical components were the same as the indirect OCT handheld. In addition, access to the VCSEL light source allowed for higher volume data sets because of the higher imaging speed.

Device Design

The camcorder design shown in Figure 5-19 preserved the optical designs for the OCT, indirect view, and fixation paths. The grip side on the right side of the camcorder was slightly curved to accommodate the curvature of the palm while holding the device. A nylon strap was inserted in the two holes located on the side to support the back of the hand. On the back of the device, the trigger button was moved so that it can be activated by the thumb. The index finger controlled the manual positioning of the fixation target located on the top of the device. The ring and little finger adjusted the focus of the device by moving the highly textured helical translation of the condensing lens. A swivel and tilt hinge was attached to the LCD display so that the display could be adjusted to the operator’s use. The display can also be folded onto the device to reduce the size of the overall device when not in operation. In this design, the plastic not used as support for optics was removed so that the hollowed enclosure was lighter than previous designs.
Figure 5-19. SolidWorks rendering of the camcorder grip 3-D printed device. (A) Isometric view. (B) Back view showing the LCD mount and trigger button. (C) Front view. (D) Side view. (E) Cross section of the optical mounts and wiring pathways in the device.

Figure 5-20. Usage of the camcorder style MEMS handheld. The forearm arm is held nearly perpendicular to the direction of the OCT beam.

Results

After assembling the device and adding the nylon strap, the finished prototype is shown in Figure 5-21. Using the VCSEL at 75 nm bandwidth and sweeping at 290 kHz in resonance, large volumetric data sets were collected of the retina with 7 μm axial resolution. Because each resonance sweep has a forward and a backwards sweep, each single acquisition produced two
sets of data. Two orthogonal 10 mm x 10 mm, 1125 x 375 sinusoidal scans were performed to generate 4 sets of data. Each scan was completed in 1.45 seconds. The interference fringe was detected using a 1.5 GHz Thorlabs PDB480C detector and sampled with the 1 GSPS AlazarTech ATS9870 acquisition card. The resulting volumetric 375 x 375 data set after resampling and registering all four sets is shown in Figure 5-22.

Figure 5-21. Picture of the assembled camcorder style OCT handheld with the screen folded out. A nylon strap is attached to the side to support the device against the back of the right hand.

Figure 5-22. (A) Registered 10 mm x 10 mm 375 x 375 en face fundus image of the fovea and optic nerve head. (B) Horizontal cross section through the optic nerve head. (C) Vertical cross section through the macula. Scale bars are 1 mm.
Discussion

The images from using the VCSEL light source showed that the MEMS handheld can acquire large fields of view of the retina. The large volumetric data set imaged both the macula and the optic nerve head. This means that a single data set could be used to detect multiple types of pathology in both areas of the retina, reducing the imaging session time per person. The motion free volumetric data set also allows for arbitrary cross sections of places of interest. A large field of view also gives some tolerance of the scan alignment to the retina because the scan does not have to be perfectly aligned to acquire images of the macula and optic nerve head.

Along with all the scan alignment improvements from the previous iteration, the one handed operation of this handheld simplified the operation of the handheld device for imaging. The reduced distance between the wrist and the OCT beam ensured that motion from the hand was not as coupled as in the grip handle handhelds. However, some issues still need to be analyzed in a clinical setting. One issue with this design is that the device is limited to right-handed operation rather than ambidextrous operation for the handle grip designs. Another issue is that the LCD is now placed on the side of the device rather than the back of the device. This may make the patient uncomfortable as it is blocks their view when imaging the patient’s left eye. However, the clearance for the screen prevents any physical contact between the device and the other eye. Lastly, changes in the nylon strap angle would improve the ergonomic use of the device when it is moved up to the patient’s eye.

Since the optical components are the same, future studies can be done to quantify the motion and analyze ease of use of this camcorder design versus the handle grip. In addition, the device will need to image patients with pathologies and compare the results with scans from commercial table top systems to test the diagnostic capabilities. The future iterations of the device will use all the best features of the previous versions so that OCT retinal screening can be performed quickly and easily.

References

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