

# Image Processing Issues with Fast, Real-Time *In Vivo* Optical Coherence Tomography Systems

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**E**arly detection and diagnosis of diseases are crucial in medicine. Healing and recovery are far easier when the diseases in question have yet to establish a strong foothold. Towards this end, medical practitioners have devised numerous techniques to diagnose diseases before they become a major concern. Such techniques can be grouped into two broad categories: *in vitro* and *in vivo*. *In vitro* techniques work by examining tissue samples for diseases within a laboratory environment. That is, tissue is removed from a live specimen and tested for suspected pathologies within a lab, usually through microscopic examination (otherwise known as a biopsy). *In vivo* techniques work by testing for diseases within the context of the living system. They attempt to correlate the physical symptoms of the patient with a list of known diseases. Most common diagnoses use only *in vivo* techniques: for example, when a doctor prescribes bed rest and lots of fluids for a case of the common cold, he usually reaches his diagnosis by checking the patient's temperature, physical comfort, and mucus output. All such checks are done *in vivo*. In extenuating circumstances, however, such as when he cannot determine whether the patient is suffering from a bad cold or the much more serious flu, he might take a sample of the patient's blood and run it through a lab. By doing so, he moves his diagnosis from an *in vivo* context to an *in vitro* one. *In vivo* techniques,

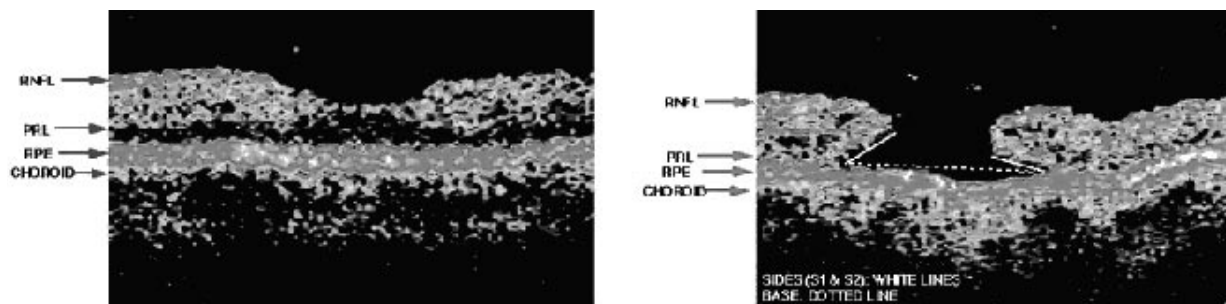


Figure 1: (Left) Image of a normal fovea. (Right) A macular hole, characterized by the absence of retinal tissue. While readily apparent when viewed using OCT, macular holes are difficult to distinguish from normal retinal tears when directly examined. (Images courtesy of the NYEEL Ocular Image Center)<sup>2</sup>

then, are commonly used within a clinical setting to diagnose diseases with *in vitro* techniques being used whenever the latter fails to reach a definitive diagnosis. This setup, though quite effective in most cases, is unfortunately imperfect. For diseases where few, if any, physical symptoms emerge until the late chronic stages, an *in vivo* examination would detect nothing until it is too late. Cancer, in all its varieties, comes to mind as one such disease. It may also be true that an *in vitro* analysis cannot be readily performed because the tissue is sensitive to sampling. Most people, for example, would object to having a piece of their eyeball sliced out for microscopic examination. In both situations, current medical diagnosis techniques remain comparatively poor with a high probability of error.

Optical Coherence Tomography (OCT) is a relatively new technology for scanning and imaging tissue anatomy.<sup>1</sup> It addresses the issues raised above by greatly enhancing the acuity and utility of visual techniques—the technology boasts a resolution of 1 to 10 micrometers and may diagnose both soft (such as skin and eye) and hard (such as teeth) tissue diseases. Beyond its incredibly high resolution, OCT is also completely benign and inherently noninvasive (unless used to image internal tissue). These qualities combined make it extremely attractive as a medical diagnostic tool. The power of OCT is demonstrated in a scanned image of a macular hole, a disease of the eye (Figure 1). Difficult to distinguish from normal retinal wear-and-tear on direct examination, the disease becomes readily apparent when viewed using OCT<sup>3</sup>. While OCT may be used in both *in vitro* and *in vivo* contexts, the focus of this paper will deal with the development of an *in vivo* OCT system, first giving a brief overview of a general OCT system.

### Workings of an OCT System

OCT operates on the same physical principles as sonar, except that broadband light rather than sound is used.<sup>4</sup> OCT systems employ broadband light because of their low coherence length (coherence is a term describing light waves that are in phase in both time and space domains). A low coherence length is desirable: The lower the length, the greater the spatial resolution an OCT system may achieve. Any OCT system consists of a light source, a beam splitter, a sample arm, a reference arm, an optical gate, and a detector. The light source in an OCT system emits near-infrared light that is split by the beam splitter into two separate light beams. One beam is sent towards the sample arm while the other is sent towards the reference arm. The sample arm beam

travels until it hits the tissue sample, where it then penetrates several micrometers deep before scattering back.<sup>5</sup> When the scattered sample beam returns, it passes through an optical gate, such as a Michelson white-light interferometer<sup>6</sup> that filters away all but the minimally scattered photons. Only minimally scattered photons are useful in constructing an image; highly scattered photons cannot effect a clean, detailed image. The reference arm beam travels until it hits and is reflected off the adjustable reference mirror. The filtered sample beam and the reference beam are recombined at the detector after they both return (Figure 2). The detector traces interference between the two light beams: The two beams interfere only when the pathlength difference between them is within the coherence length of the source.<sup>7</sup> When interference does occur, a depth-resolved reflectivity profile is generated for that part of the sample by measuring the light intensities of the backscattered photons as a function of their axial and transverse positions in the tissue. A series of adjacent scans as the sample arm travels transversely across the sample then yields a complete reflectivity profile.<sup>8</sup> This entire process is known as the acquisition phase of a scan.

A constructed image of the tissue sample is then generated from the reflectivity profile through a series of image processing steps. First, the reflectivity profile is scaled and mapped to a smaller, more manageable subset of itself. Secondly, the light intensities of the profile are mapped to values in either a false color domain or a gray-scale one. Now formatted as image data, the profile undergoes additional image processing, such as distortion removal, before being displayed on a host computer. Depending on the application, additional image processing may occur to tailor the output to the application's needs. Collectively, this set of steps is referred to as the processing phase of a scan. Unlike the acquisition phase, the processing phase is dependent on the implementation of each OCT system and may vary.

### Issues with *In Vivo* OCT Systems

An *in vivo* OCT system must deal with additional issues not addressed in the basic setup. First is the issue of image contamination. Patients, being live biological organisms, are always in motion. Even when supposedly sitting still, their eyes blink, their hearts beat, and minute vibrations course throughout their bodies. Consequently, the tissue sample in an *in vivo* OCT system is never at rest, which poses problems for any OCT system. If during a scan-

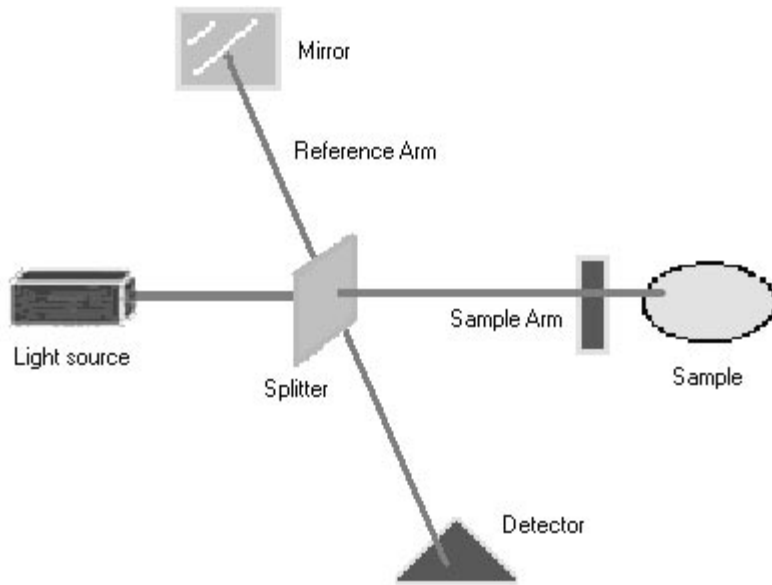


Figure 2: A typical OCT setup. The light source emits a laser beam, which is split into two by the splitter. One beam goes towards the sample arm and is backscattered by the sample. The other heads to the reference arm and is reflected back by the mirror. The two beams combine at the detector, which checks to see whether they interfere. Interference leads to a reflectivity profile found by measuring the backscattered photon intensities as a function of their position in the tissue.<sup>7</sup>

ning process the tissue under the scanning region shifts and moves, the resulting image will lack clear boundaries; it would be blurry. For large degrees of movement, the image becomes useless. The term motion artifacts describes the set of image contamination caused by motion. Motion artifacts generally arise from the patient moving about; however, it may also arise when the sample arm moves in a manner undefined in its specification. For example, scans of internal tissue are performed via a human-controlled catheter inserted into an anesthetized patient. Wiggling or shaking the catheter during a scan will result in motion artifacts.

The second issue is speed. *In vivo* systems lack the luxury of time given to their *in vitro* counterparts. Given a time consumption of  $x$  seconds from acquisition to display, and  $n$  desired number of images, the total time spent in scanning would equal  $nx$  seconds. For either a small  $x$  or  $n$ , the time commitment is minimal. However, the number of desired images is typically large (in the hundreds), so  $x$  must be small. A small  $x$  is also advantageous in terms of patient comfort—especially for internal scans where patients are anesthetized beforehand. The less time required to perform a scan, the less time the patient needs to be put under, and the less chance of complications or discomfort. Moreover, a large  $x$  also worsens the motion artifact problem: Motion artifacts alone will only contaminate an image of

the current tissue sample (bad enough as it is). Motion artifacts coupled with a slow process time may result in a contaminated image of a tissue region that is no longer even the current region being scanned.

### Designing an *In Vivo* OCT System

One possible *in vivo* design addresses the motion artifact and speed issues by optimizing the processing phase of an OCT scan. The rationale is that a faster processing phase would accelerate system performance and consequently alleviate the more extreme motion artifacts. At the Optics Group in the Research Laboratory of Engineering, this is the design we chose to implement.

As previously mentioned, the processing phase of an OCT scan consists of the conversion of a reflectivity profile of the tissue to a reconstructed image of the tissue. Optimizing the speed of the processing phase would therefore require optimizing the conversion algorithm that transforms a reflectivity profile to a displayable image. Under our design, we resolved the transformation into four key steps: light intensity homogenization, color domain mapping, removing scanning distortions, and converting between coordinate-spaces. Optimizing the conversion algorithm would require optimizing these four steps.

ABCDEFGHIJKLMNOPQRSTUVWXYZ  
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 ABCDEFGHIJKLMNOPQRSTUVWXYZ  
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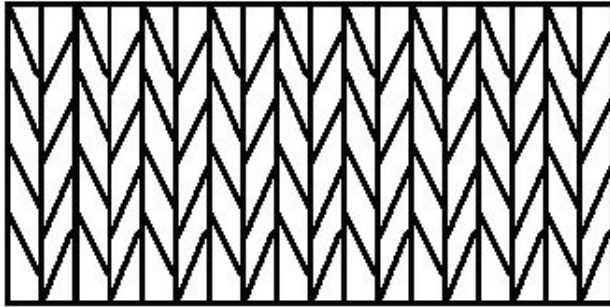


Figure 3: (Top) Writing a continuous sentence on a word processor that outputs both left to right and right to left reverses the orientation of every other line (in gray). In this example, the word processor is assumed to hold only 26 letters per line. (Bottom) A similar situation occurs in a reflectivity profile: because the sample arm traverses the sample crosswise, the orientation of every downward scan is opposite that of every upward scan. This effect is known as bi-column inversion.

### Light Intensity Homogenization

The first step involves homogenizing the light intensity values, making relatively equal intensities exactly equal. The point of OCT is to image tissue structure such that important features are easily discernible. Relatively minute differences in light intensities should therefore reflect minute differences in the tissue, while relatively large differences in light intensities should reflect large differences in the tissue. For example, a light intensity of 100 and a light intensity of 1000 differ significantly from each other and probably represent different physical layers in the tissue; these two intensities should not be homogenized. On the contrary, a light intensity of 100 and a light intensity of 101 are nearly equal and probably represent the same physical layer in the tissue; these two intensities should be homogenized. Any conversion algorithm must perform accordingly.

### Color Domain Conversion

The second step concerns the conversions of the light intensity domain and the color domain. Colors are described on a computer according to a Red, Green, and Blue (RGB) specification that allocates  $x$  bits to Red,  $y$  bits to G, and  $z$  bits to Blue. The exact number of bits to allocate per color depends on the total number of bits currently assigned per color value. For example, under a typical 16-bit specification, the bit allocation may be 5-6-5: 5 bits to Red, 6 bits to Green, and 5 bits to Blue. However, this is a convention-

al allocation—there is nothing to prevent a 16-bit allocation scheme that assigns all 16 bits to, say, Blue. The RGB specification itself is also not strictly enforced. Colors may be described in terms of RBG or any other permutations of the RGB schemata. When mapping the light intensity values of the reflectivity profile against the color values of a color domain, the conversion algorithm divides, by bits, the light intensity values into the appropriate color representation of the host computer.

### Bi-Column Inversion

The third process involves ameliorating distortions introduced into the reflectivity profile. As noted before, a reflectivity profile is formed from consecutive adjacent scans as the sample arm travels transversely across the tissue. The transverse motion of the sample arm, while efficient, leads to a negative side effect: The orientation of every downward transverse scan is opposite to that of an upward one. To grasp the idea, think of typing a continuous sentence (without carriage returns) on a word processor that outputs both from left to right and from right to left. Every other line of text would read in the opposite direction from the previous line. The same is true of a scanned constructed image, except that every column rather than line is inverted. This phenomenon is known as bi-column inversion (Figure 3). Converting a reflectivity profile to a displayable image requires reorienting every other scan column in the profile.

### Coordinate Space Mapping

The final step entails coordinate space conversion. In some situations it makes sense to display an image in other coordinate systems other than Cartesian. Catheter scans of internal tissue and retinal scans are instances where a polar representation is preferable. A conversion scheme from Cartesian to polar is unfortunately problematic. Not all integer coordinates in Cartesian space map directly to integer coordinates in polar space. However, images are always internally represented as a collection of color values with integer coordinates. Any conversion scheme must therefore ensure that noninteger coordinates are mapped to integer ones. Such a mapping, though, introduces other complications: Depending on its implementation, data overload and loss can occur. Two distinct points in the Cartesian representation may be mapped to the same point in the polar representation, leading to data overloading and subsequently to data loss at that point.

### References

1. Huang D, Swanson EA, Lin CP et al. "Optical Coherence Tomography," *Science* 1991, V254 1178-1181.
2. The New York Eye and Ear Infirmary. "Macular Hole and Normal Fovea," [www.nyee.edu/glaucoma/oct-data.htm](http://www.nyee.edu/glaucoma/oct-data.htm)
3. Swanson, EA, Izatt JA, Hee MR et al. "In-vivo Retinal Imaging by Optical Coherence Tomography," *Opt Lett* 1993, V18 1860-1866.
4. The New England Eye Center. "Optical Coherence Tomography," [www.neec.com/medical/OCT.html](http://www.neec.com/medical/OCT.html)
5. Cottrell GW, Morhenn V, Chen Z. "Early detection of Basal Cell Carcinoma using Optical Coherence Tomography and Pattern Recognition Techniques," Technical Report, Mar 2000, UC San Diego.

## Implementing an *In Vivo* OCT System

The implemented algorithm optimized three of the four steps in the processing phase. The light intensity homogenization step was optimized by mapping the reflectivity profile onto a logarithmic scale. In the interest of increasing processing speed, a less accurate bit-masking algorithm replaced a real logarithm function. This implementation reduces the number of required mathematical operations by a linear factor. Color domain conversions were handled by stipulating an RGB specification of 5-6-5 and by mapping the light intensities into a color lookup table. The light intensity values become the indices to a predefined table of color values. Passing the reflectivity profile through the color lookup table resulted in formatted color image data. Coordinate space conversions were handled in a similar manner using a coordinate-space lookup table. Having only integer coordinates in the lookup table enforced integer-to-integer coordinate mapping. Linear interpolation then assigned values to any unmapped points in the polar space. Performance was faster using this implementation than using pure mathematical transformations by an exponential factor in time, but more costly by a linear factor in space. The savings in time occur only with pointer arithmetic (to reference the lookup tables); the loss in space resulted from the needed memory to hold the color and coordinate-space lookup tables. Bicolumn inversions were treated by memory swapping data. This step of the processing phrase saw no improvement.

Overall, the design improved from earlier ones by several factors in processing speed. The rate of process and display measured at between 7~10 fps, which is an improvement on earlier systems running at under 1 fps. The improved speed, however, still falls quite short of video frame rate (typically ~ 30 fps). It is highly likely that hardware changes to the OCT setup (i.e., improved sample arm speed) would be necessary in conjunction with optimizing algorithms to achieve a real-time system. Improvements in motion artifacts were not clocked under the new system due to a lack of live test subjects at the time.

## Further Research and Applications

In the *in vivo* context, there is still much work to be done to remove motion artifacts and achieve a real-time system. OCT in general, however, is also wide open to further research. One of the most exciting research areas today is in extending OCT imaging to the three-dimension-

al realm. By stacking consecutive, cross-sectional OCT images along the z-axis, a three-dimensional representation of the scanned tissue sample may be obtained. Depending on the number of cross-sectional images used, the 3D images can become incredibly detailed. The possibilities for coupling 3D images with a real-time *in vivo* system are profound: An exact, virtual replica of the tissue sample would allow doctors to rotate, manipulate, and examine the tissue from every angle without ever touching it.

Another area attracting much research is the combination of OCT imaging with artificial intelligence. At its heart, *in vivo* diagnosis techniques do nothing more than match a set of symptoms with a set of possible diseases. For example, a strep throat diagnosis involves following a checklist of symptoms:

- \* Does the patient have a sore throat?
- \* Is the patient feverish?
- \* Does the patient have white pus on the tonsils?
- \* Does the patient have tender lymph nodes?
- \* Is the patient coughing?

From the answers to these questions alone, a physician can give an accurate diagnosis. The same holds true for diagnosing diseases based on OCT images—a list of physical characteristics in the images corresponds to a diagnosis for the disease. This paradigm of matching a set of patterns (the symptoms) to a set of outcomes (diseases) is essentially a rule-based system; the symptoms are antecedents to rules whose consequences are the diagnoses. This is a well-known area of research in AI. It may one day be possible to fully automate diagnosis using OCT: A computer generates scanned images of the tissue sample, matches the images to a database linking sets of images to diseases, and outputs a diagnosis.

OCT may one day expand to other fields outside of medicine. For example, the technology is ideally suited to developmental and molecular biology, as well as industrial uses. Because of its high resolution and nondestructive qualities, OCT may have uses in materials production as an imaging tool for polymers and composites. In summation, it must be noted that the potential for OCT is still expanding, with its promise yet to be fully realized.

## Acknowledgements

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6. University of Florida Medical College. "Optical Coherence Tomography," [www.medinfo.ufl.edu/other/profmed/slides/luttge/slide20.html](http://www.medinfo.ufl.edu/other/profmed/slides/luttge/slide20.html)
7. Everett M. "Optical Coherence Tomography," <http://lasers.llnl.gov/lasers/mtp/oct.html>
8. Lankenau IE, Welzel J, Birngruber R et al. "In Vivo Tissue Measurements with Optical low Coherence Tomography," SPIE 1997, Paper 2981-11 78-84.

## Suggested Readings

1. Rollins A, Yazdanfar S, Kulkarni M et al. "In Vivo Video Rate Optical Coherence Tomography," Optics Express 1998, V3.6 219.
2. Yazdanfar S, Kulkarni M, Izatt J. "High resolution imaging of in vivo cardiac dynamics using color Doppler optical coherence tomography," Optics Express 1997, V1.13 424.
3. Brezinski ME, Pitris C, Boppart SA et al. "Micron scale optical biopsy with optical coherence tomography," Journal of Clinical Oncology 1997, V15.3 972.
4. Ghanta RK, Fujimoto JG. "Ultrahigh Resolution Ophthalmic Structural Imaging Using Optical Coherence Tomography," HST Forum 2002 <http://hst.mit.edu/forum/abstracts>.