Optical coherence tomography

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Optical coherence tomography tomogram of a fingertip.

Optical coherence tomography (OCT) is an optical signal acquisition and processing method. It captures micrometer-resolution, three-dimensional images from within optical scattering media (e.g., biological tissue). Optical coherence tomography is an interferometric technique, typically employing near-infrared light. The use of relatively long wavelength light allows it to penetrate into the scattering medium. Confocal microscopy, another similar technique, typically penetrates less deeply into the objective.

Depending on the properties of the light source (superluminescent diodes and ultrashort pulsed lasers have been employed), Optical coherence tomography has achieved sub-micrometer resolution (with very wide-spectrum sources emitting over a ~100 nm wavelength range)

Optical coherence tomography is one of a class of optical tomographic techniques. A relatively recent implementation of optical coherence tomography, frequency-domain optical coherence tomography, provides advantages in signal-to-noise ratio, permitting faster signal acquisition. Commercially available optical coherence tomography systems are employed in diverse applications, including art conservation and diagnostic medicine, notably in ophthalmology where it can be used to obtain detailed images from within the retina.

Introduction

Starting from white-light interferometry for *in vivo* ocular eye measurements [1] [2] imaging of biological tissue, especially of the human eye, was investigated by multiple groups worldwide. A first two-dimensional *in vivo* depiction of a human eye fundus along a horizontal meridian based on white light interferometric depth scans has been presented at the ICO-15 SAT conference in 1990[3]. Further developed 1990 by Naohiro Tanno [4][5], then a professor at Yamagata University, and in particular since 1991 by Huang et al.[6], optical coherence tomography (OCT) with micrometer resolution and cross-sectional imaging capabilities has become a prominent biomedical tissue-imaging technique; it is particularly suited to ophthalmic applications and other tissue imaging requiring micrometer resolution and millimeter penetration depth[7]. First *in vivo* OCT images – displaying retinal structures – were published in 1993. [8] [9] OCT has also been used for various art conservation projects, where it is used to analyze different layers in a painting. OCT has critical advantages over other medical imaging systems. Medical ultrasonography, magnetic resonance imaging (MRI) and confocal microscopy are not suited to morphological tissue imaging: the first two have poor resolution; the last lacks millimeter penetration depth.[10][11]

OCT is based on low coherence interferometry.[12][13][14] In conventional interferometry with long coherence length (laser interferometry), interference of light occurs over a distance of meters. In OCT, this interference is shortened to a distance of micrometers, thanks to the use of broadband light sources (sources that can emit light over a broad range of frequencies). Light with broad bandwidths can be generated by using superluminescent diodes (superbright LEDs) or lasers with extremely short pulses (femtosecond lasers). White light is also a broadband source with lower powers.

Light in an OCT system is broken into two arms -- a sample arm (containing the item of interest) and a reference arm (usually a mirror). The combination of reflected light from the sample arm and reference light from the reference arm gives rise to an interference pattern, but only if light from both arms have travelled the "same" optical distance ("same" meaning a difference of less than a coherence length). By scanning the mirror in the reference arm, a reflectivity profile of the sample can be obtained (this is time domain OCT). Areas of the sample that reflect back a lot of light will create greater interference than areas that don't. Any light that is outside the short coherence length will not interfere. This reflectivity profile, called an A-scan, contains information about the spatial dimensions and location of structures within the item of interest. A cross-sectional tomograph (B-scan) may be achieved by laterally combining a series of these axial depth scans (A-scan). En face imaging (C-scan) at an acquired depth is possible depending on the imaging engine used.

Laypersons Explanation

Optical Coherence Tomography, or 'OCT', is a technique for obtaining sub-surface images of translucent or opaque materials at a resolution equivalent to a low-power microscope. It is effectively 'optical ultrasound', imaging reflections from within tissue to provide cross-sectional images.

OCT is attracting interest among the medical community, because it provides tissue morphology imagery at much higher resolution (better than 10 µm) than other imaging modalities such as MRI or ultrasound.

The key benefits of OCT are:

- Live sub-surface images at near-microscopic resolution
- Instant, direct imaging of tissue morphology
- No preparation of the sample or subject
- No ionizing radiation

OCT delivers high resolution because it is based on light, rather than sound or radio frequency. An optical beam is directed at the tissue, and a small portion of this light that reflects from sub-surface features is collected. Note that most light is not reflected but, rather, scatters. The scattered light has lost its original direction and does not contribute to forming an image but rather contributes to *glare*. The glare of scattered light causes optically scattering materials (e.g., biological tissue, candle wax, or certain plastics) to appear opaque or translucent even while they do not strongly absorb light (as can be ascertained through a simple experiment — e.g., shining a red laser pointer through one's finger). Using the OCT technique, scattered light can be filtered out, completely removing the glare. Even the very tiny proportion of reflected light that is not scattered can then be detected and used to form the image in, e.g., a scanning OCT system employing a microscope.

The physics principle allowing the filtering of scattered light is optical coherence. *Only* the reflected (non-scattered) light is coherent (i.e., retains the optical phase that causes light rays to propagate in one or another direction). In the OCT instrument, an optical interferometer is used in such a manner as to detect *only* coherent light. Essentially, the interferometer strips off scattered light from the reflected light needed to generate an image. In the process depth and intensity of light reflected from a sub-surface feature is obtained. A three-dimensional image can be built up by scanning, as in a sonar or radar system.

Within the range of noninvasive three-dimensional imaging techniques that have been introduced to the medical research community, OCT as an echo technique is similar to ultrasound imaging. Other

medical imaging techniques such as computerized axial tomography, magnetic resonance imaging, or positron emission tomography do not utilize the echo-location principle.

The technique is limited to imaging 1 to 2 mm below the surface in biological tissue, because at greater depths the proportion of light that escapes without scattering is too small to be detected. No special preparation of a biological specimen is required, and images can be obtained 'non-contact' or through a transparent window or membrane. It is also important to note that the laser output from the instruments is low – eye-safe near-infra-red light is used – and no damage to the sample is therefore likely.

Theory

The principle OCT is white light or low coherence interferometry. The optical setup typically consists of an interferometer (Fig. 1, typically Michelson type) with a low coherence, broad bandwidth light source. Light is split into and recombined from reference and sample arm, respectively.

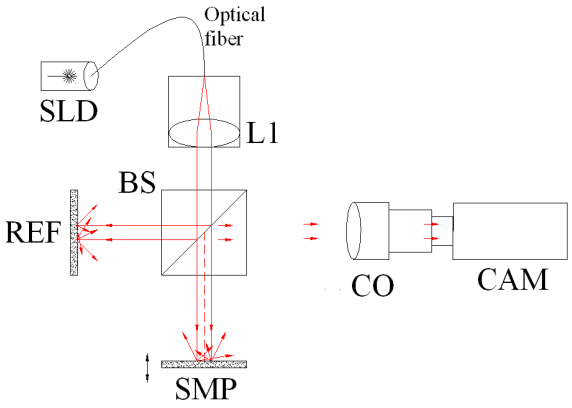

Fig. 1 Full-field OCT optical setup. Components include: super-luminescent diode (SLD), convex lens (L1), 50/50 beamsplitter (BS), camera objective (CO), CMOS-DSP camera (CAM), reference (REF) and sample (SMP). The camera functions as a two-dimensional detector array, and with the OCT technique facilitating scanning in depth, a non-invasive three dimensional imaging device is achieved.

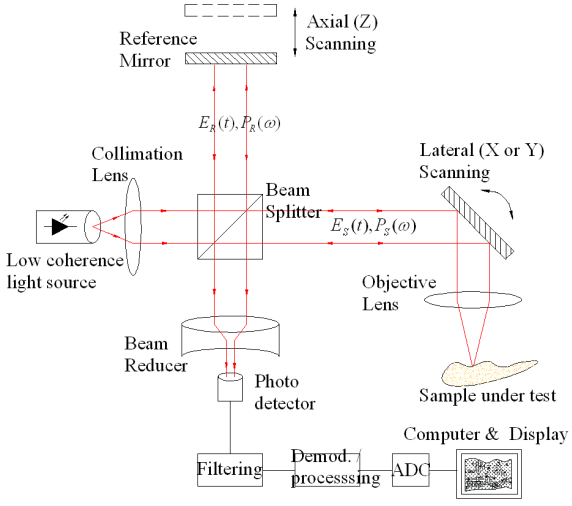

Fig. 2 Typical optical setup of single point OCT. Scanning the light beam on the sample enables

non-invasive cross-sectional imaging up to 3 mm in depth with micrometer resolution.

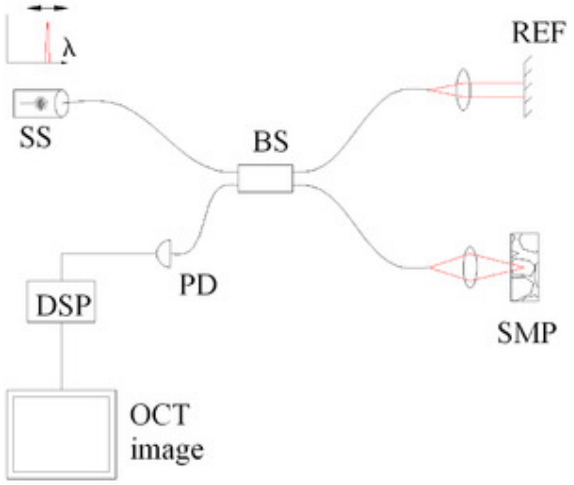

Fig. 3 Spectral discrimination by swept-source OCT. Components include: swept source or tunable laser (SS), beamsplitter (BS), reference mirror (REF), sample (SMP), photodetector (PD), digital signal processing (DSP)

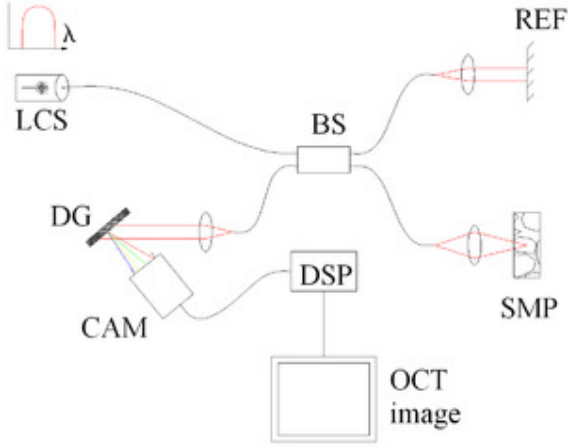

Fig. 4 Spectral discrimination by fourier-domain OCT. Components include: low coherence source (LCS), beamsplitter (BS), reference mirror (REF), sample (SMP), diffraction grating (DG) and full-field detector (CAM) act as a spectrometer, and digital signal processing (DSP)

Time Domain OCT

In time domain OCT the pathlength of the reference arm is translated longitudinally in time. A property of low coherence interferometry is that interference, i.e. the series of dark and bright fringes, is only achieved when the path difference lies within the coherence length of the light source. This interference is called auto correlation in a symmetric interferometer (both arms have the same reflectivity), or cross-correlation in the common case. The envelope of this modulation changes as pathlength difference is varied, where the peak of the envelope corresponds to pathlength matching.

The interference of two partially coherent light beams can be expressed in terms of the source intensity, I_S, as

$$I = k_1 I_S + k_2 I_S + 2\sqrt{(k_1 I_S) \cdot (k_2 I_S)} \cdot Re\left[\gamma\left(\tau\right)\right] \qquad (1)$$

where $k_1 + k_2 < 1$ represents the interferometer beam splitting ratio, and $\gamma(\tau)$ is called the complex degree of coherence, i.e. the interference envelope and carrier dependent on reference arm scan or time delay τ, and whose recovery of interest in OCT. Due to the coherence gating effect of OCT the complex degree of coherence is represented as a Gaussian function expressed as[14]

$$\gamma\left(\tau\right) = \exp\left[-\left(\frac{\pi \Delta\nu \tau}{2\sqrt{\ln 2}}\right)^2\right] \cdot \exp\left(-j 2\pi \nu_0 \tau\right) \qquad (2)$$

where $\Delta\nu$ represents the spectral width of the source in the optical frequency domain, and ν_0 is the centre optical frequency of the source. In equation (2), the Gaussian envelope is amplitude modulated by an optical carrier. The peak of this envelope represents the location of sample under test microstructure, with an amplitude dependent on the reflectivity of the surface. The optical carrier is due to the Doppler effect resulting from scanning one arm of the interferometer, and the frequency of this modulation is controlled by the speed of scanning. Therefore translating one arm of the interferometer has two functions; depth scanning and a Doppler-shifted optical carrier are accomplished by pathlength variation. In OCT, the Doppler-shifted optical carrier has a frequency expressed as

$$f_{Dopp} = \frac{2 \cdot \nu_0 \cdot v_s}{c} \qquad (3)$$

where ν_0 is the central optical frequency of the source, v_s is the scanning velocity of the pathlength variation, and c is the speed of light.


interference signals in TD vs. FD-OCT

The axial and lateral resolutions of OCT are decoupled from one another; the former being an equivalent to the coherence length of the light source and the latter being a function of the optics. The coherence length of a source and hence the axial resolution of OCT is defined as

$$\begin{aligned} l_c &= \frac{2\ln 2}{\pi} \cdot \frac{\lambda_0^2}{\Delta\lambda} \\ &\approx 0.44 \cdot \frac{\lambda_0^2}{\Delta\lambda} \end{aligned} \qquad (4)$$

Frequency Domain OCT (FD-OCT)

In frequency domain OCT the broadband interference is acquired with spectrally separated detectors (either by encoding the optical frequency in time with a spectrally scanning source or with a dispersive detector, like a grating and a linear detector array). Due to the Fourier relation (Wiener-Khintchine theorem between the auto correlation and the spectral power density) the depth scan can be immediately calculated by a Fourier-transform from the acquired spectra, without movement of the reference arm.[15] [16] This feature improves imaging speed dramatically, while the reduced losses during a single scan improve the signal to noise proportional to the number of detection

elements. The parallel detection at multiple wavelength ranges limits the scanning range, while the full spectral bandwidth sets the axial resolution.

Spatially Encoded Frequency Domain OCT (aka Spectral Domain or Fourier Domain OCT)

SEFD-OCT extracts spectral information by distributing different optical frequencies onto a detector stripe (line-array CCD or CMOS) via a dispersive element (see Fig. 4). Thereby the information of the full depth scan can be acquired within a single exposure. However, the large signal to noise advantage of FD-OCT is reduced due the lower dynamic range of stripe detectors in respect to single photosensitive diodes, resulting in an SNR (signal to noise ratio) advantage of ~10 dB at much higher speeds. Since OCT at 1300 nm with a photo array, the dynamic range is not a serious problem at this wavelength range. The drawbacks of this technology are found in a strong fall-off of the SNR, which is proportional to the distance from the zero delay and a sinc-type reduction of the depth dependent sensitivity because of limited detection linewidth. (One pixel detects a quasi-rectangular portion of an optical frequency range instead of a single frequency, the Fourier-transform leads to the sinc(z) behavior). Additionally the dispersive elements in the spectroscopic detector usually do not distribute the light equally spaced in frequency on the detector, but mostly have an inverse dependence. Therefore the signal has to be resampled before processing, which can not take care of the difference in local (pixelwise) bandwidth, which results in further reduction of the signal quality.However,the fall-off is not a serious problem with the development of new generation CCD or Photo array with a larger number of pixels.

Synthetic array heterodyne detection offers another approach to this problem without the need to high dispersion.

Time Encoded Frequency Domain OCT (also swept source OCT)

TEFD-OCT tries to combine some of the advantages of standard TD and SEFD-OCT. Here the spectral components are not encoded by spatial separation, but they are encoded in time. The spectrum either filtered or generated in single successive frequency steps and reconstructed before Fourier-transformation. By accommodation of a frequency scanning light source (i.e. frequency scanning laser) the optical setup (see Fig. 5) becomes simpler than SEFD, but the problem of scanning is essentially translated from the TD-OCT reference-arm into the TEFD-OCT light source. Here the advantage lies in the proven high SNR detection technology, while swept laser sources achieve very small instantaneous bandwidths (=linewidth) at very high frequencies (20-200 kHz). Drawbacks are the nonlinearities in the wavelength, especially at high scanning frequencies. The broadening of the linewidth at high frequencies and a high sensitivity to movements of the scanning geometry or the sample (below the range of nanometers within successive frequency steps).

Full Field OCT

Full-field OCT (also called en face OCT) is an original approach of OCT, based on white-light interference microscopy. Tomographic images are obtained by combination of interferometric images recorded in parallel by a detector array such as a CCD camera. Whereas conventional OCT produces B-mode (axially-oriented) images like ultrasound imaging, full-field OCT acquires tomographic images in the en face (transverse) orientation.

Full-field OCT is an alternative method to conventional OCT to provide ultrahigh resolution images (~ 1 µm in all 3 dimensions), using a simple halogen lamp instead of a complex laser-based source. Various studies have been carried out demonstrating the performance of this technology for three-

dimensional imaging of ex vivo and in vivo specimens. Full-field OCT can be used for non-invasive histological studies without sample preparation.

Scanning schemes

Focusing the light beam to a point on the surface of the sample under test, and recombining the reflected light with the reference will yield an interferogram with sample information corresponding to a single A-scan (Z axis only). Scanning of the sample can be accomplished by either scanning the light on the sample, or by moving the sample under test. A linear scan will yield a two-dimensional data set corresponding to a cross-sectional image (X-Z axes scan), whereas an area scan achieves a three-dimensional data set corresponding to a volumetric image (X-Y-Z axes scan), also called full-field OCT.

Single point (confocal) OCT

Systems based on single point, or flying-spot time domain OCT, must scan the sample in two lateral dimensions and reconstruct a three-dimensional image using depth information obtained by coherence-gating through an axially scanning reference arm (Fig. 2). Two-dimensional lateral scanning has been electromechanically implemented by moving the sample[16] using a translation stage, and using a novel micro-electro-mechanical system scanner.[17]

Parallel OCT

Parallel OCT using a charge-coupled device (CCD) camera has been used in which the sample is full-field illuminated and en face imaged with the CCD, hence eliminating the electromechanical lateral scan. By stepping the reference mirror and recording successive *en face* images a three-dimensional representation can be reconstructed. Three-dimensional OCT using a CCD camera was demonstrated in a phase-stepped technique[18], using geometric phase-shifting with a Linnik interferometer[19] , utilising a pair of CCDs and heterodyne detection[20], and in a Linnik interferometer with an oscillating reference mirror and axial translation stage.[21] Central to the CCD approach is the necessity for either very fast CCDs or carrier generation separate to the stepping reference mirror to track the high frequency OCT carrier.

Smart detector array for parallel TD-OCT

A two-dimensional smart detector array, fabricated using a 2 µm complementary metal-oxide-semiconductor (CMOS) process, was used to demonstrate full-field OCT.[22] Featuring an uncomplicated optical setup (Fig. 3), each pixel of the 58x58 pixel smart detector array acted as an individual photodiode and included its own hardware demodulation circuitry.

Selected Applications

Optical coherence tomography is an established medical imaging technique. It is widely used, for example, to obtain high-resolution images of the retina and the anterior segment of the eye. Researchers are also seeking to develop a method that uses frequency domain OCT to image coronary arteries in order to detect vulnerable lipid-rich plaques[1].

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