Biomedical Optics
OCT

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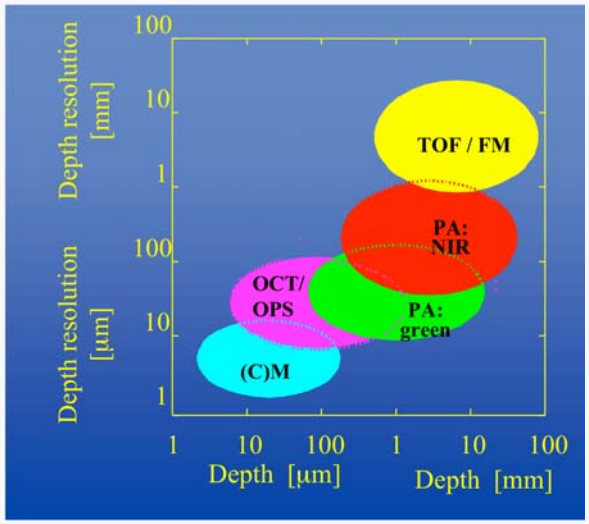
Imaging Methods in Tissue



C(M) : (confocal) microscopy

OCT: optical coherence tomography

OPS: orthogonal polarization spectral imaging

PA: photoacoustics

TOF: time-of-flight tomography

FM: frequency-modulated tomography

Optical Coherence Tomography

- Imaging technique
- Based on intensity differences in backscattered light from tissue
- Similar to ultrasound, but higher resolution
- Superficial tissue structures
- Time of flight ?

General characteristics

- perform cross-sectional measures of tissue in situ similar to US
  - *time for a pulse to travel*
- detection is based on low coherence interferometry
  - *reflected infrared light*

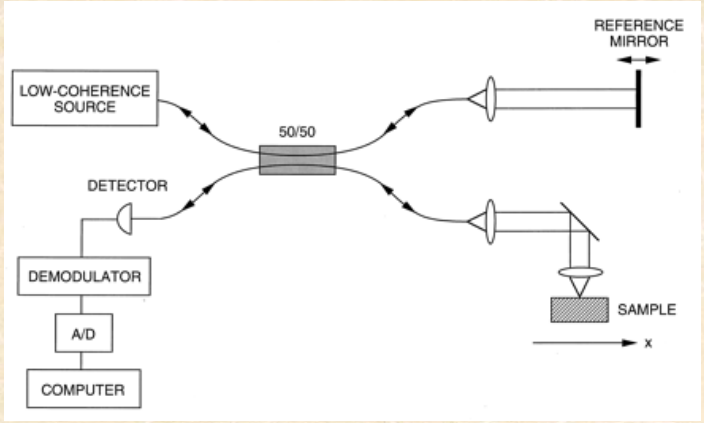
General characteristics

- penetration depth ≈ 2-3 mm
  - *wavelength dependent*
- resolution axial ≈ 4-20 μm
  - *detector dependent*
- resolution lateral ≈ 5-20 μm
  - *spot size*

OCT based on coherence measurement

- Signals are only detected when the optical path length in the sample and reference arm are within the coherence length of the source

Set-up of OCT

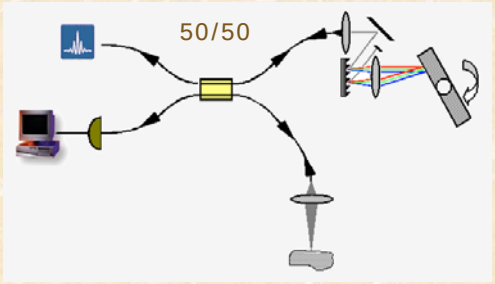


- Interference between the light reflected from the tissue and the light reflected from the reference mirror occurs only when the two path lengths are matched to within the coherence length of the light source

Optical Coherence Tomography

Ti:Sapphire laser
λ_0 = 800 nm
$\Delta\lambda$ = 125 nm

Double pass RSOD



Lock-in Amplifier+
Digital processing

Sample

Coherence and Source Requirements

- Temporal coherence
- Spatial coherence
- Partial Coherence
- Coherence time
- Coherence Length

Spatial coherence

- Spatial coherence is measured by a wave front with a constant phase all over space. It means that between any two points in space the phase difference is constant with time.
- A laser light has spatial coherence when the phase difference between two points in space is constant in time.

Spatial coherence, cont

- When a laser operates in a single basic transverse mode (TEM_{00}), it has the maximum spatial coherence.
- The spatial coherence is the cause of the high directionality of the laser beam.
  - Spatial coherence is important in applications where all the power is needed in a single spot (diffraction limited focusing).

Spatial Coherence

- Spatial coherence is the dependence of fringe visibility on the spatial extent of the source.
- The spread in wavelengths among the sources is small enough so that the coherence length is much greater than the range of OPD in the measurement.
- Therefore, fringe visibility is not affected by the bandwidth of the power spectrum.

Temporal coherence

- Temporal Coherence means that the light has a single wavelength (or a single frequency), and this is the property of mono-chromaticity
- A wave has complete temporal coherence when the phase of the wave at a certain instant of time (Δt) along the travelling wave front, is equal to the phase of the wave after it advance a distance L at a time L/c for every L

Temporal coherence, cont

- It means that in a time (Δt), while the wave advances a distance of c(Δt) it keeps its shape as the original wave
- The narrower the linewidth ($\Delta \nu$) of the light source, the better is its temporal coherence
- The temporal coherence is a measure of the ability of the radiation to perform interference, as a result of differences in path lengths between the two beams.

Temporal Coherence

- Temporal coherence is the dependence of fringe visibility on the power spectrum of the source.

Coherence properties

- Light is assumed as electromagnetic radiation

$$E = E_0 e^{i(k \cdot r - \omega t + \phi)}$$

- Consists of wave-trains with different lifetimes
- Average lifetime, τ_0, is called coherence time

$$\tau_0 = \tau_{ave} = 1/\Delta\nu$$

Coherence length

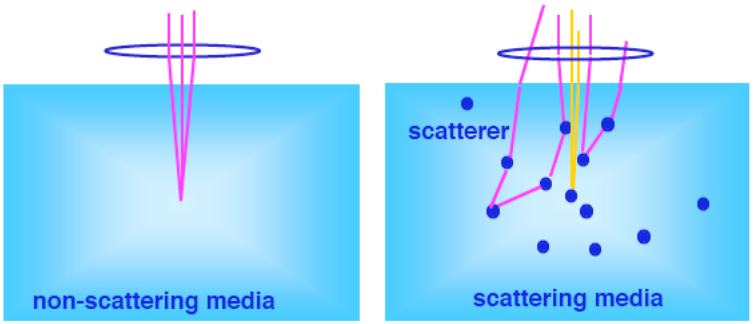
- **Coherence Length (L_c)** is the maximum path difference possible for a specific temporal coherence, which still shows interference.
- This specific temporal coherence is related to specific linewidth ($\Delta\lambda$) by the formula: $L_c = c/(\Delta\nu)$
  - $\Delta\nu$ = Frequency linewidth of radiation, in units of Hertz [Hz]
  - c = Speed of light in vacuum, in units of [m/s]
- Narrowing the linewidth, increase its coherence length
- This is the reason why it is recommended to use a single (longitudinal) mode laser in applications related to interference (such as holography)

Optical Tomographic Imaging of Tissue Structure and Physiology

Challenge: ***Scattering of photon destroy localization***

Mean free scattering path:

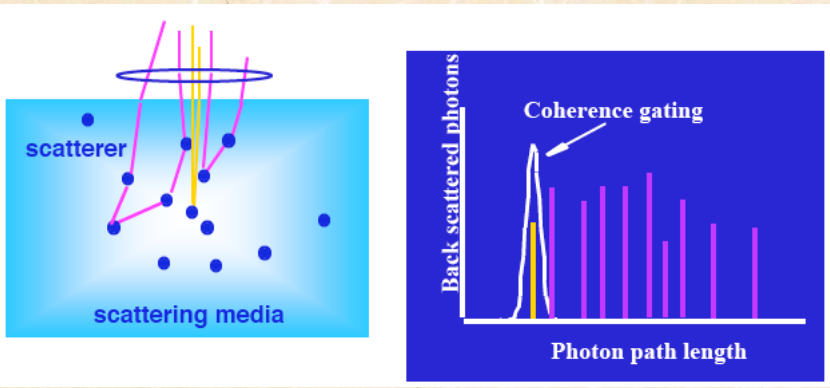
Skin tissue: $1/\mu_s \sim 50\ \mu m$ **Blood:** $1/\mu_s \sim 8\ \mu m$



Optical Tomographic Imaging of Tissue Structure and Physiology

- Technology:
  - Time of flight (only ballistic photons or minimally scattered photons are selected)
  - Photon migration (amplitude and phase of photon density wave are measured)
  - Optical coherence tomography (coherence gating are used to select minimally scattered photons)

Optical Coherence Tomography: Coherence Gating



Interference of monochromatic light

- Light is assumed as electromagnetic radiation

$$\boldsymbol{E} = \boldsymbol{E}_0 e^{i(\boldsymbol{k}\cdot\boldsymbol{r}-\omega t+\phi)}$$

- Interference: Superposition of waves

$$\boldsymbol{E} = \boldsymbol{E}_1 + \boldsymbol{E}_2 =$$

$$\boldsymbol{E}_1 e^{i(\boldsymbol{k}\cdot\boldsymbol{r}-\omega t+\phi_1)} + \boldsymbol{E}_2 e^{i(\boldsymbol{k}\cdot\boldsymbol{r}-\omega t+\phi_2)}$$

- Detection of light waves:

$$\boldsymbol{I} \propto \left\langle \boldsymbol{E}^2 \right\rangle$$

Correlation function

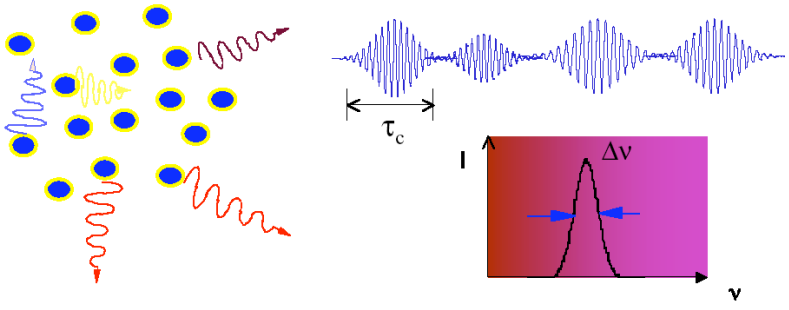
- Defining a normalized correlation function

$$\gamma_{12}(\tau) \equiv \frac{\Gamma_{12}(\tau)}{\sqrt{I_1 I_2}}$$

- We get

$$I_p(t) = I_1 + I_2 + 2\sqrt{I_1 I_2}\,\gamma_{12}(\tau)\cos(2\pi\upsilon_0\tau)$$

Photon sources



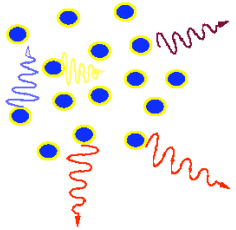
Atoms or molecules radiate wavetrains of finite length

- **More than one wavelength (spectral bandwidth)**
- **Fixed phase relation only within individual wavetrain**

Coherence

Correlation of light wave at two points in space-time:

$$\Gamma(r_1,t_1;r_2,t_2) = \langle E(r_1,t_1)E(r_2,t_2)\rangle$$

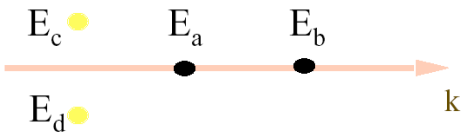


Temporal Coherence (longitudinal)

$$\Gamma = \langle E_a(t)E^*_b(t)\rangle$$

Spatial Coherence (lateral)

$$\Gamma = \langle E_c(t)E^*_d(t)\rangle$$

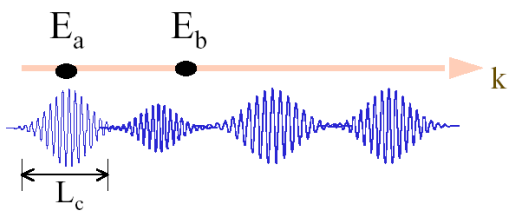


Temporal Coherence

Correlation of light wave along the light propagation direction

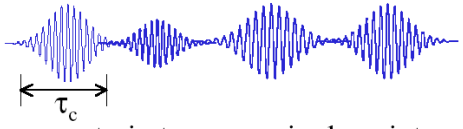
$\Gamma = \langle E_a(t) E^*_b(t) \rangle$

$= \langle E(t+t_{ba})\, E^*(t) \rangle$



Coherence length:

The length of the wavetrain where there is definite phase relation.



Coherence time:

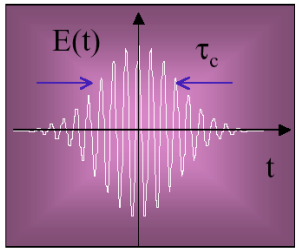
The time for the elementary wavetrain to pass a single point

$L_c = c\,\tau_c$

Temporal Coherence

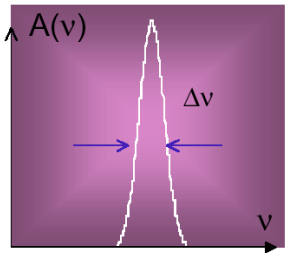
Temporal coherence is a measure of spectral bandwidth

A high (good) temporal coherence gives a narrow spectral bandwidth ("pure" light of single wavelength (color))



Fourier transform pair

$A(\nu) = \int_{-\infty}^{\infty} E(t) e^{-i2\pi\nu t} dt$

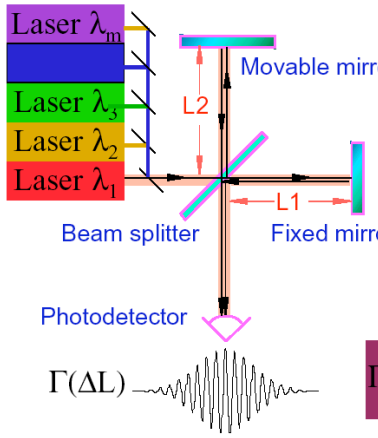


$\tau_c \cong 1/\Delta\nu$

Coherence lengths of light sources

Source	Mean wavelength λ (nm)	Linewidth Δλ (nm)	Coherence length ΔL_c
Thermal IR (8000-12000 nm)	10000	≈4000	≈25000 nm ≈ 2,5
Mid-IR (500-5000 nm)	4000	≈2 000	≈8000 nm = 2λ
White light	550	≈300	≈900 nm = 1,6λ
Mercury arc	546,1	≈1,0	≈0,03 cm
Stabilized He-Ne laser	632,8	$\approx 10^{-6}$	≈400 m
Special He-Ne laser	1153	$8{,}9*10^{-11}$	$15*10^{6}$ m

Interference with Partial Coherence Light Source



$I_1(\nu_1) = 2*I_0(\nu_1)[1+\cos(2\pi\Delta L\nu_1)]$

$I_2(\nu_2) = 2*I_0(\nu_2)[1+\cos(2\pi\Delta L\nu_2)]$

$I_3(\nu_3) = 2*I_0(\nu_3)[1+\cos(2\pi\Delta L\nu_3)]$

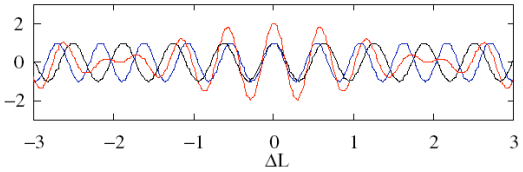
.....

$I_m(\nu_2) = 2*I_0(\nu_2)[1+\cos(2\pi\Delta L\nu_m)]$

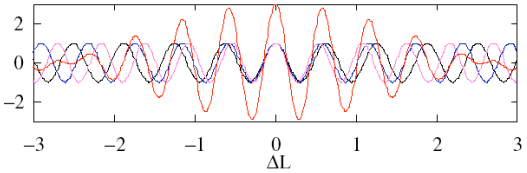
$$\Gamma(\Delta L, \nu_1, \nu_2 .. \nu_m) = 2\sum_{1}^{m} I_0(\nu_i)\cos(2\pi\Delta L\nu_i)$$

Interference with Partial Coherence Light Source

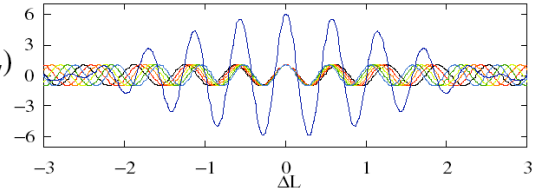
$\Gamma(\Delta L,\nu_1,\nu_2)$



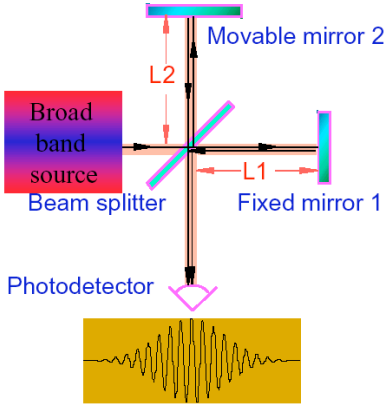
$\Gamma(\Delta L,\nu_1,\nu_2,\nu_3)$



$\Gamma(\Delta L,\nu_1,\nu_2,.....\nu_7)$



Interference with partial coherence light source

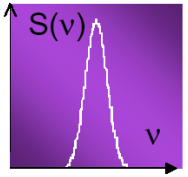


For discrete light with different wavelength

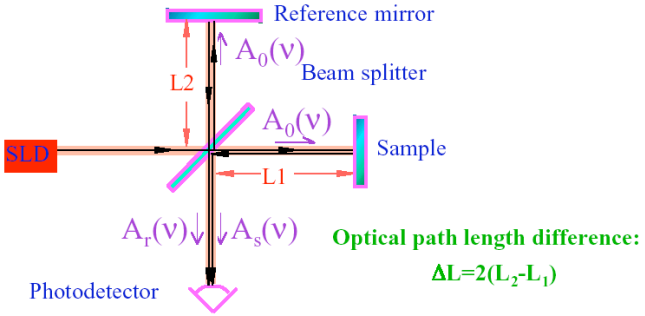
$$\Gamma(\Delta L,\nu_1,\nu_2..\nu_m)=2\sum_1^m I_0(\nu_i)\cos(2\pi\Delta L\nu_i)$$

For continuous spectra with spectral density of S(ν):

$$\Gamma(\Delta L)\approx 2I_0\int_0^\infty S(\nu)\cos(2\pi\Delta L\nu)d\nu$$



Interference of partially coherent light



Assume light coupled equally into reference arm and sample arm with spectral amplitude of $A_o(\nu)$. The light coupled back to the detect from the sample and reference arm is given by:

$$A_r(\nu)=e^{i2\pi\nu L_r}K_rA_o(\nu)$$

$$A_s(\nu)=e^{i2\pi\nu L_s}K_sA_o(\nu)$$

Interference of partially coherent light

If the time delay (τ) between light in reference and sample paths is changed by translating the reference mirror, total power detected at the interferometer output is given by a time-average of the squared light amplitude

$$I_t(\tau)=\left\langle|E_r(t)+E_s(t)|^2\right\rangle=I_r+I_s+\Gamma_{oct}(\Delta L)$$

$$\Gamma_{oct}(\Delta L)=2\int_0^\infty K_rK_sS(\nu)\cos(2\pi\Delta L\nu)d\nu$$

Assuming that there is no spectral modulation in the reflectivity of both the sample and reference arms

$$\Gamma_{oct}(\Delta L)=2K_rK_s\int_0^\infty S(\nu)\cos(2\pi\Delta L\nu)d\nu$$

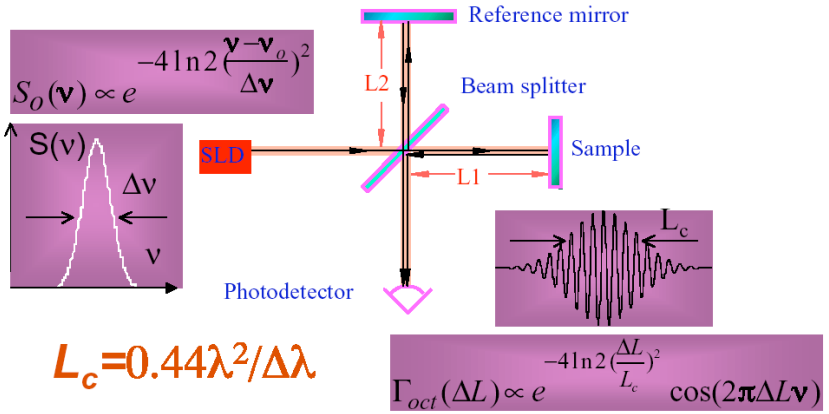
If the source spectral distribution is a Gaussian function

$$S_O(\nu)\propto e^{-4\ln 2\left(\frac{\nu-\nu_o}{\Delta\nu}\right)^2}$$

$$\Gamma_{oct}(\tau)\propto e^{-4\ln 2\left(\frac{\Delta L}{L_c}\right)^2}\cos(2\pi\Delta L\nu)$$

Where L_c is the coherence length of the partial coherence source given by

Optical Coherence Tomography



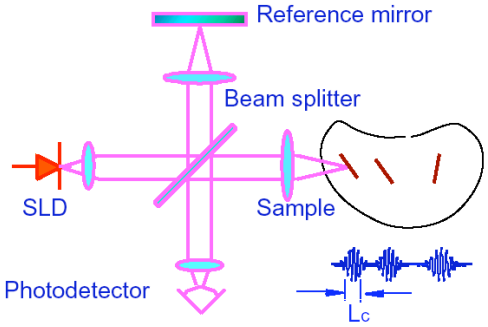
$L_c = 0.44\lambda^2/\Delta\lambda$

$\Gamma_{oct}(\Delta L) \propto e^{-4\ln 2(\frac{\Delta L}{L_c})^2} \cos(2\pi\Delta L\nu)$

Interference fringes observed only when optical path lengths are matched within coherence length of the source

Optical Coherence Tomography

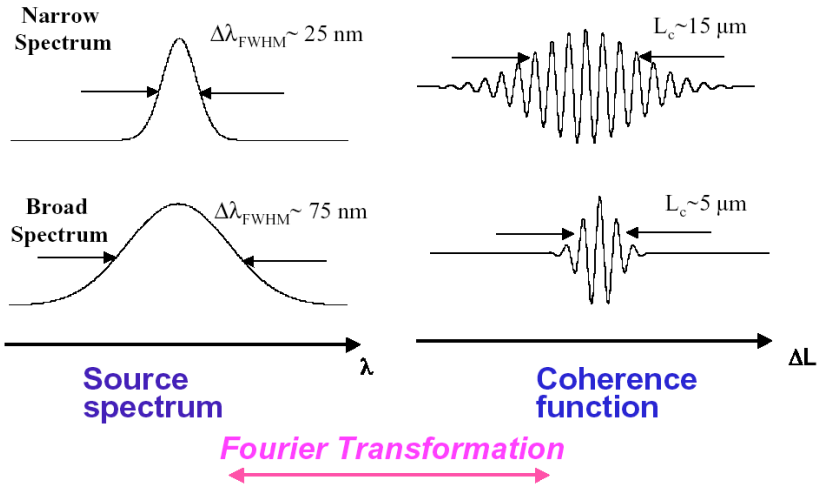
—— Michelson interferometer with a broad band partially coherent source



Axial spatial resolution: $L_c = 0.44\lambda^2/\Delta\lambda$

Coherent Length

$L_c = 0.44\lambda^2/\Delta\lambda$

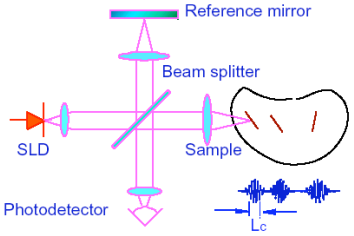


Fourier Transformation

Optical Coherence Tomography

—— Michelson interferometer with a broad band partial coherent source

- *Fringe amplitude proportional to backscattered light*
- *Longitudinal (depth) resolution: L_c*
- *Coherence length: $L_c = 0.44\lambda^2/\Delta\lambda$, (2~15 μm)*
- *Lateral resolution by focusing optics (1~10 μm)*
- *Probing depth: $1/\mu'_s$~ $5/\mu'_s$*



Resolution of OCT

$$L_c = \frac{4\ln 2}{\pi}\frac{\lambda^2}{\Delta\lambda}$$

L_c = coherence length
λ = center wavelength
$\Delta\lambda$ = optical bandwidth

$$\Delta z = \frac{L_c}{2n_g}$$

Δz = longitudinal resolution
n_g = group index

$$n_g = n - \lambda\frac{dn}{d\lambda}$$

Resolution of OCT, cont

$$\Delta x = \frac{4\lambda}{\pi}\bullet\frac{f}{d}$$

f = focal length
d = spot size of objective lens

$$b = 2z_R = \pi\frac{(\Delta x)^2}{2\lambda}$$

b = focus depth
z_R = Rayleigh range

Lightsource Parameters

Wavelength and bandwidth determine the axial resolution (ΔL):

$$\Delta L = \frac{2\ln 2}{\pi}\frac{\lambda^2}{\Delta\lambda}$$

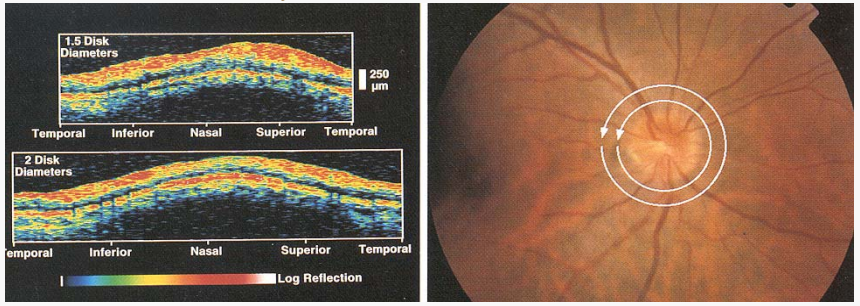
Typical resolutions are:

	SLD	*Ti:Sapphire laser*
λ_0 =	1300 nm	800 nm
$\Delta\lambda$ =	50 nm	125 nm
ΔL =	15 μm	2 μm

Lateral resolution is determined by the size of the focal spot

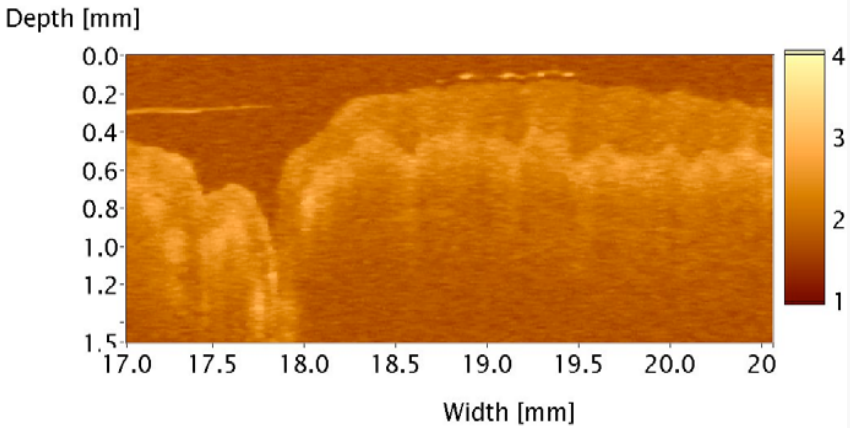
Optical Coherence Tomography

- Peripapillary area
- Nerve fiber layer thickness

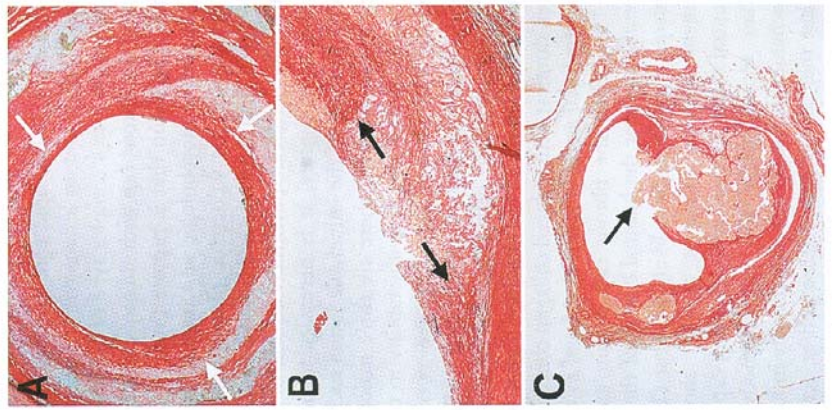


Dermatology

Epidermis finger

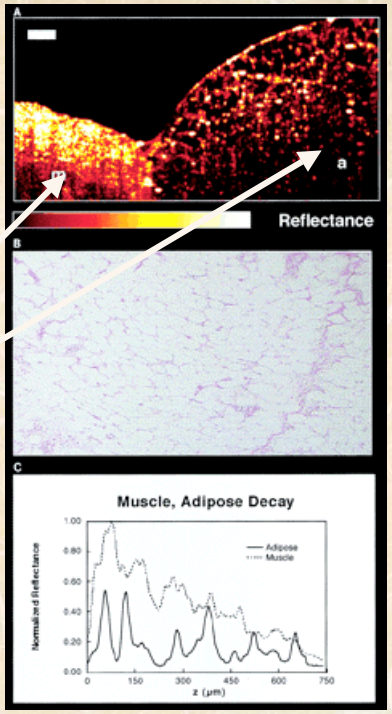


Cardiology: Vulnerable Plaque

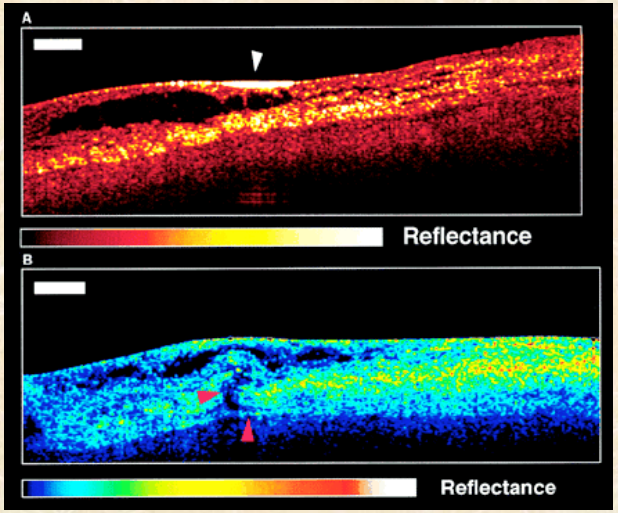


Plaques

- Contrast between lipid- and water-based tissue.
  - m cardiac mucle
  - a adipose tissue

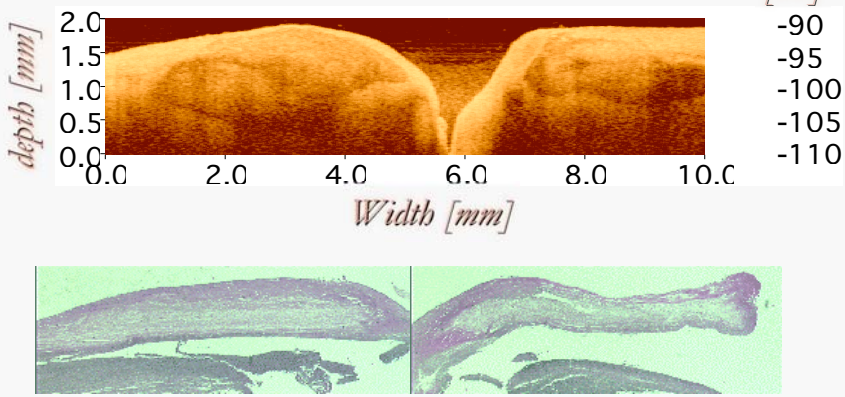


Plaques with fine structures

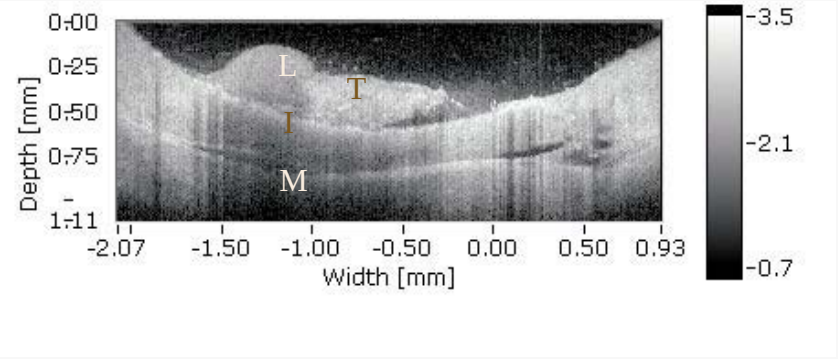


Plaque Imaging: 1300 nm, 15 µm

- Human thoracic aorta



Plaque Imaging: 800 nm, 5 µm

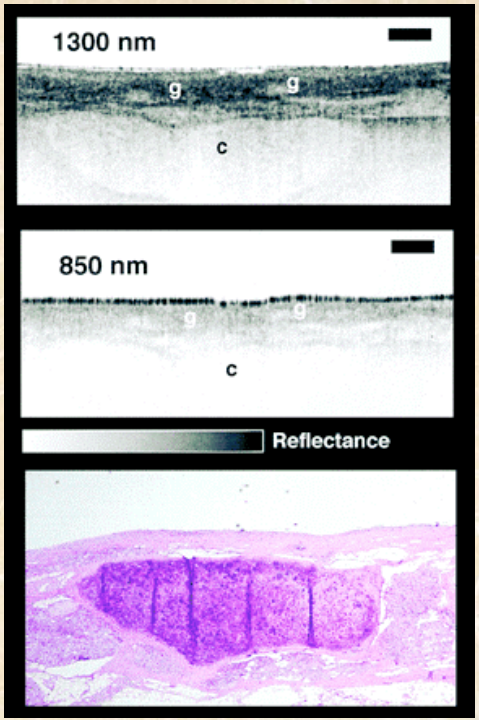


Human femoral artery

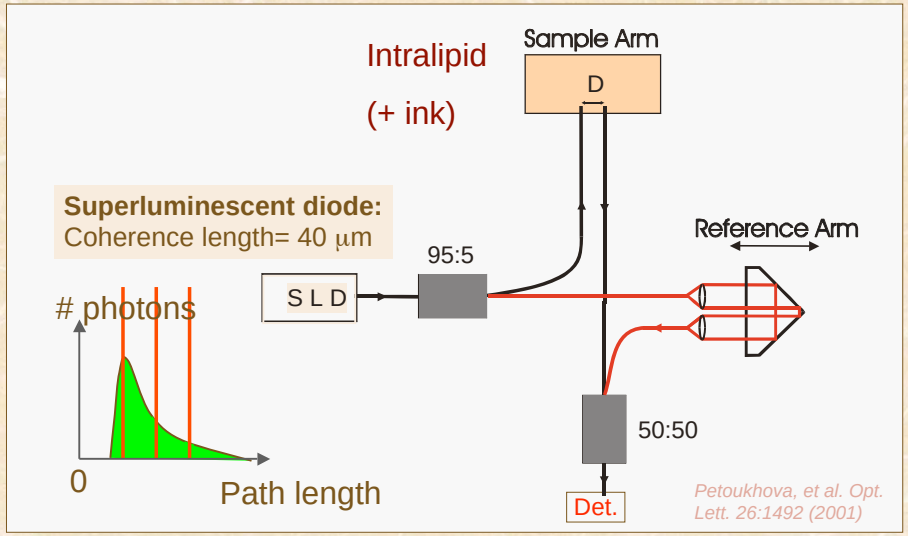
L: Lumen
T: Thrombus
I: Intima
M: Media

Image depth vs wavelength

- 1300 nm (upper)
- 850 nm (middle)
- histology (lower)

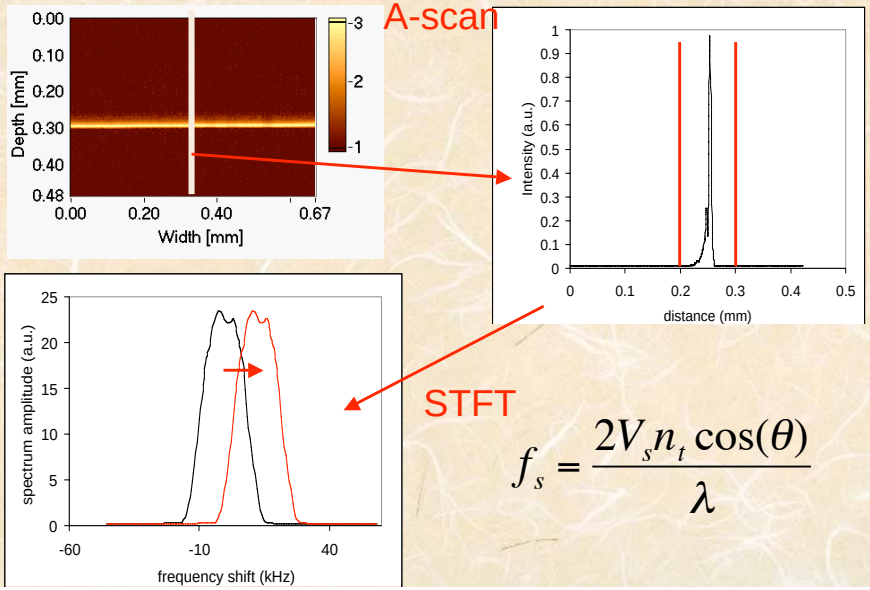


From laser Doppler... to low coherence Doppler



Petoukhova, et al. Opt. Lett. 26:1492 (2001)

OCT signal analysis: flow



$$f_s = \frac{2V_s n_t \cos(\theta)}{\lambda}$$

Detector current

- The interferometric detector current, $\tilde{i}_d(t)$ generated by a moving scatterer in the sample is given by:

$$\tilde{i}_d(t) = A(t)\cos[2\pi(f_r - f_s)t + \Phi(t)]$$

$A(t)$ is the amplitude of the reflectivity as a function of depth

$\Phi(t)$ is a phase term

Coherent demodulation

- Complex envelope of the interferogram

$$i_d(t) = A(t)\exp[-j\{2\pi f_s t + \Phi(t)\}]$$

- Short time Fourier transform(STFT)

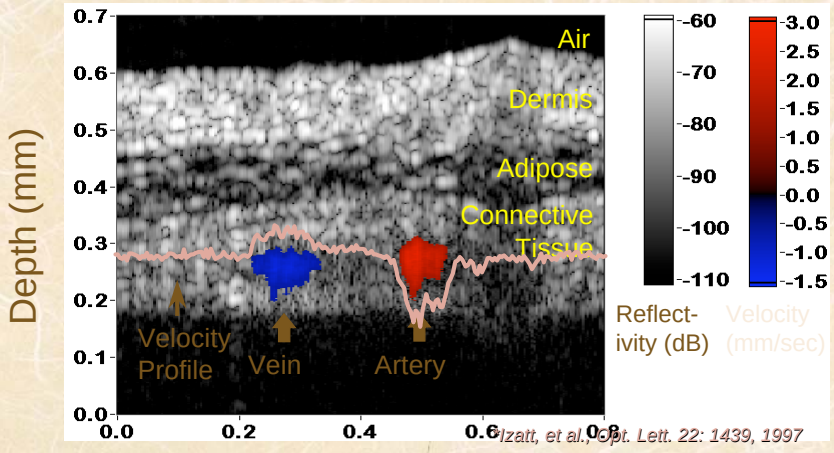
$$V_s = \frac{f_s \lambda_0}{2n_t \cos\theta}$$

V_s is the mean velocity

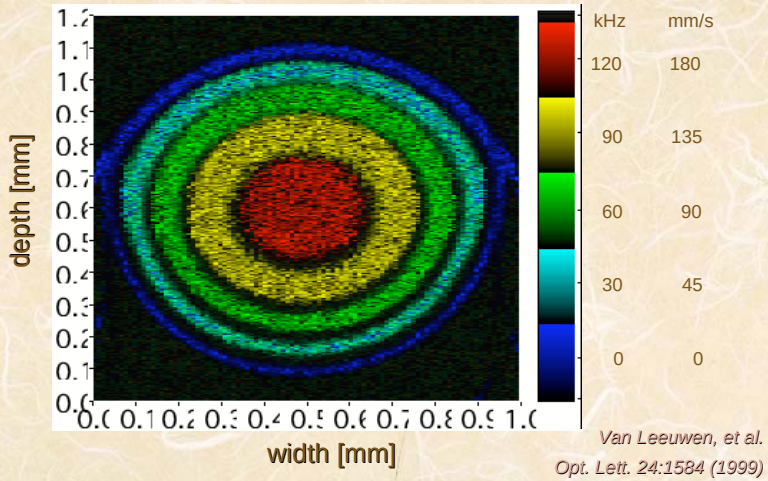
n_t is the mean tissue index of refraction

θ is the angle between the incident beam and direction of motion of scatterers within the sample

Color Doppler OCT (CD OCT)

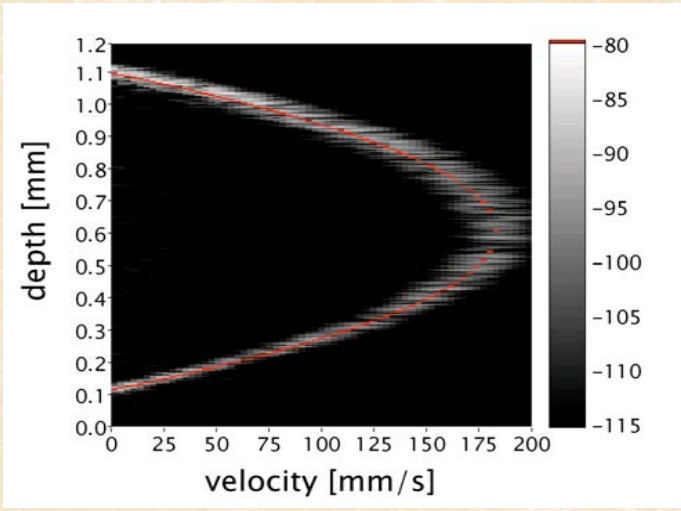


CD OCT: High Velocity Flow Profiles

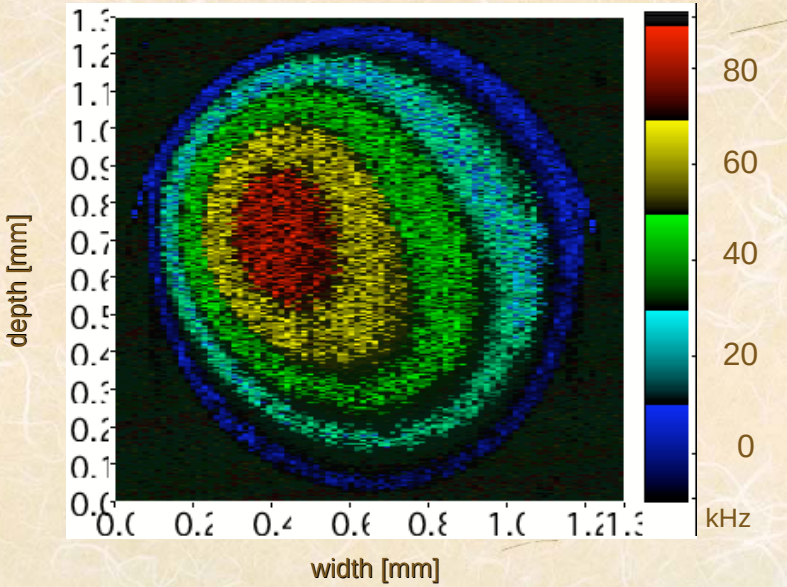


Van Leeuwen, et al.
Opt. Lett. 24:1584 (1999)

CD OCT: Flow Profiles



CD OCT: Flow Profiles



OCT radar