Optical Coherence Tomography

Inferring architectonic structures and connectivity in the brain

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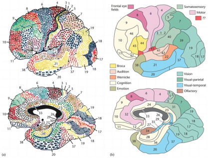
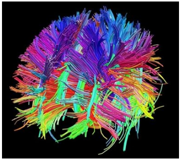
Great interest in architectonic structures

- diseases and disorders
- fMRI
- connectivity





⇒Projects on *ex vivo* imaging

MRI (sequences, post processing, registration to *in vivo*)

- + whole brain
- + higher resolution
- + some architectonics structures revealed
- - brain dependant (aging, fixation, PMI...)
- - a lot of cortical areas can't be delimited

Histology (validation for MRI, guide)

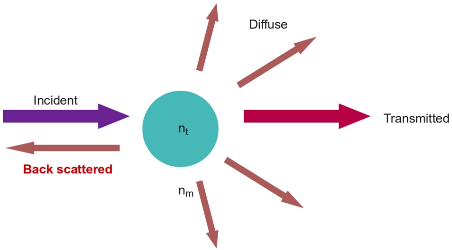
- + whole brain
- + cellular resolution
- + gold standard for architectonic structures
- - labor intensive
- - distortions /deformations due to cutting, mounting and staining
- - different dyes for different interests (cells, myelinated fibers)

⇒ New direction: **OCT**

New direction

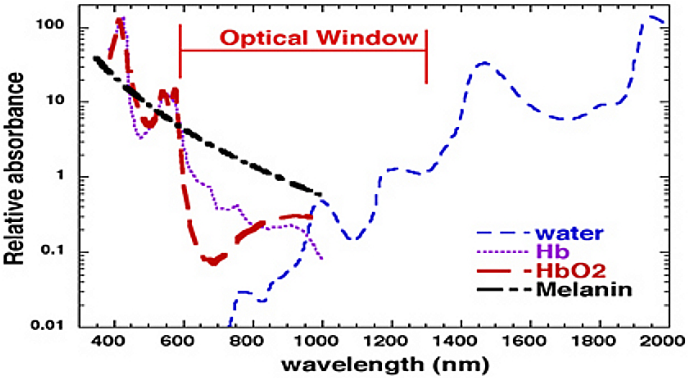
- What is OCT ?
  - Optical: use of light
  - Coherence: use of low coherence interferometry
  - Tomography: 3D volume
- Why use OCT?
  - high resolution : up to 1 μm
    $\Rightarrow$ cells (neurons) : **cytoarchitecture**
    $\Rightarrow$ fibers : **myelooarchitecture & connectivity**
  - relies on intrinsic optical properties
    $\Rightarrow$ no staining
  - image the fixed blockface
    $\Rightarrow$ no or less deformation (compare to histology)

Tissue Optics : Basics



- Cells (*e.g.* neurons)
- Myelinated fibers (the myelin sheath has a high refractive index)

Tissue Optical Window

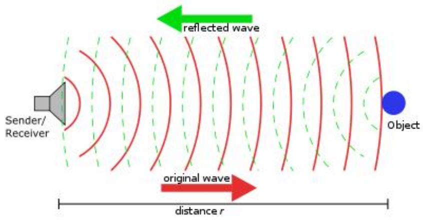


Optical Coherence Tomography

1. Principle
2. Spectral Domain OCT/OCM
3. Image Processing

Principle

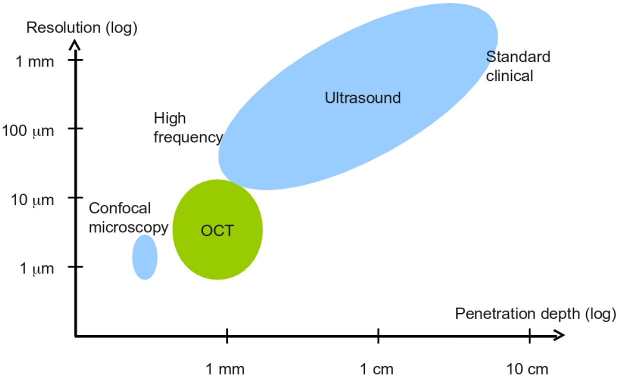
- Introduced by Fujimoto [1]
- 3D technique with high resolution
- Analogue to UltraSound



Speed of sound : 1480 $m.s^{-1}$ (in water)
Speed of light : $3x10^8$ $m.s^{-1}$

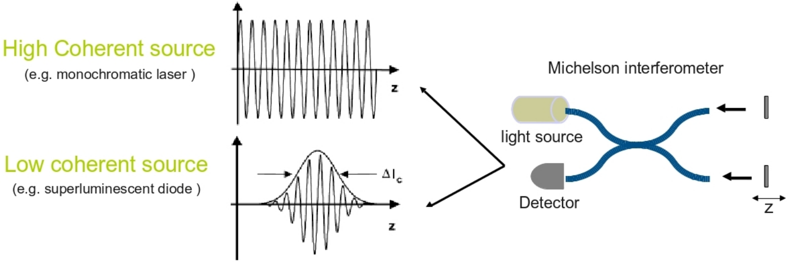
[1] David Huang, Eric A. Swanson, Charles P. Lin, Joel S. Schuman, William G. Stinson, Warren Chang, Michael R. Hee, Thomas Flotte, Kenton Gregory, Carmen A. Puliafito and James G. Fujimoto, "Optical Coherence Tomography ," Science, Vol. 254, 1991.

Principle : Resolution / Penetration

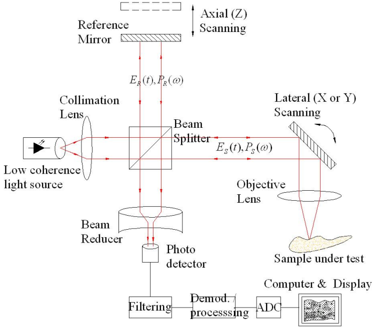


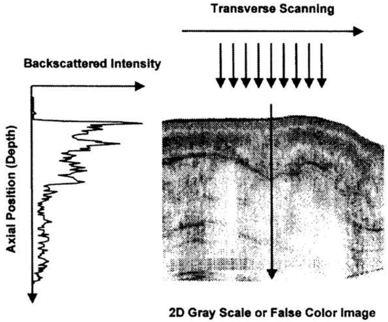
Principle : Interferometry

Light is too fast ⇒ Interference between the reflected light and a reference light

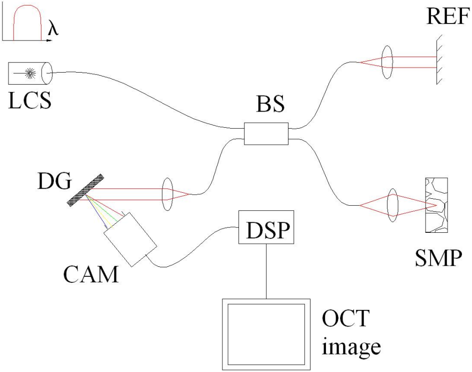


Principle : Time Domain OCT (TD-OCT)





Spectral Domain OCT (SD-OCT)[2]



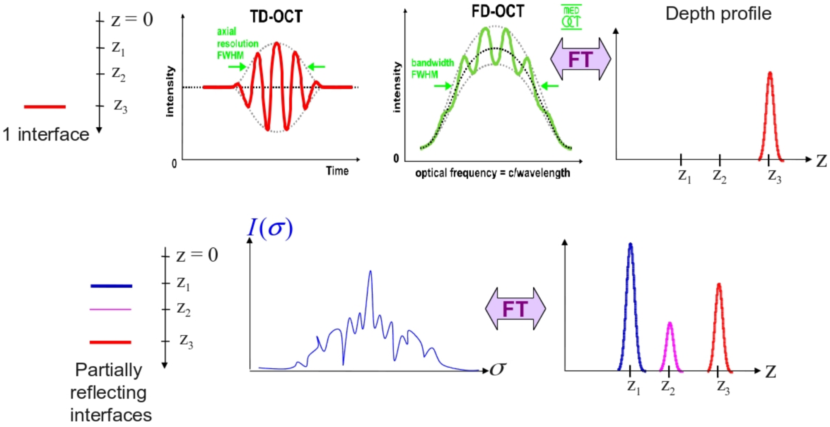
Optical Coherence Microscopy

Objective in the sample arm
⇒ Better resolution

- No movement of the reference mirror
- Faster (1 spectra = 1depth profile)
- Reduced losses

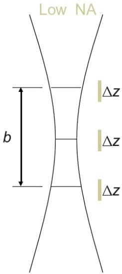
[2] V. J. Srinivasan, et al., "Optical coherence microscopy for deep tissue imaging of the cerebral cortex with intrinsic contrast", Optics Express, 20(3), 2012

SD-OCT vs TD-OCT



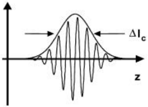
Example

Resolutions and depth of focus



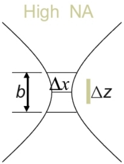
- Axial Resolution : depends on light source bandwith $\Delta\lambda$

$$l_c = \frac{2\ln 2}{\pi}\frac{\lambda_0^2}{\Delta\lambda}$$



- Lateral Resolution : depends on the objective (Numerical Aperture)

$$\Delta x = \frac{2\lambda_0}{\pi \mathrm{NA}}$$



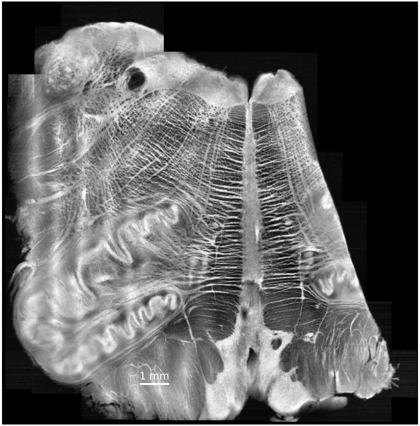
- Depth of focus : depends on the objective (Numerical Aperture)

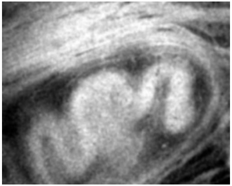
$$b = \pi\frac{\Delta x^2}{2\lambda_0}$$

Example : Medulla (brain stem)

SuperLuminescent Diode (SLD)

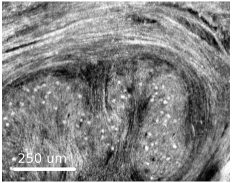
- $\lambda_0 = 1310$nm
- $\Delta\lambda$=170nm





Obj. 10x, NA 0.3

Axial res. 3.5 µm
Lateral res. 3 µm
Depth of focus 20 µm

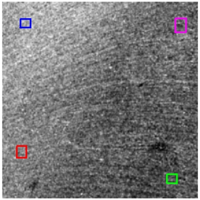


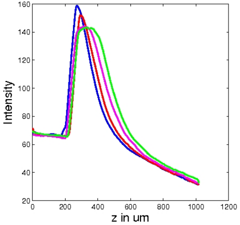
Obj. 40x, NA 0.8

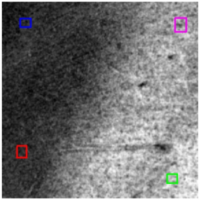
Axial res. 3.5 µm
Lateral res. 1 µm
Depth of focus 3 µm

Image Processing

- 1 acquired volume = 1.5 mm x 1.5 mm x 1.5 mm (10x obj.)
- Average Intensity Projection over 400 μm below the surface
- Maximum Intensity Projection over 400 μm below the surface
- XY translation stage
- Stitching: Fiji plug-in based on Fourier shift theorem [3]







[3] S. Preibisch, S. Saalfeld, P. Tomancak, "Globally optimal stitching of tiled 3D microscopic image acquisitions", Bioinformatics, 25(11), 2009

Image Processing

Isocortex, Brodmann areas 36 and 20

Average Intensity Projection

Cytoarchitecture

Maximum Intensity Projection

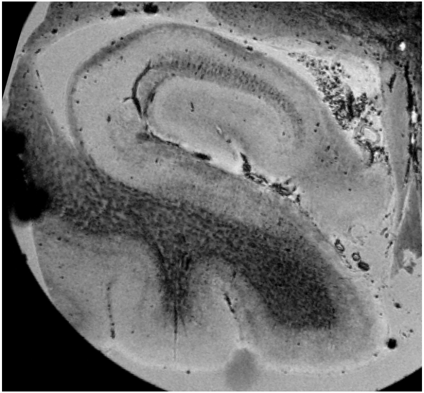
Myeloarchitecture

Architectonics Structures

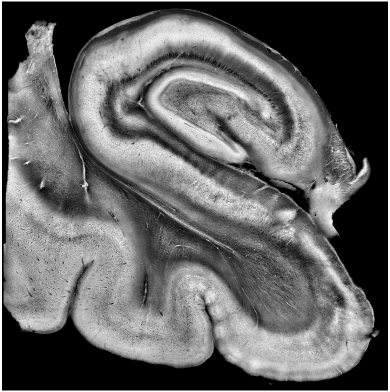
1. *ex vivo* MRI vs. OCT
2. Cortical boundary: EC / PC
3. Nissl stain *vs.* OCT: isocortex
4. Assessment of deformations

ex vivo MRI *vs.* OCT: hippocampus

7T, FLASH, 60 μm^3, TE=22ms, TR=55ms, FA=25°, 1 run



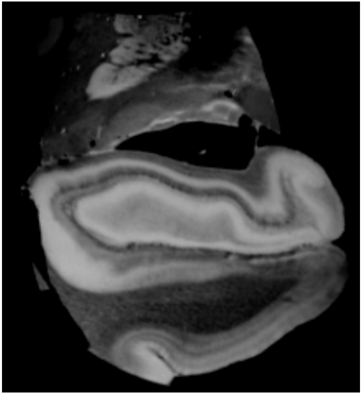
OCT
lateral resolution: 3 μm



73 y.o., Male, PMI < 24hrs, length of fixation 4 months

Entorhinal / Perirhinal Cortex boundary

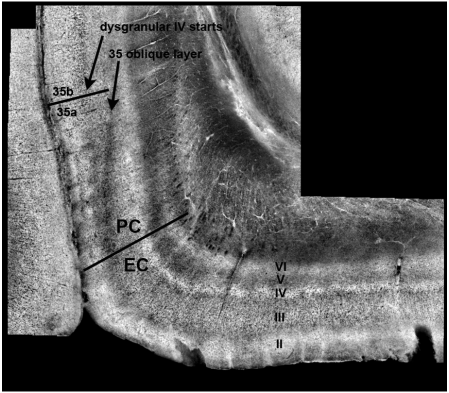
7T, FLASH, 100 μm^3, TE=20ms, TR=40ms, FA=20°



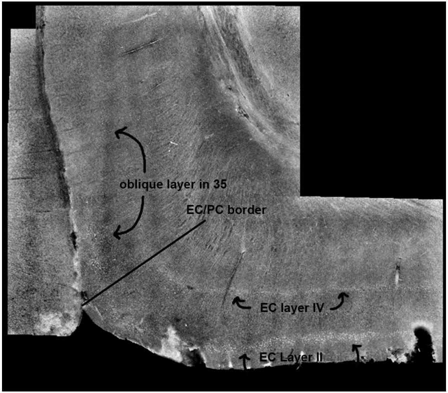
67 y.o., Male, PMI 12hrs

Entorhinal / Perirhinal Cortex boundary

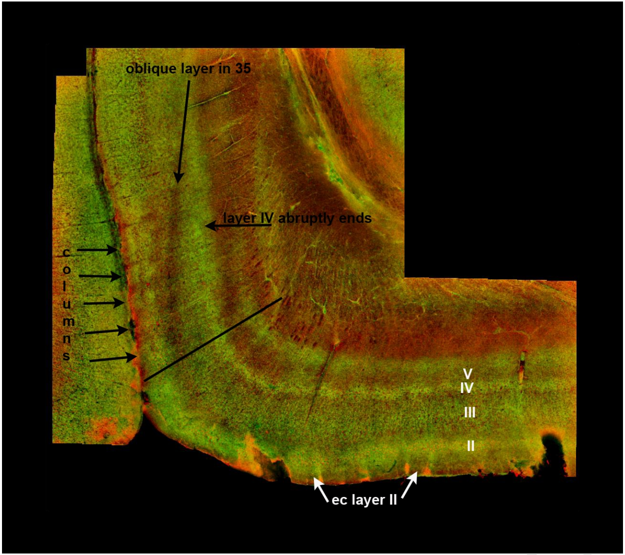
Average Intensity Projection



Maximum Intensity Projection



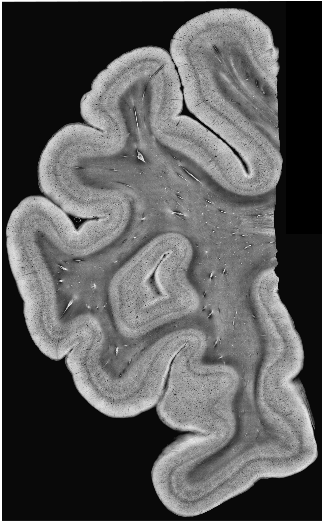
Entorhinal / Perirhinal Cortex boundary



Nissl Stain *vs.* OCT: isocortex

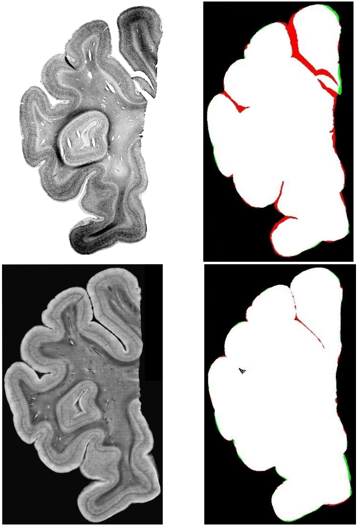
Gold standard: Nissl stain

OCT (Average Intensity)



Deformations: registration to the blockface

Blockface



Connectivity

OCT-based Tractography

1. Principle and Process
2. Comparison with DTI

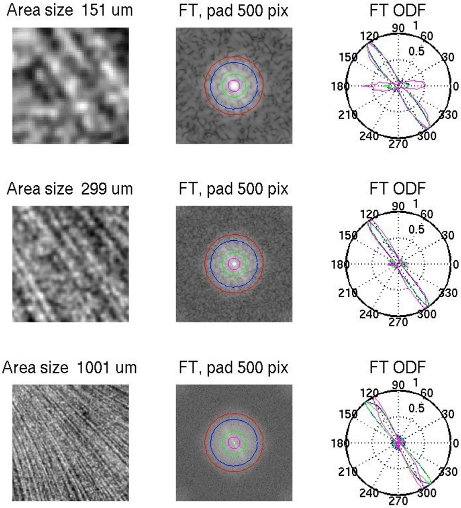
Principle and Process

- Maximum Intensity Projection
- Resolution for the Orientation Density Function (ODF) (*area*)
- Frequency Domain[4]

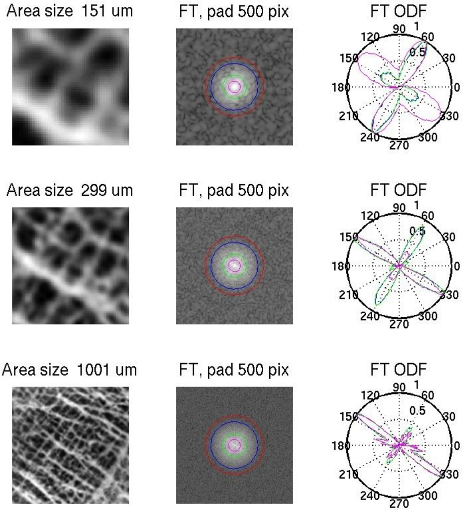
1. Hanning window
2. Padding (*pad*)
3. Fourier Transform
4. ODF reconstruction (*radius*)
5. Preferential Direction(s) (*maxima of the ODF*)

[4] C. J. Goergen, H. Radhakrishnan, D. E. Sosnovik, S. Sakadzi, and V. J. Srinivasan, "Optical coherence tractography using intrinsic contrast", Optics Letters, 37(18), 2012

Influence of radius: simple case

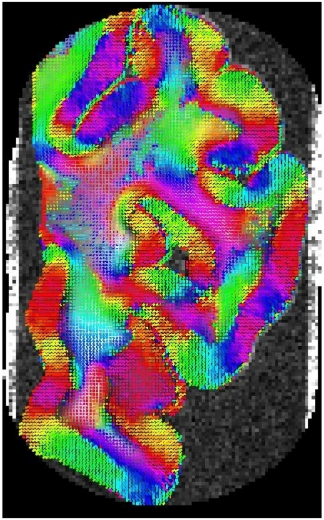


Multiple directions

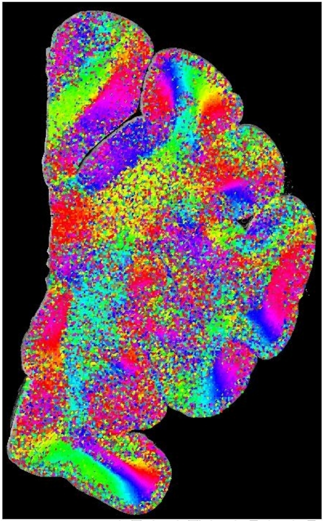


DTI vs. OCT

DTI: 4.7T, 300μm^3, 2 low-b img, 20 dir, b=2048, TE=28ms, TR=320ms, FA=180°



OCT: lateral resolution = 3μm
ODF :area 300μm, step 150μm



Future work

- **3D reconstruction / 3D ODF**
  - **Vibrotome + XYZ Translation Stages**
    - Tim Ragan, Phil Knodle (Tissue Vision) [5]
    - Octopμs
  - **Imaging a volume of human brain (several cm^3)**
- **Registration with MRI**
- **Comparison with DTI and DSI**
- **Polarization-sensitive OCT** [6]

[5] T. Ragan, J.D. Sylvan, K. Kim, et al, "High-resolution whole organ imaging using two-photon tissue cytometry," J. Biomed. Opt. 12(1), 2012.

[6] Wang, H., et al., "Reconstructing micrometer-scale fiber pathways in the brain: Multi-contrast optical coherence tomography based tractography", NeuroImage, 58(4), 2011.