Optical Coherence Tomography

missing link in medical imaging

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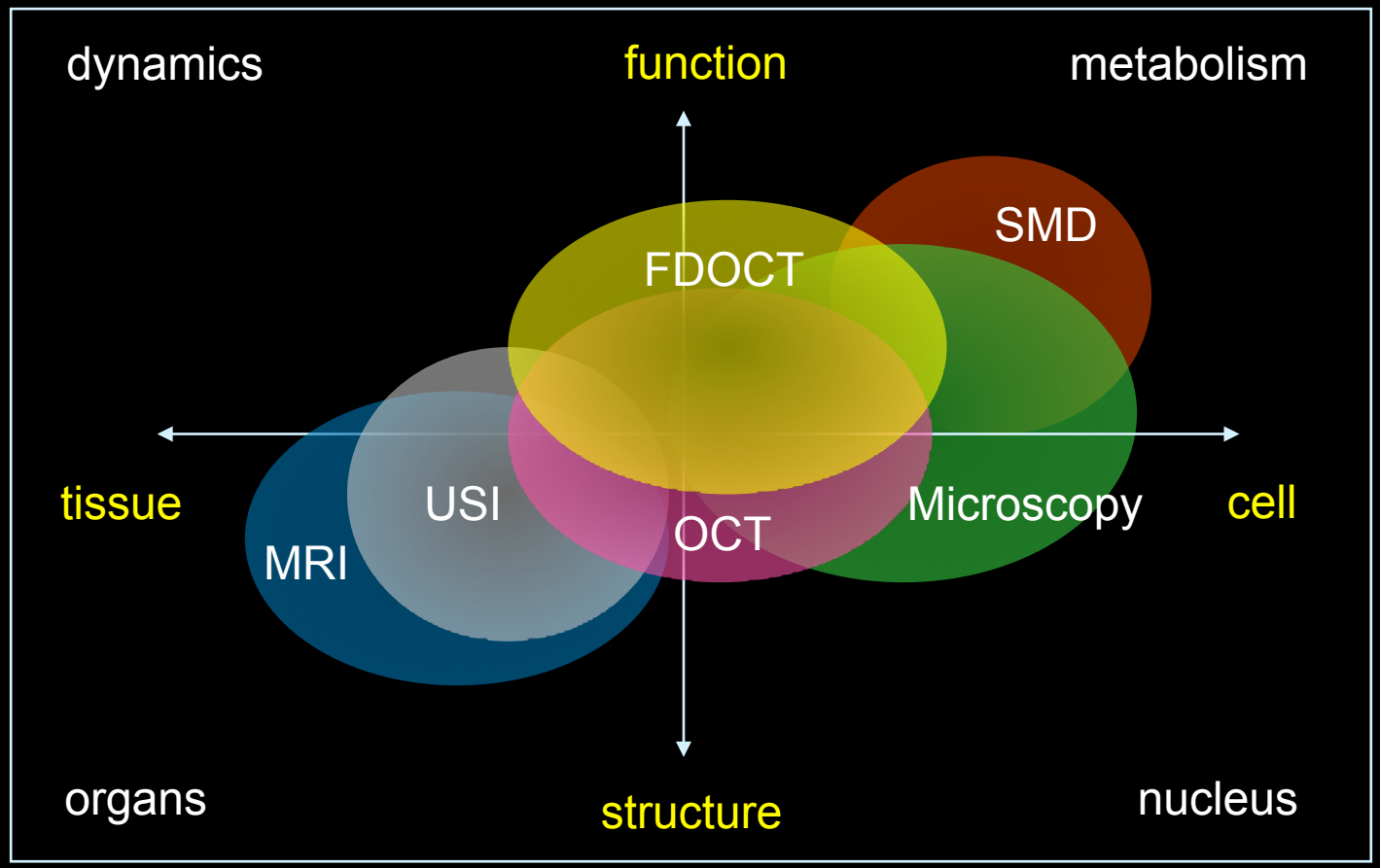
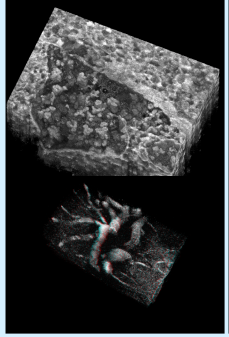
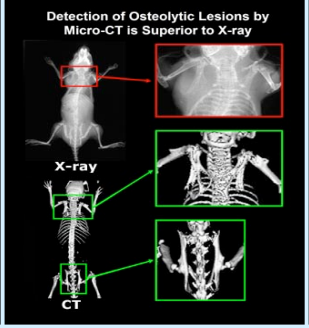
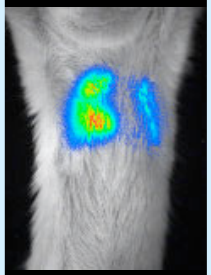
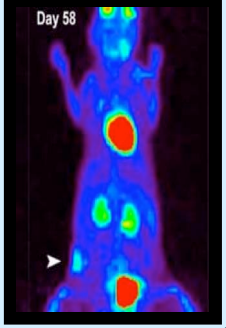
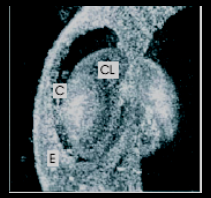

dynamics
function
metabolism
SMD
FDOCT
tissue
USI
MRI
OCT
Microscopy
cell
organs
structure
nucleus

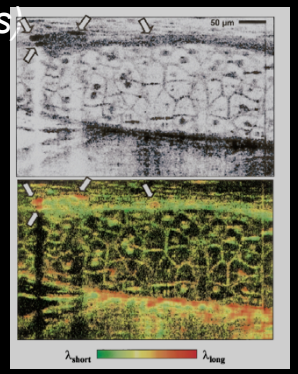
Tomographic Methods

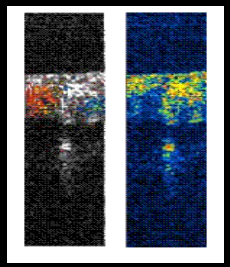
Method	OCT	µCT	MRI	USI	ODT	PET
Resolution	+++	++	-	-	-	-
Non Hazard	+++	- -	++	++	+-	-
Tissue depth	-	+++	+++	++	+	+++
Speed	+++	-	-	++	- -	- -
Molecular contrast	- +	-	+	- -	+++	++
flow	+++	- -	- +	+ +	- -	- -
						

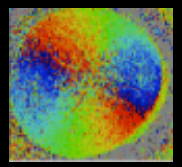
En-lightening Information

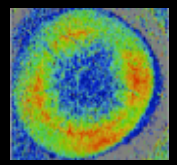
Property of Light	*Sample Property*
Intensity	*Reflectivity (refractive index gradients)*
Spectrum	*Absorption, Scattering*
Phase	*Dispersion, dynamic structural changes*
Polarization	*Retardance, Rotation*
Flourescence	*Lifetime, molecular compostion*

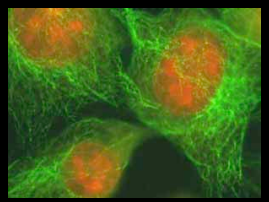












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OCT impact

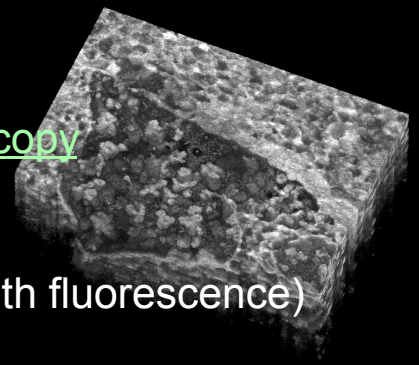
OCT - Selected Chapters

Structural

Optical Coherence Tomography

Applications: retinal Imaging, full anterior chamber, endoscopy

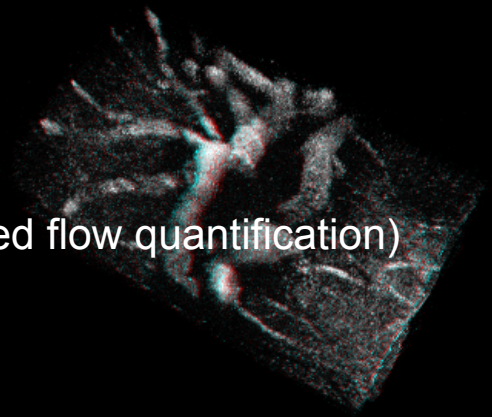
Optical Coherence Microscopy with extended focus depth
(endocrine pancreas, mouse breast, brain, combination with fluorescence)



Ultrahigh Speed FDOCT

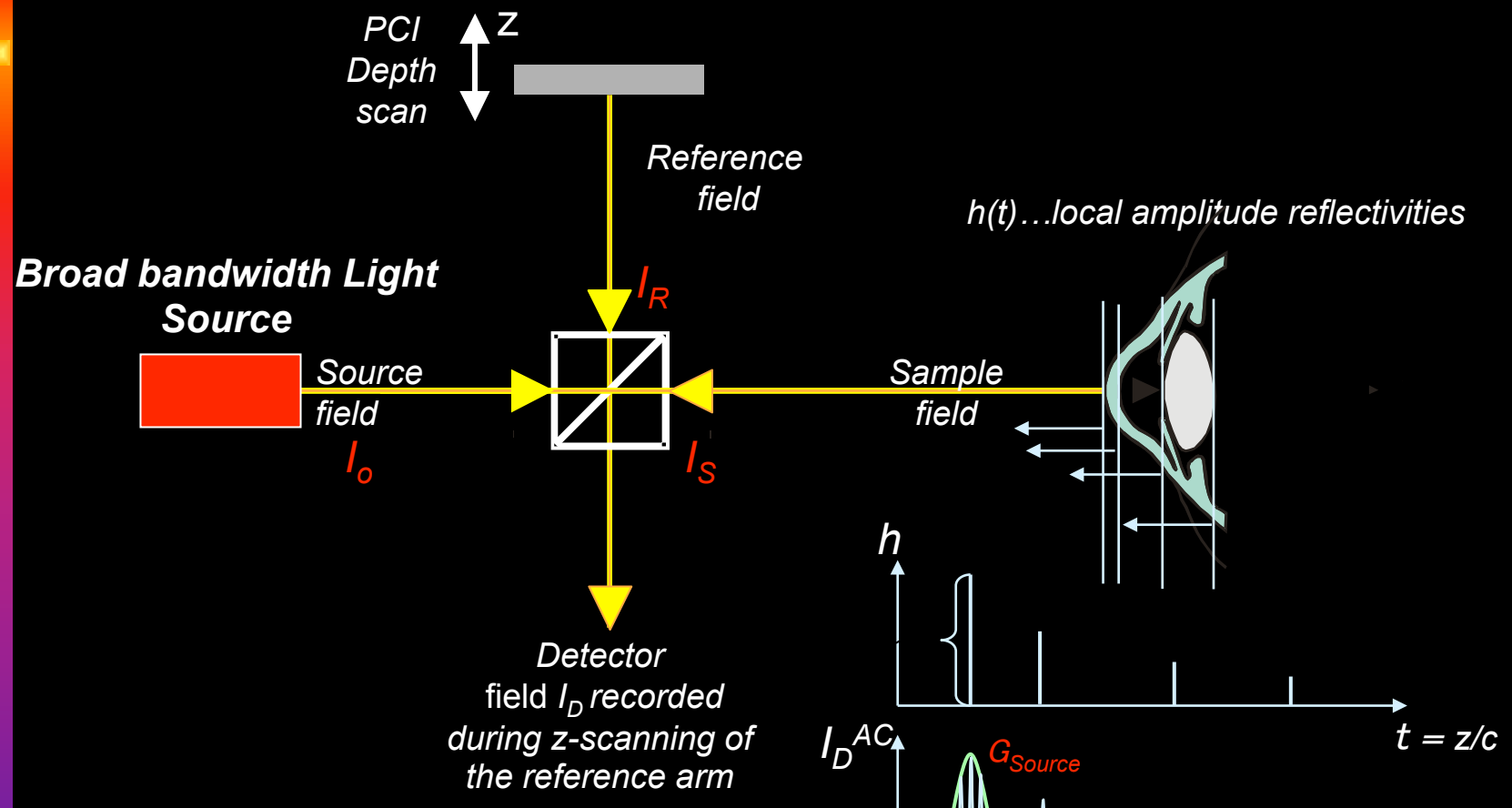
Functional

Doppler µ-Tomography
(optical vivisectioning of retinal vessels, intensity based flow quantification)



Optical Testing of Retinal Physiology
(frequency encoded testing of receptor response)

Partial Coherence Interferometry



$$I_D(t) = \underbrace{I_S + I_R}_{I_D^{DC}} + \underbrace{2\,\mathrm{Re}\,[G_{Source}(t) \times h(t)]}_{I_D^{AC} \propto 2\sqrt{I_S I_R}}$$

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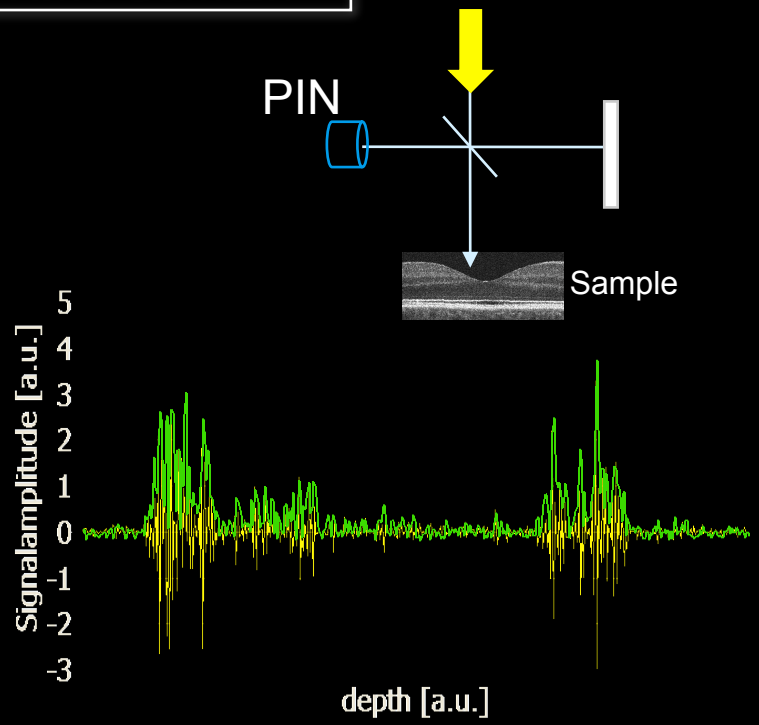
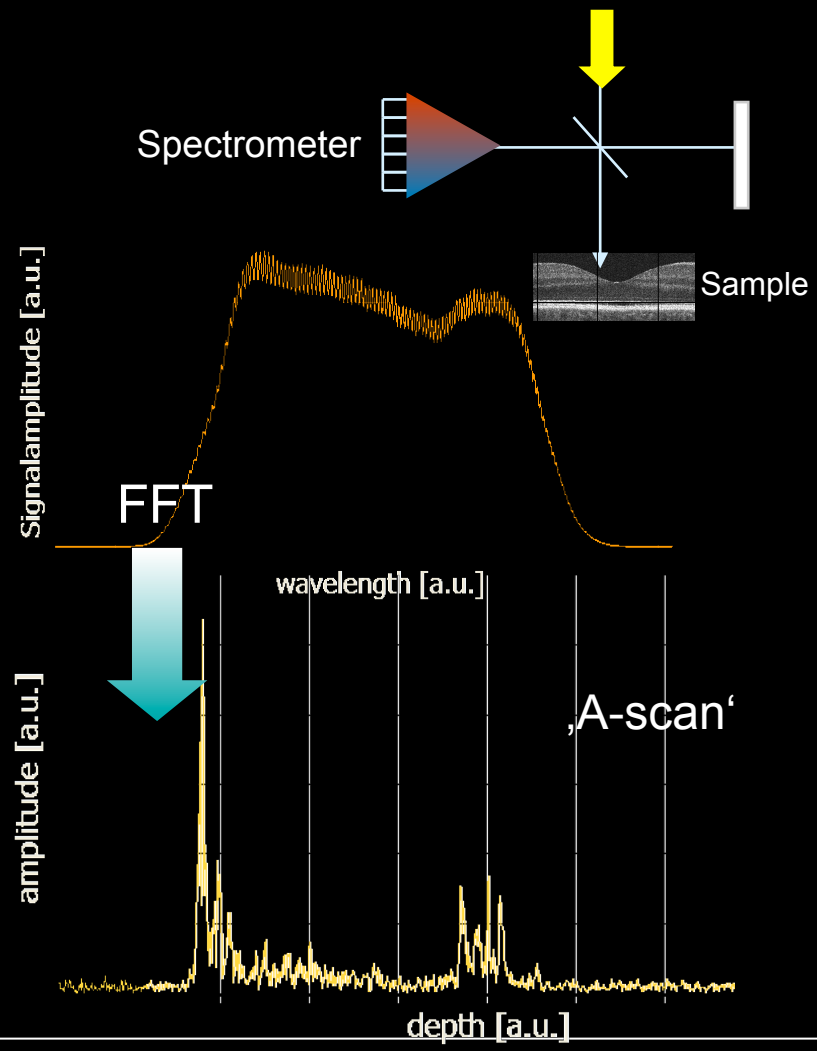
OCT Methods

Time domain



A-scan

Fourier domain

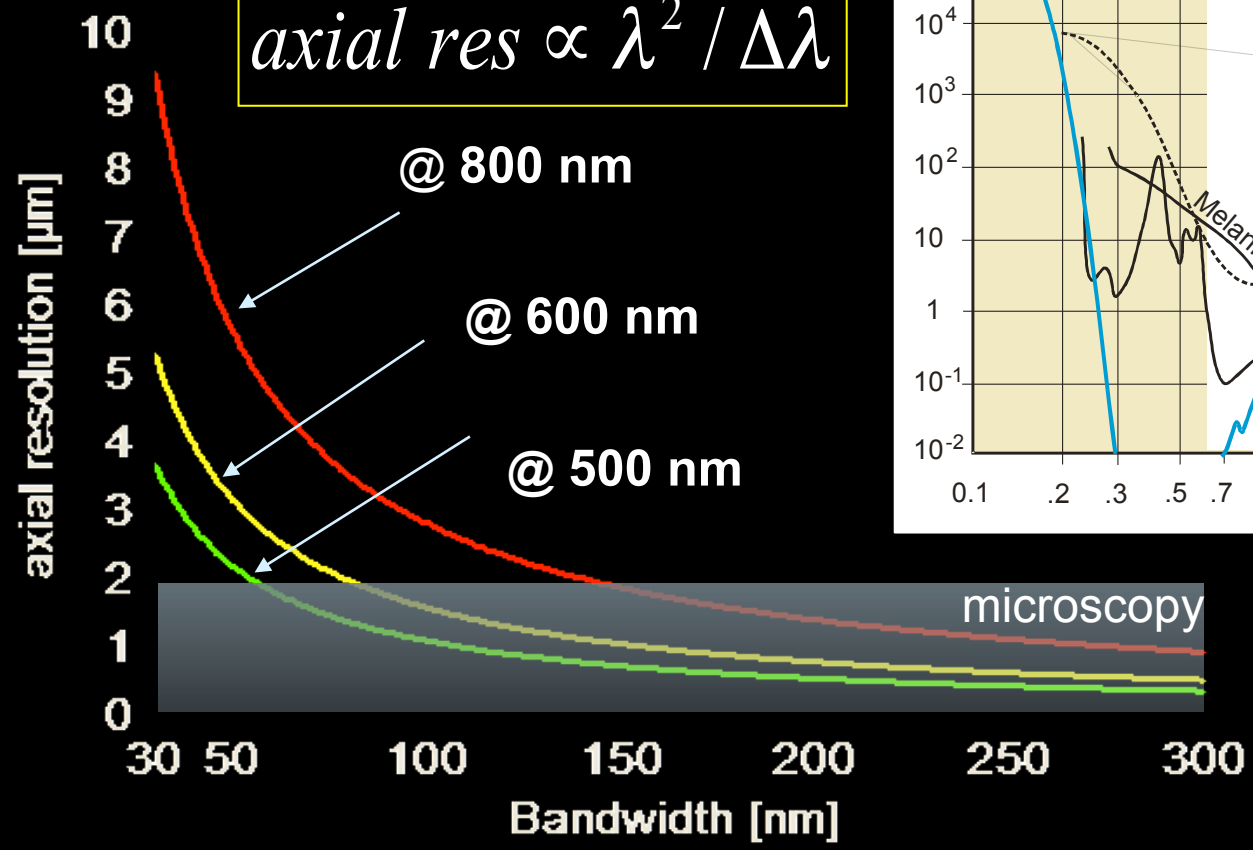


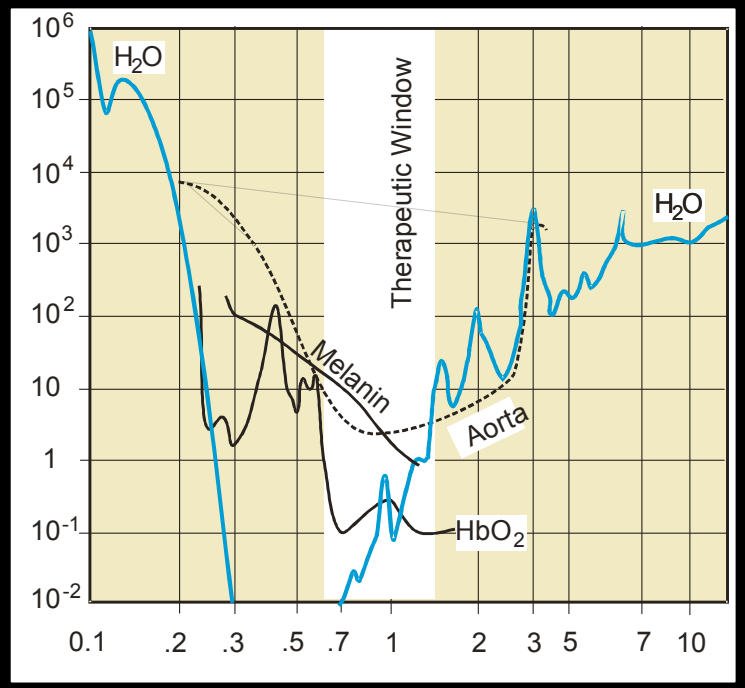
‚A-scan'

Resolution

OCM depth resolution is decoupled from transverse resolution

$$axial\ res \propto \lambda^2 / \Delta\lambda$$

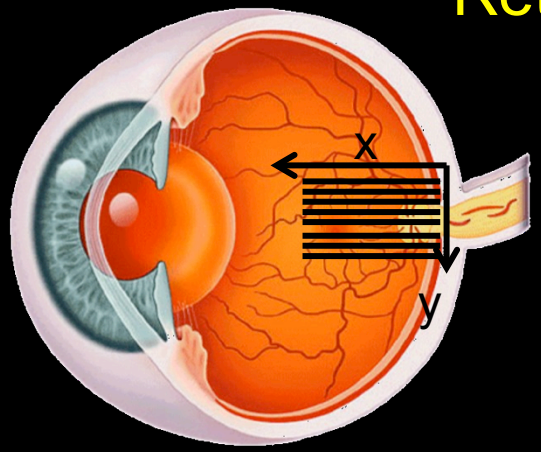


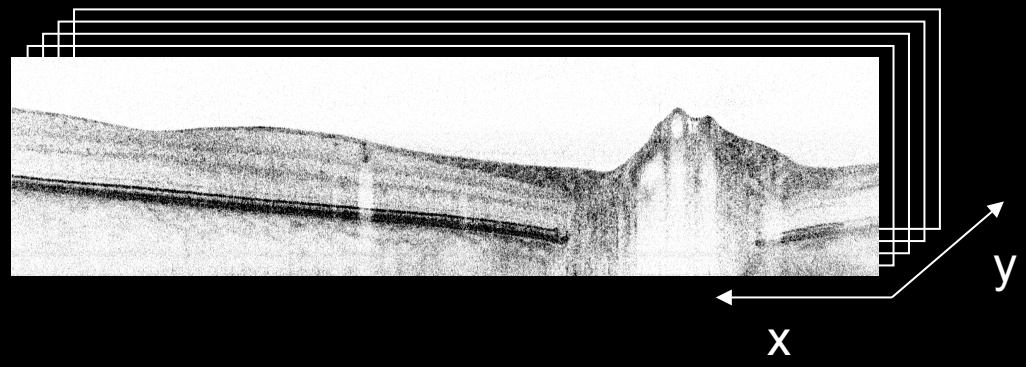


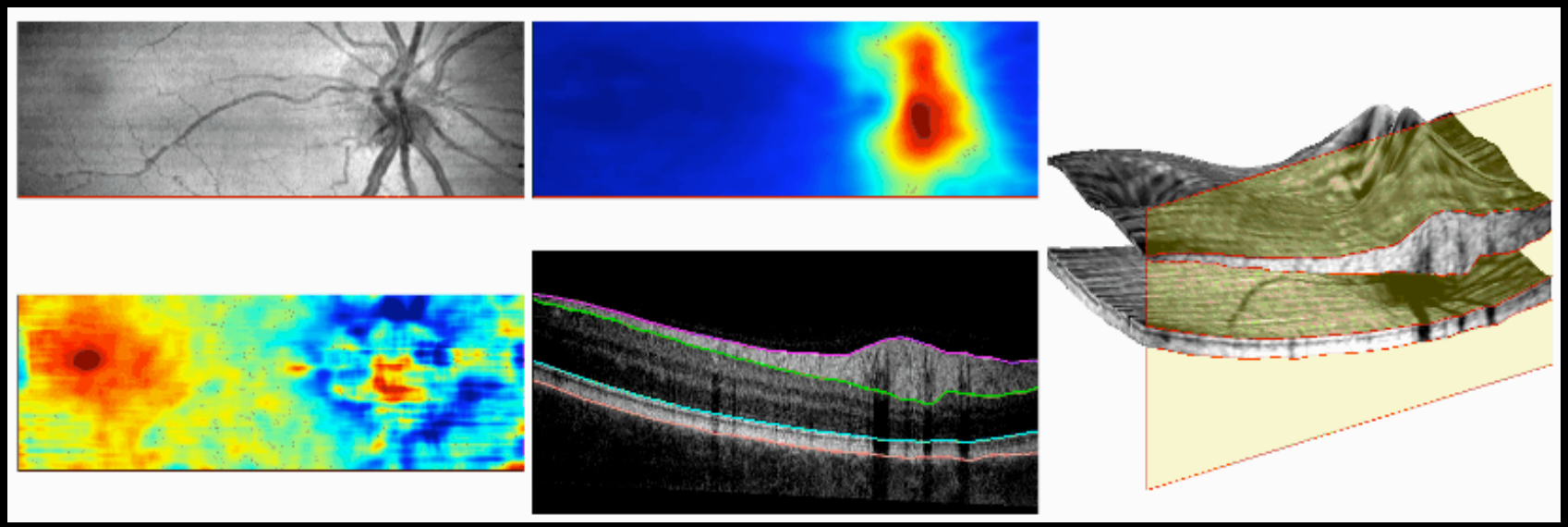
Assumptions: Gaussian Spectrum

Ophthalmology

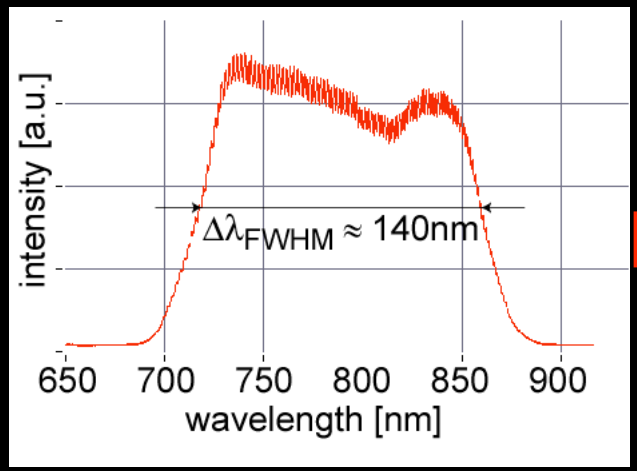
Retinal in-vivo tomography





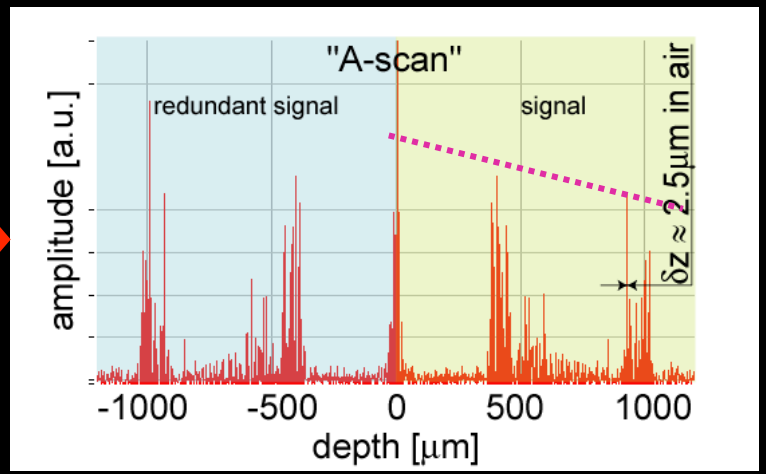


FDOCT Drawbacks



λ -> k

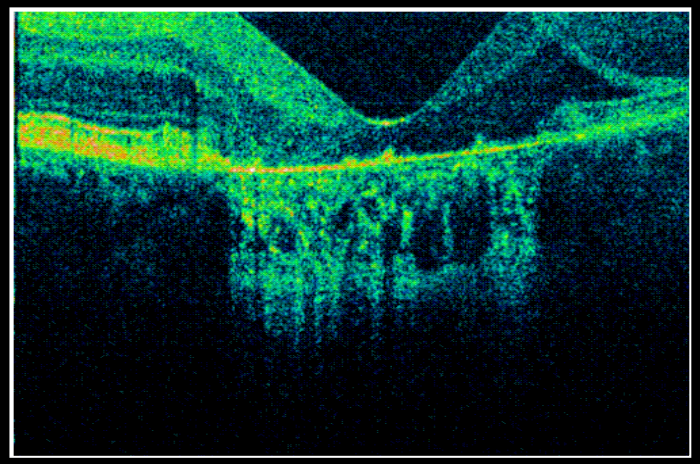
FFT

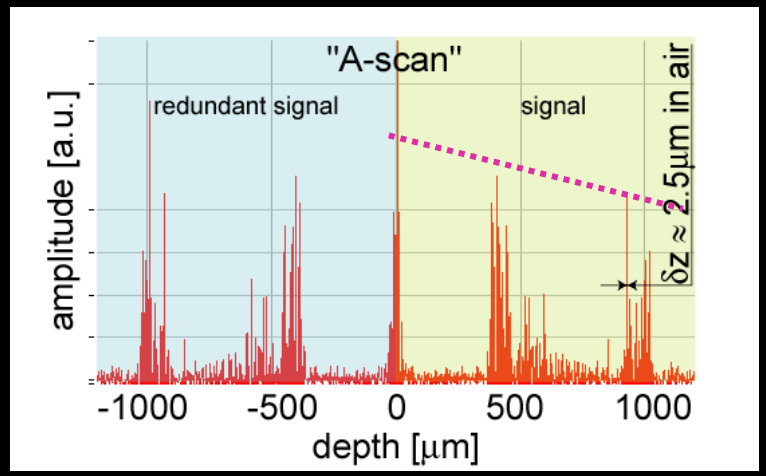


Main drawbacks (spectrometer-based FDOCT):

- Rigid depth range (sampling by array pixel number)
- Depth dependent sensitivity
- Fringe washout for moving structure
- Mirrored/redundant structure terms

FDOCT Drawbacks





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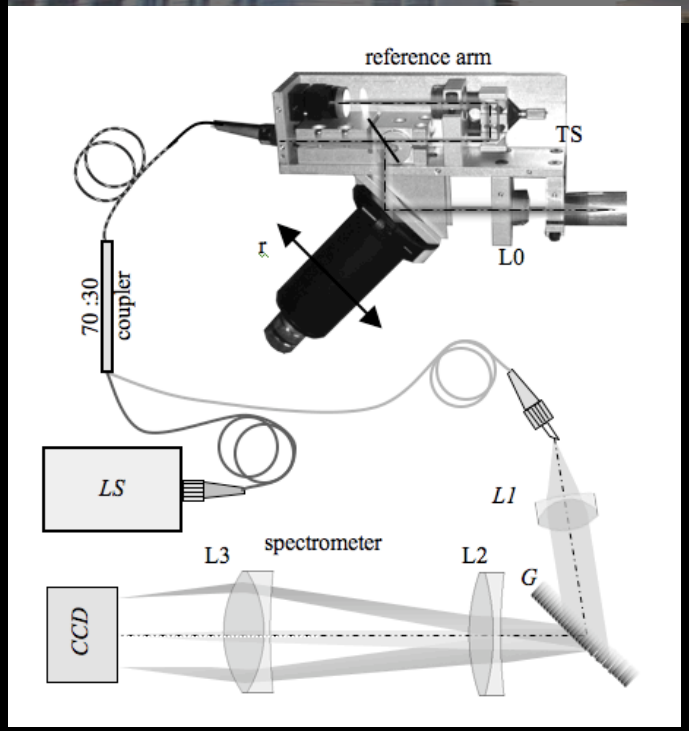
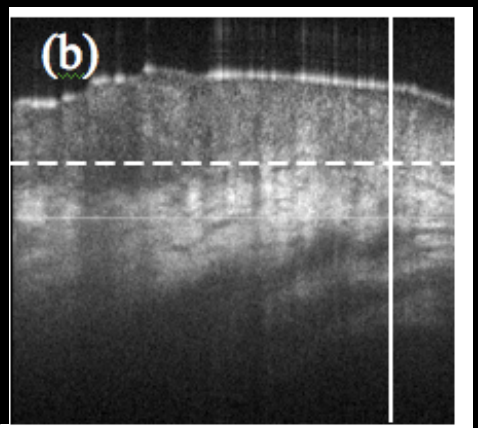
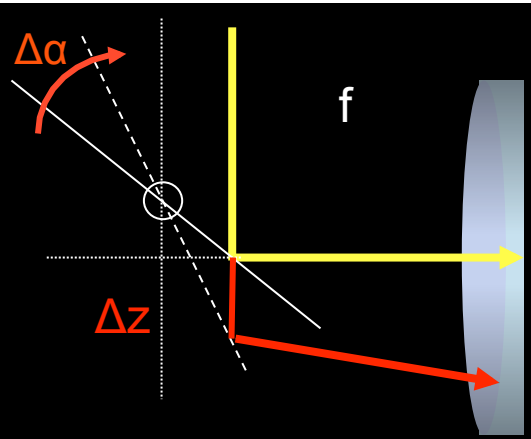
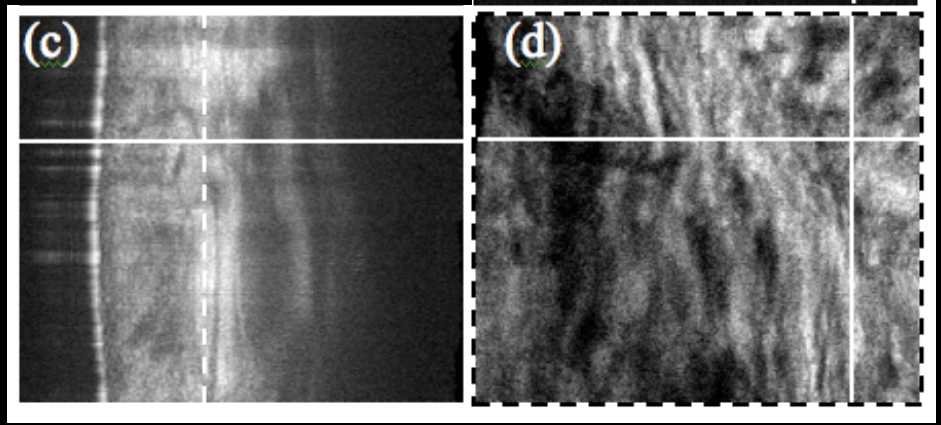
Tissue imaging – Complex Ambiguity



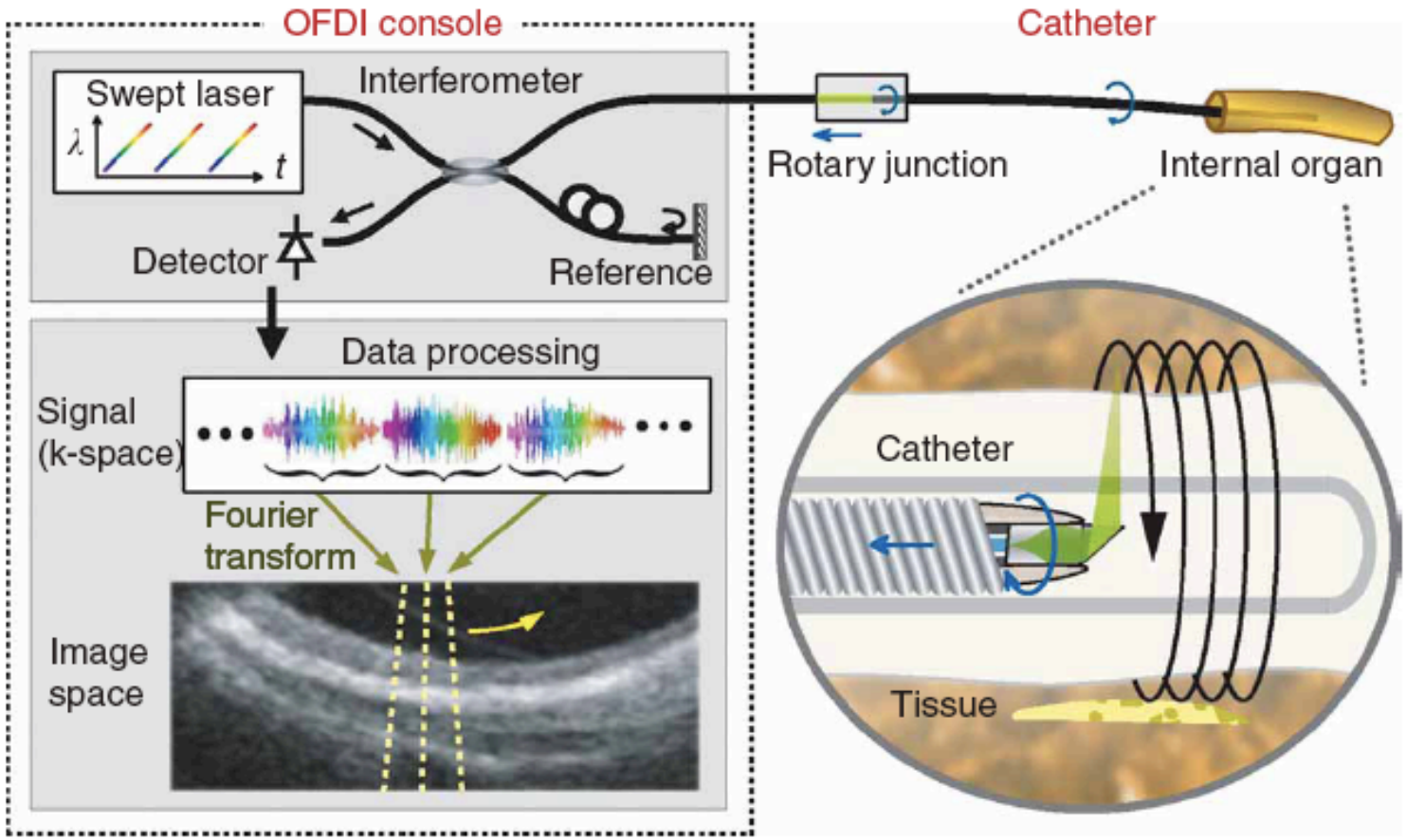
Tomogram of human inner lip (3mm x 2.5mm)
Wavelength 1300nm
Axial resolution 10µm







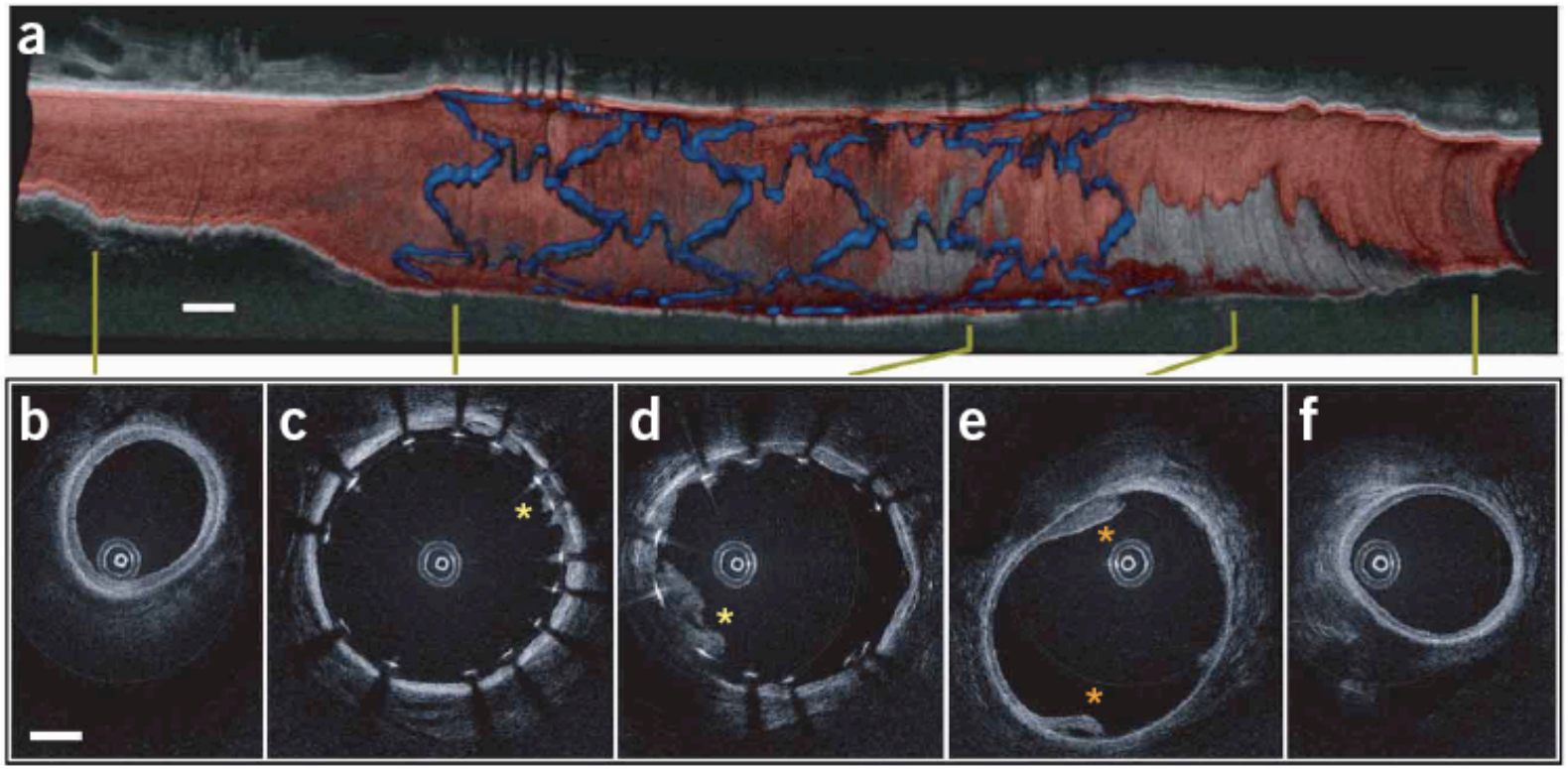
Endoscopic OCT – swept source OCT



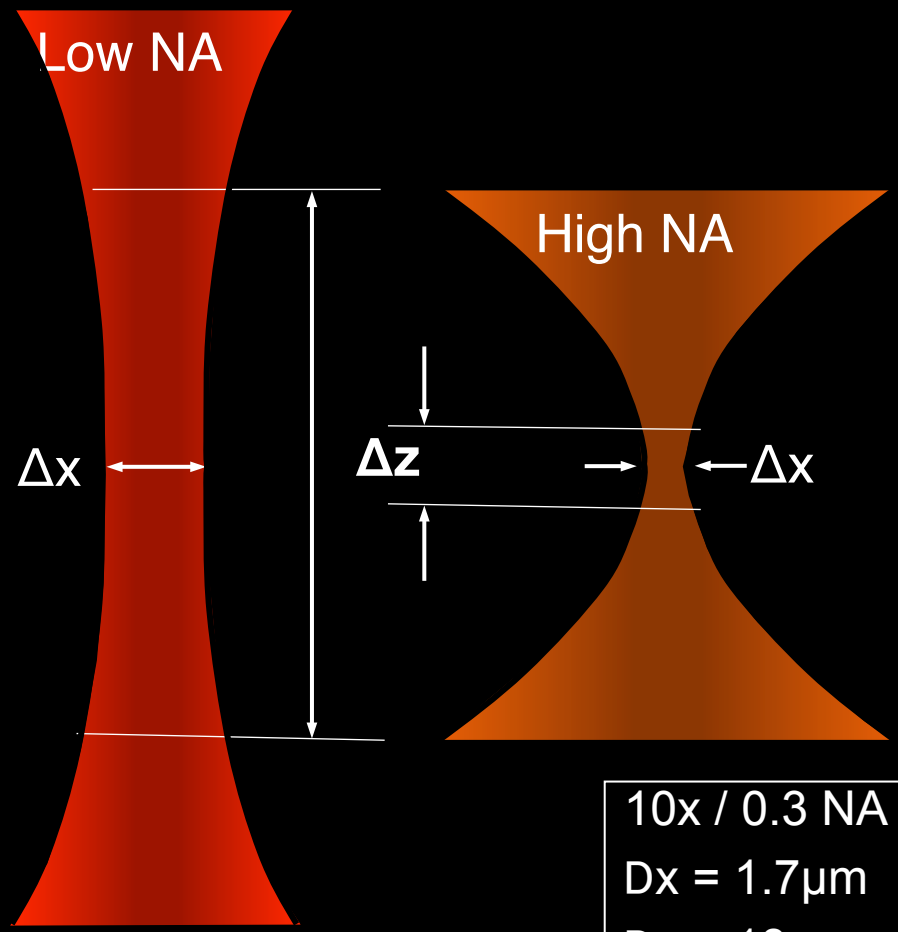
Endoscopic OCT

porcine coronary artery with stent in-vivo

scale bar 1mm, acquired in 6 sec



Optical Coherence Microscopy OCM



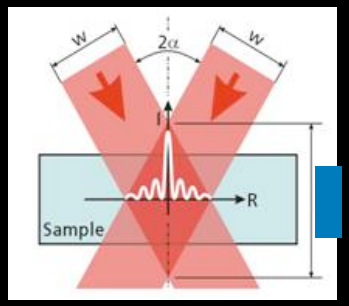
10x / 0.3 NA / 800nm

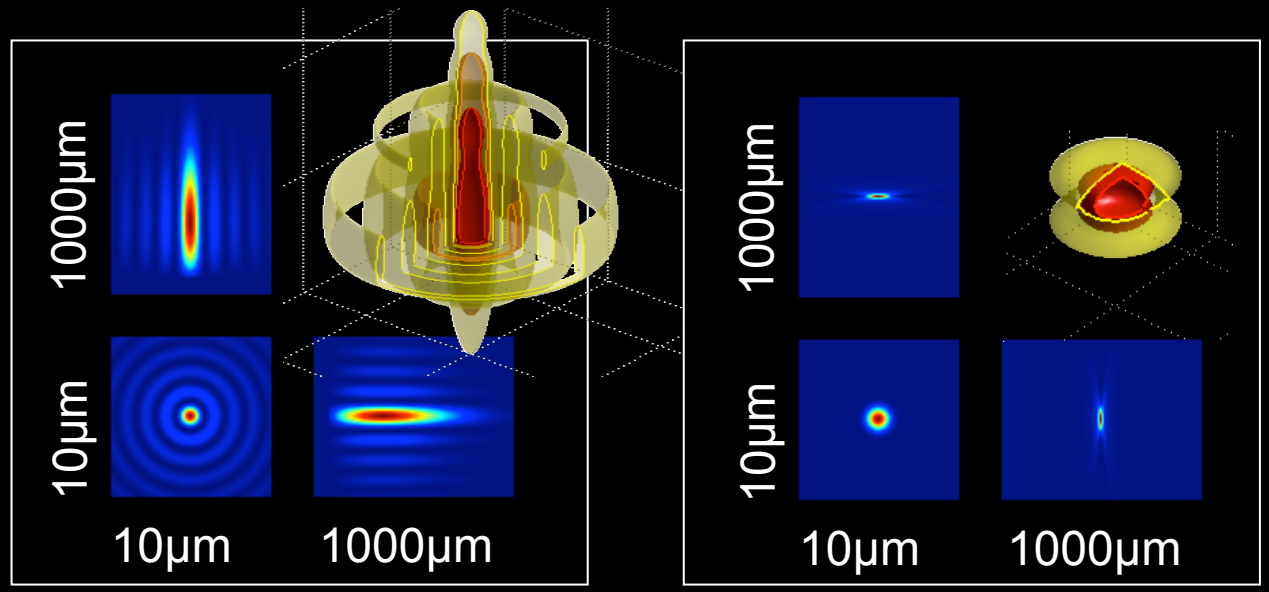
Dx = 1.7µm ☑

Dz = 18 µm ☹

Optical needle

Achieving a long illumination needle by creating an interference pattern in the sample space





Leitgeb et al, Opt. Lett 2006

Optical needle

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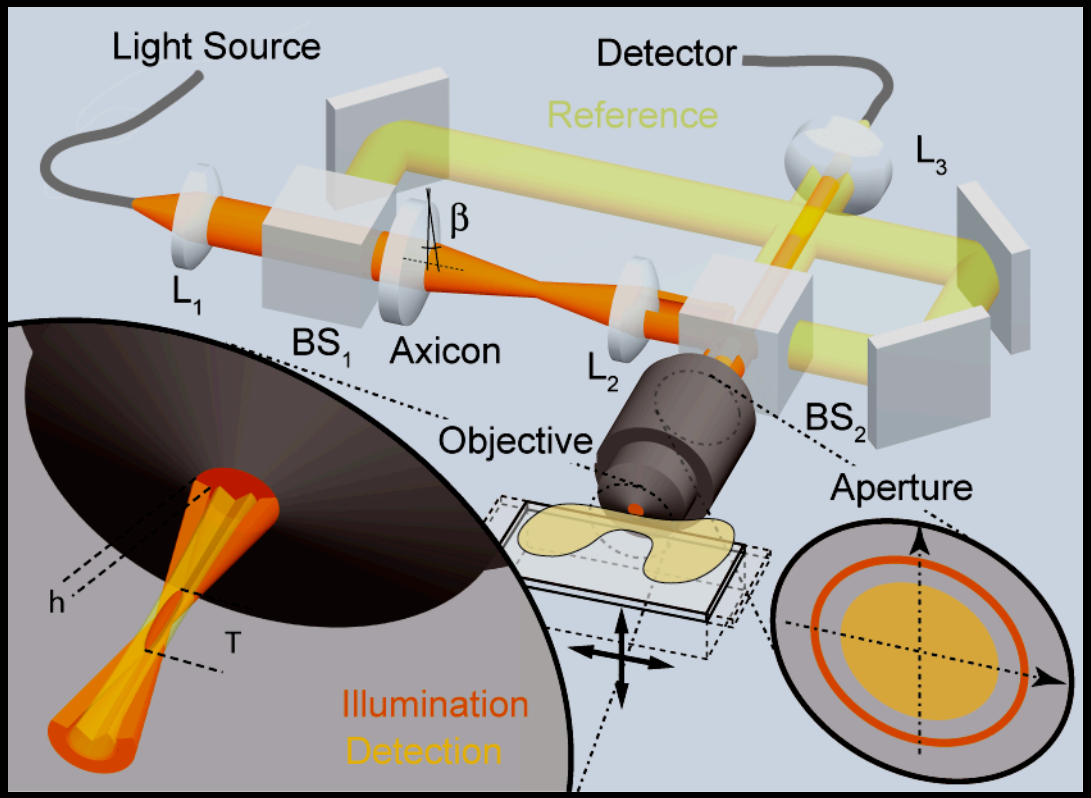
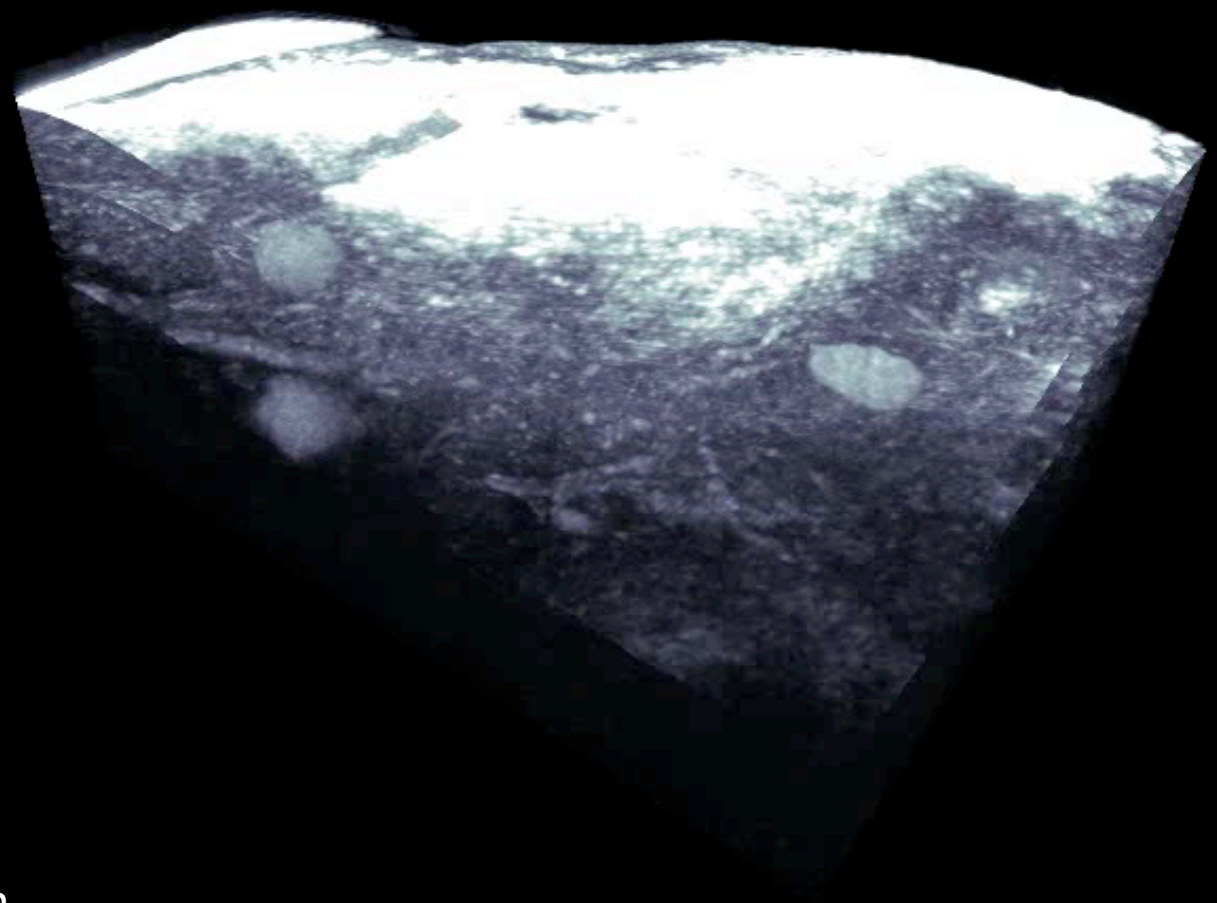


Applications – Pancreas Imaging

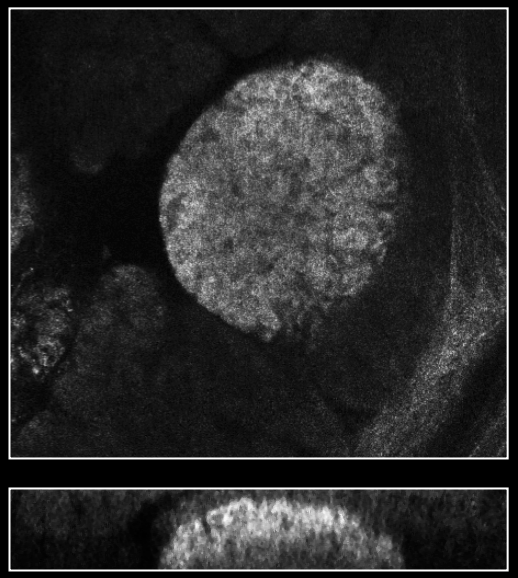
Application to diabetes research (visualization of Langerhans islets within unprepared mouse pancreas in-vitro and in-vivo)



2 x 1.5 mm

Comparision xf-OCM - confocal Microscopy

Mouse Pancreas, in vitro

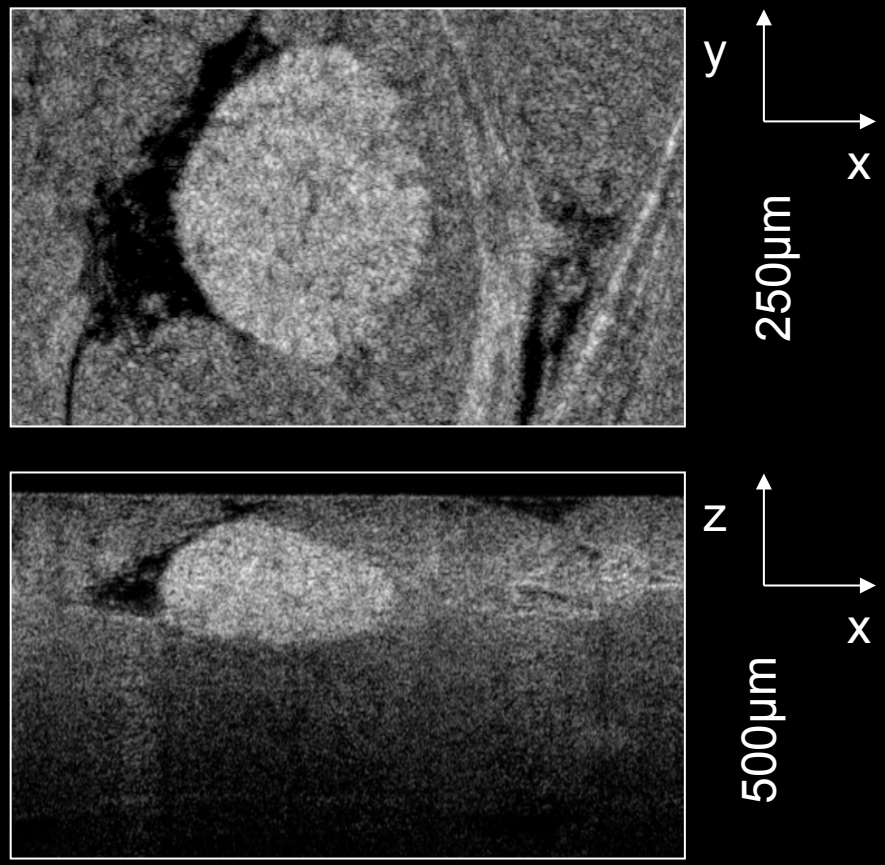


Confocal microscopy

NA 0.8, 20x water immersion

@633nm

400µm



xf-OCM

NA 0.23, 10x air objective

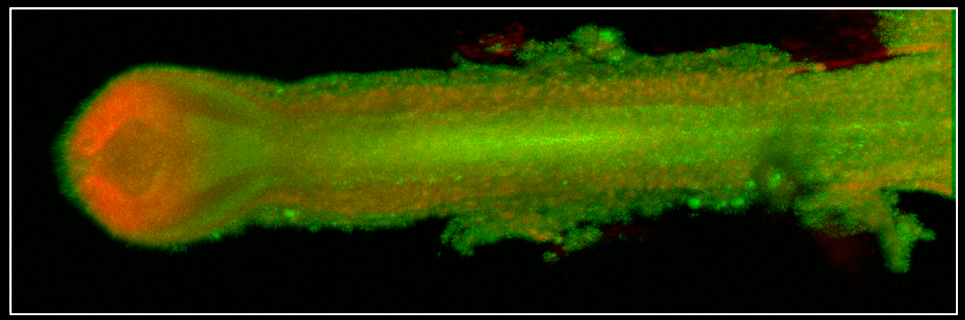
@800nm

Combination xf-FDOCM-Fluorescence - Rat Hair Follicle

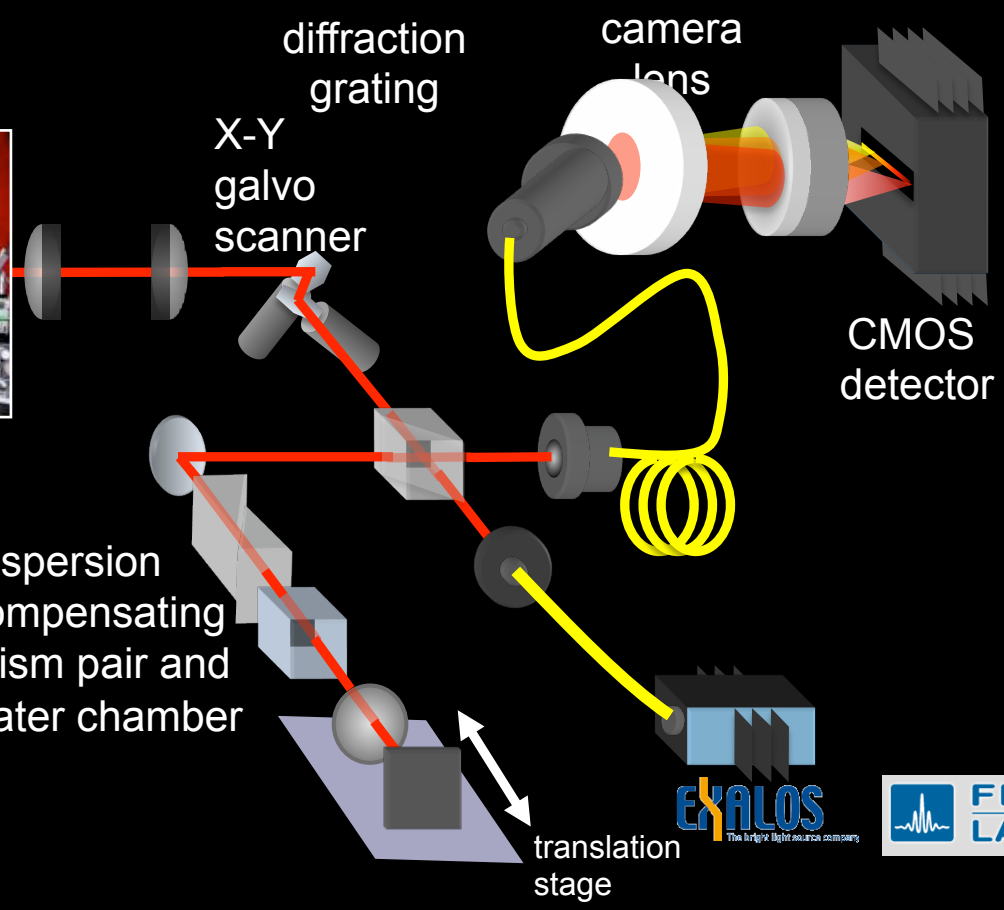
Collaboration with stem cell laboratory, EPFL : lineage specification and cell differentiation

400um x 1.2mm

xf-OCM / FLM
@800nm
& 650nm



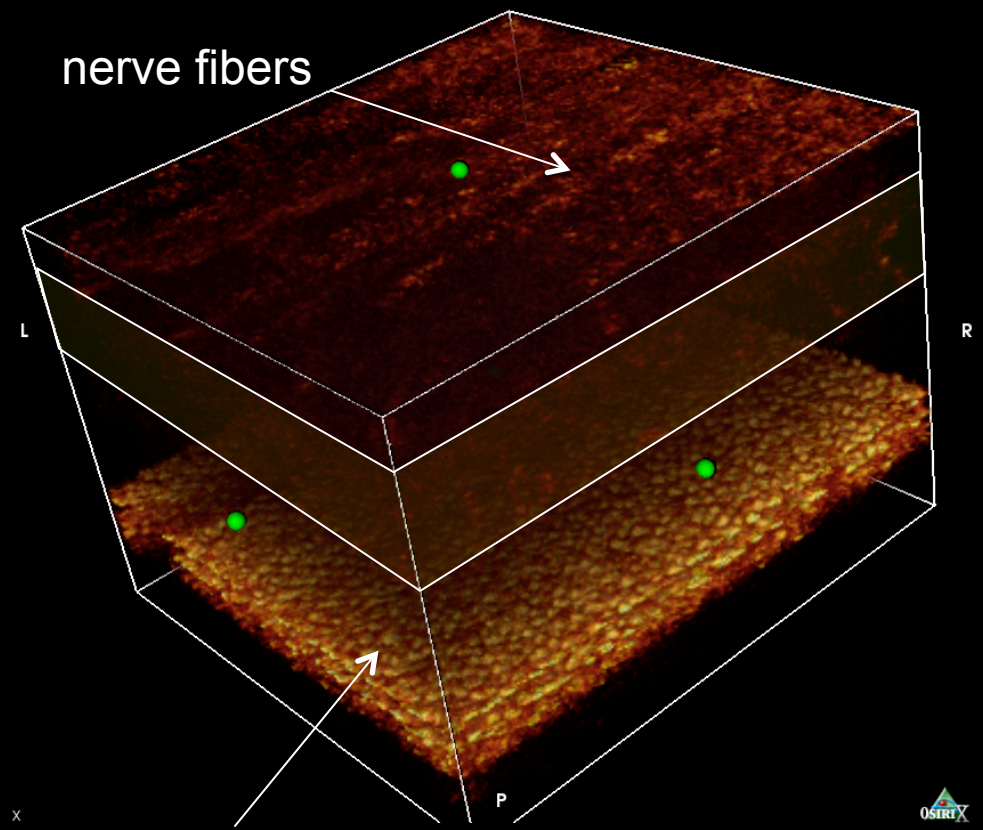
Ultra-high Speed FDOCT

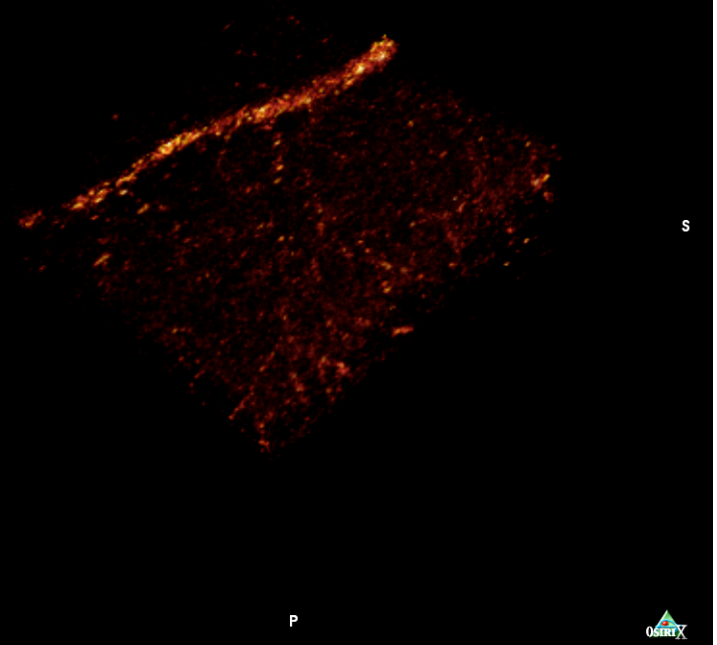


λ	830 nm
Δλ	45 nm
Axial resolution	6.7 µm
Line rate	up to 200 kHz
Sensitivity	92dB -103dB
Sensitivity decay	-9 dB / 2 mm
Power @ cornea	550 µW

Ultra-high Speed FDOCT

300 x 400 x 600 µm (200 x 500 x 600 pixels) taken in only 0.5sec
at 200.000 depth scans / sec

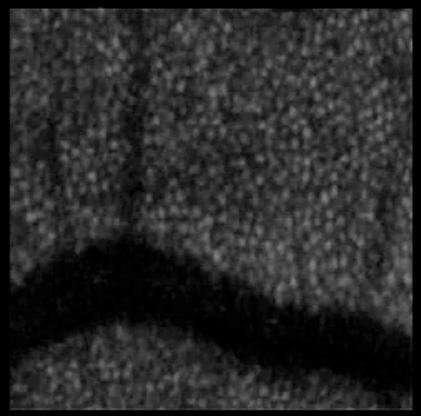


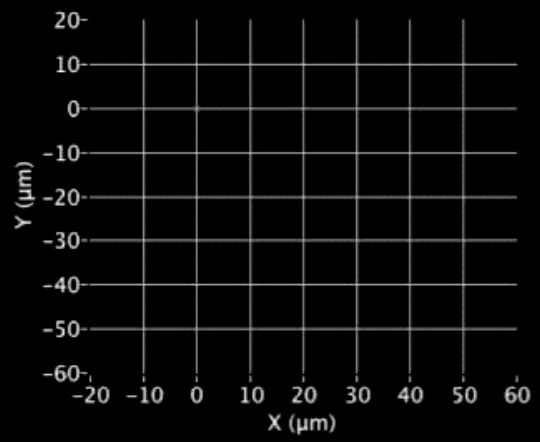


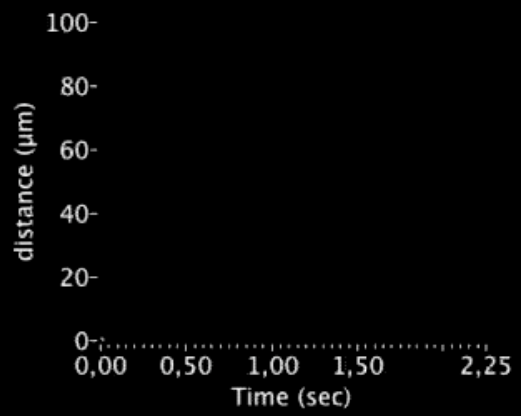
Photoreceptor Imaging without adaptive Optics

CMOS camera at 200kHz
10 full volumes per second (200x 100 x 800)
300µm x 300µm patch

0.00 sec







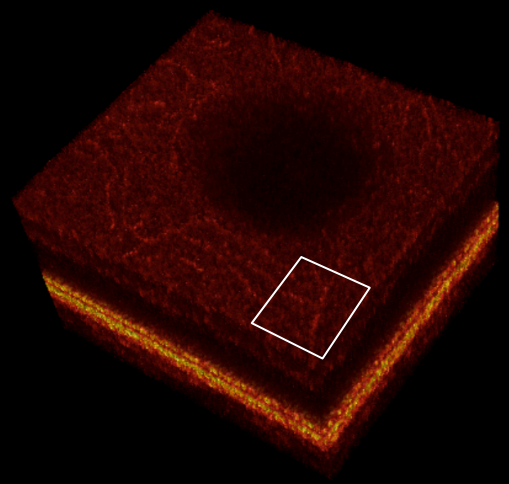
Fundus projection

X-Y course of eye motion

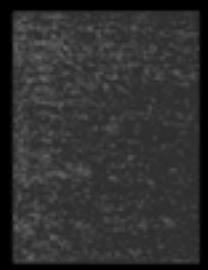
eye motion distance

Perfusion Imaging

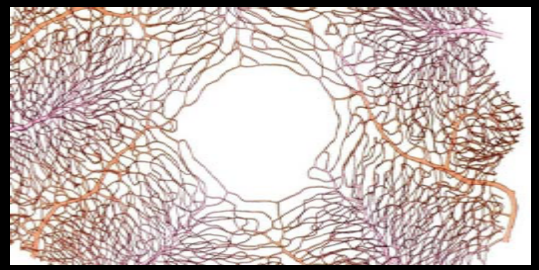
600 x 600 x 600 µm (200 x 500 x 600 pixels) taken in only 0.5sec at 200.000 depth scans / sec



Volume series taken at 13 volumes / sec

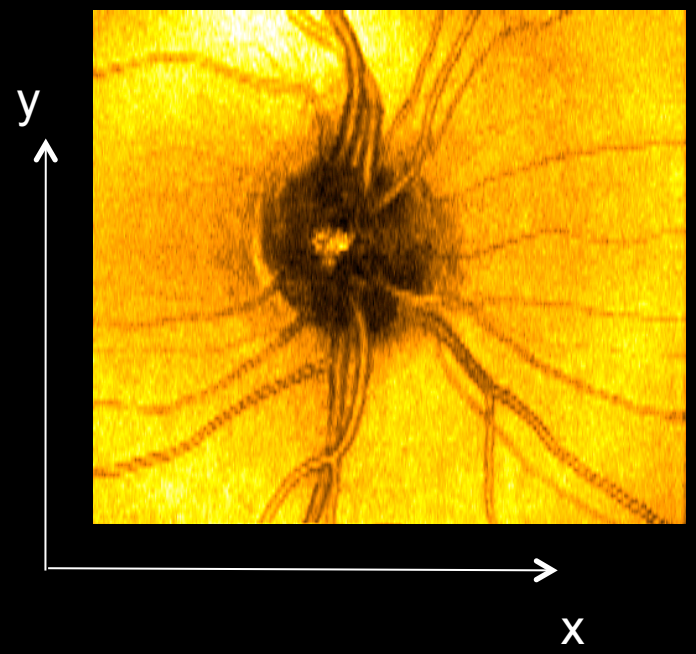


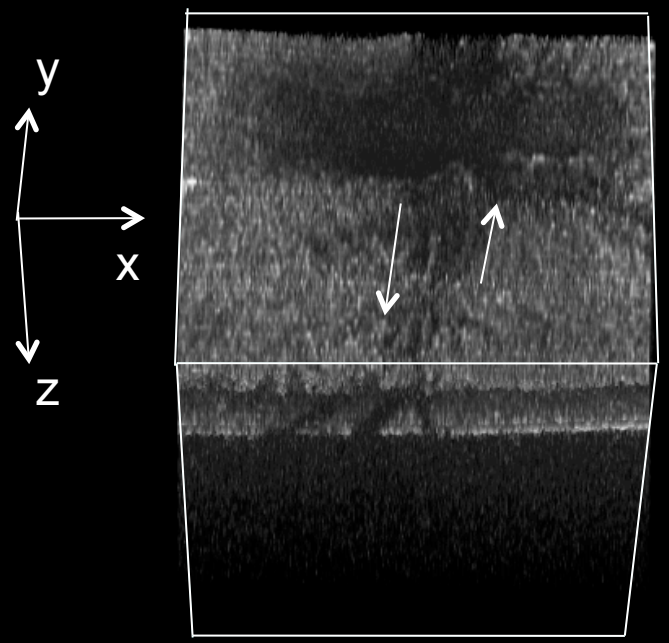
foveal microcirculation



Perfusion Imaging

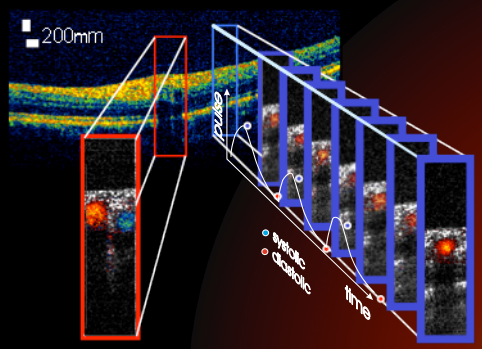
Volume series taken at
13 volumes / sec



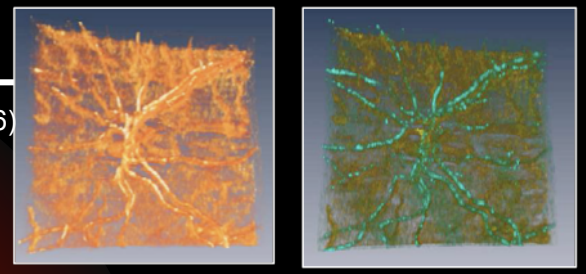


Selection of Perfusion Imaging and Contrasting Methods

Phase sensitive –
Leitgeb et al., Opt. Express (2003)

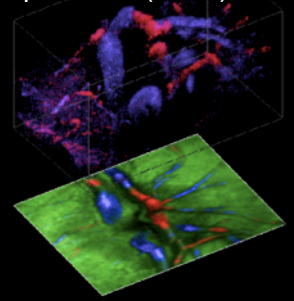


Optical Angiography –
Makita et al., Opt. Express 14 (2006)

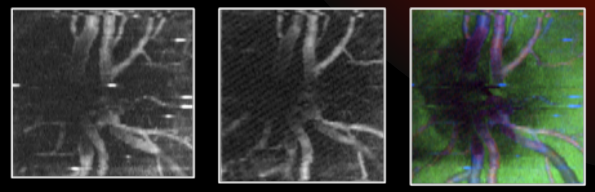


Perfusion Imaging with OCT

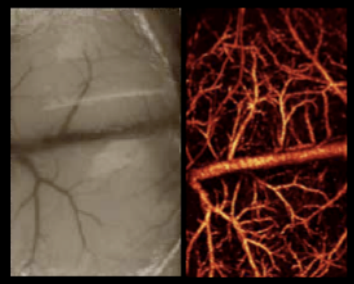
Resonant Doppler –
Bachmann et al., Opt. Express 15 (2007)



Joint time and frequency domain Doppler –
Szkulmowski et al, Opt. Express 16 (2008),
Tao et al. Opt. Express 16 (2008)

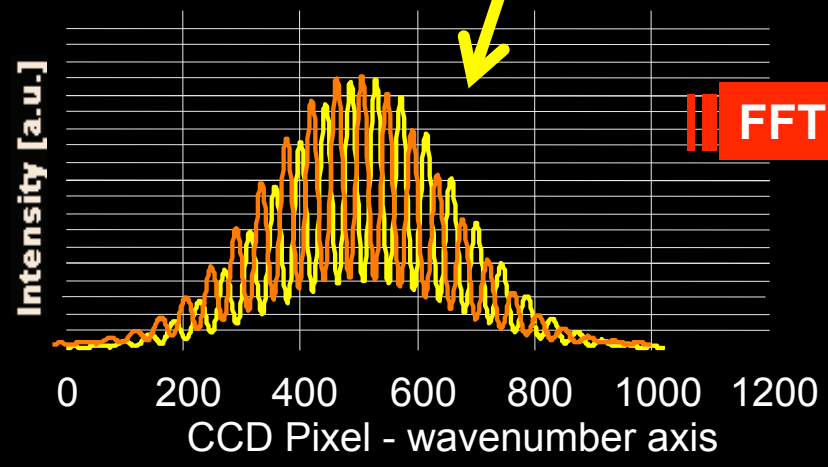


Optical Micro-Angiography (OMAG) –
Wang et al. Opt. Express 15 (2007)

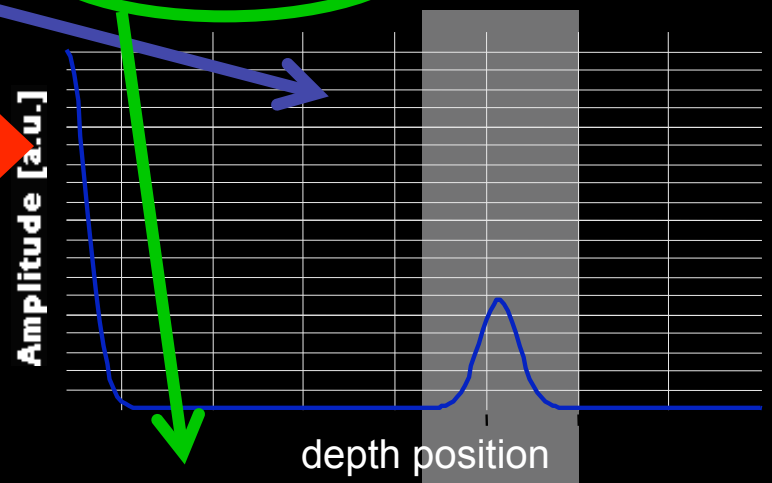


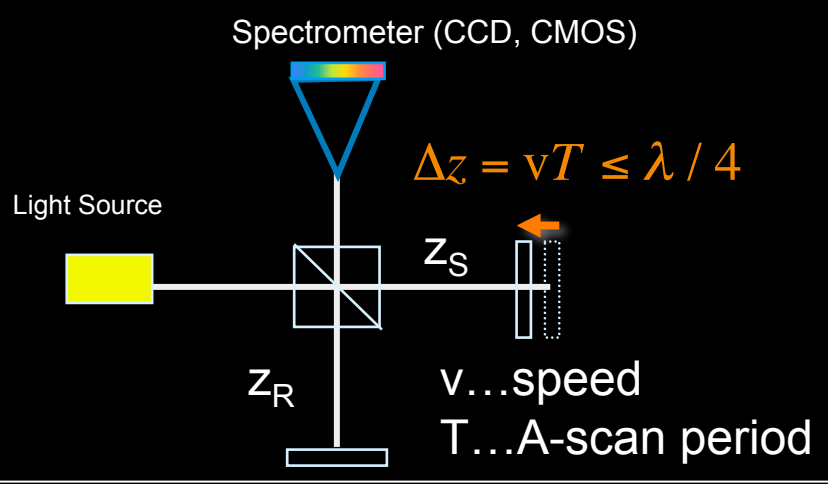
Method - Doppler FDOCT

$$FFT\{I(k)\} = \hat{I}(z)\exp(i\Phi(z) + 2ikvT)$$

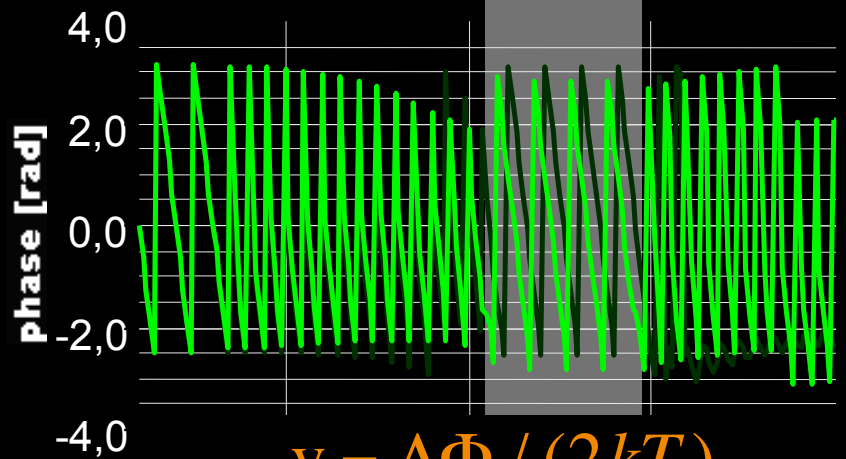


FFT





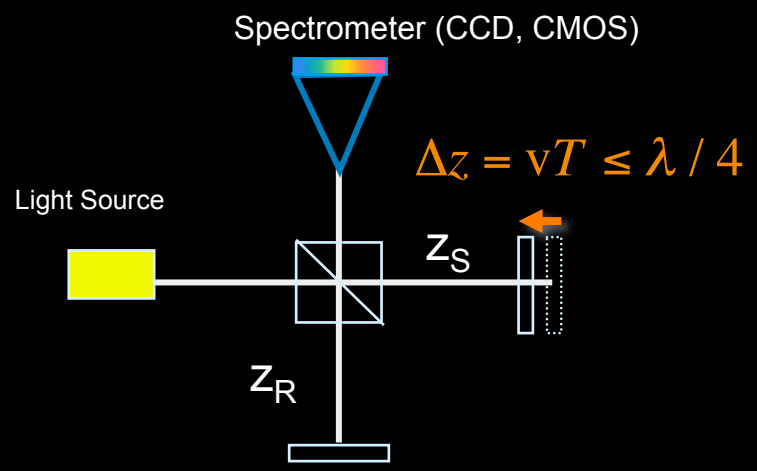
$$\Delta z = vT \leq \lambda / 4$$



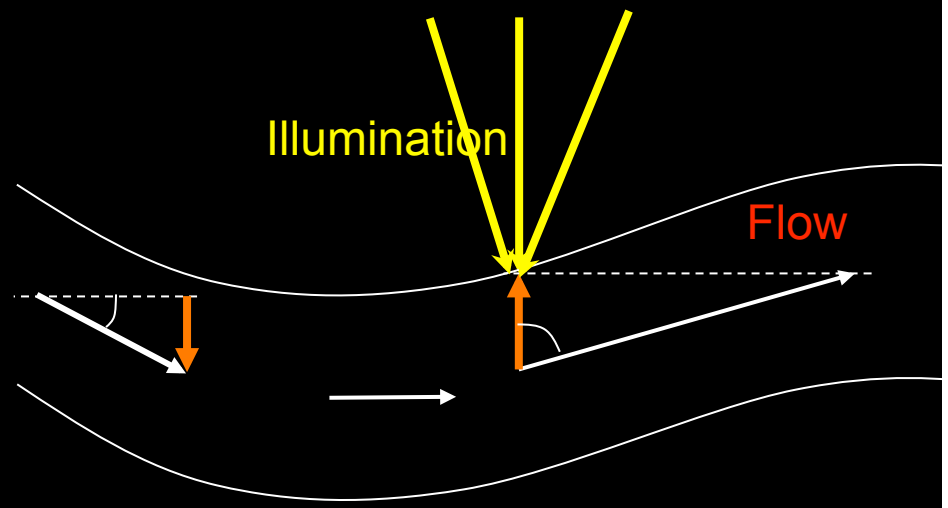
$$v = \Delta\Phi / (2kT)$$

R.A.Leitgeb

Method - Doppler FDOCT



$$\Delta z = vT \leq \lambda / 4$$



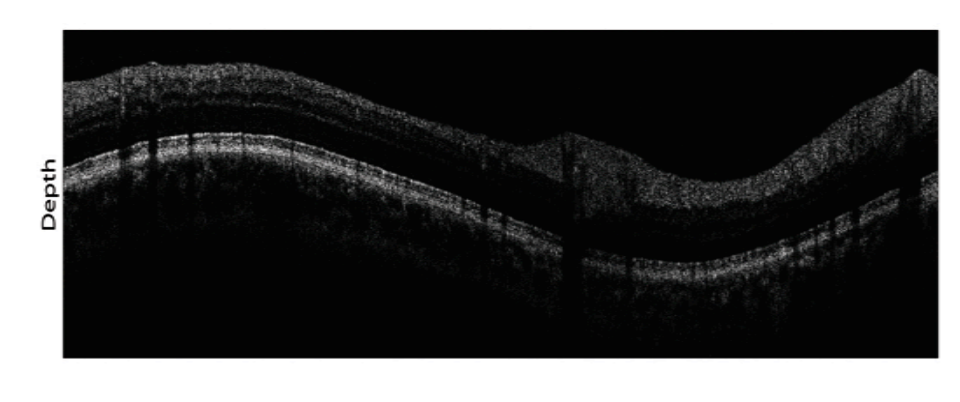
Werkmeister et al, Opt. Lett. 2009

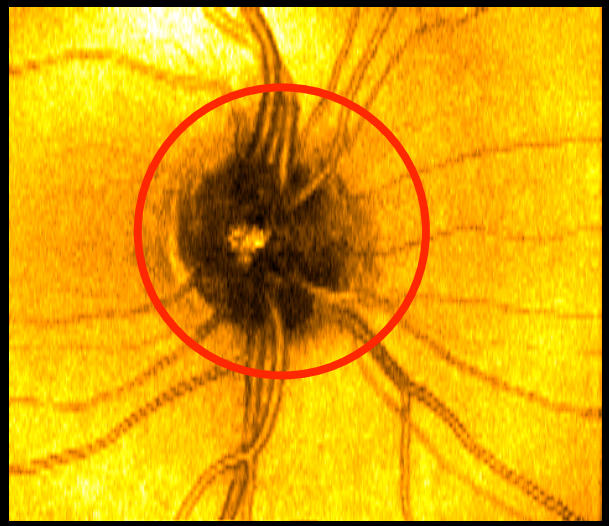
Within order 10µs typical exposure time of CCD retinal blood moved only 10nm !!!

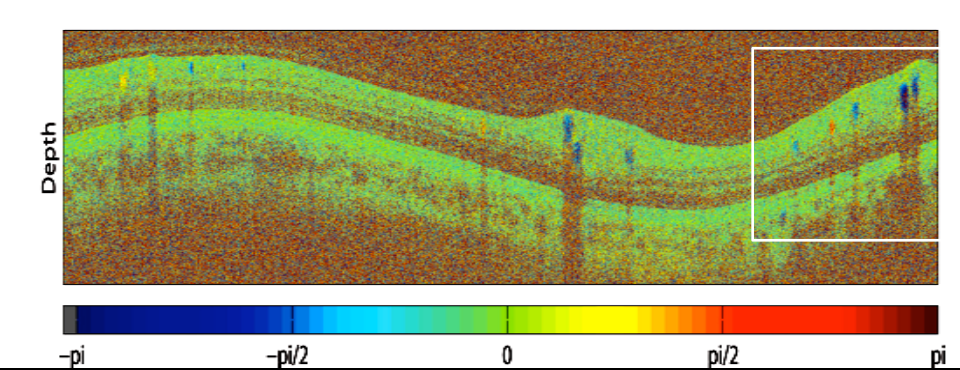
Like looking at lake Geneva from airplane and detect height changes corresponding to thickness of a single hair.

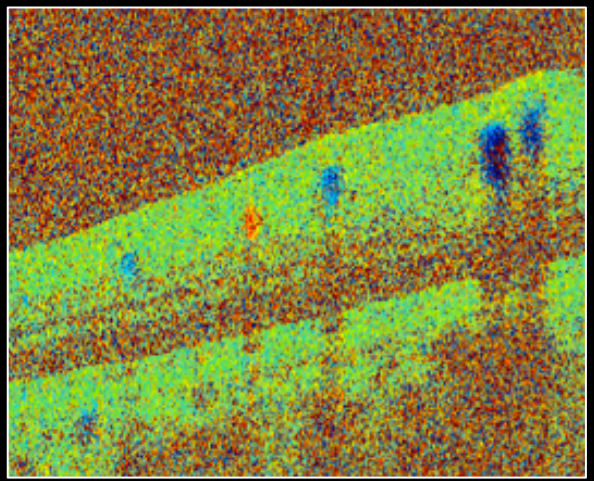
Method - Doppler FDOCT

Circumpapillary scans
8000 A-scans, 30kHz scan rate

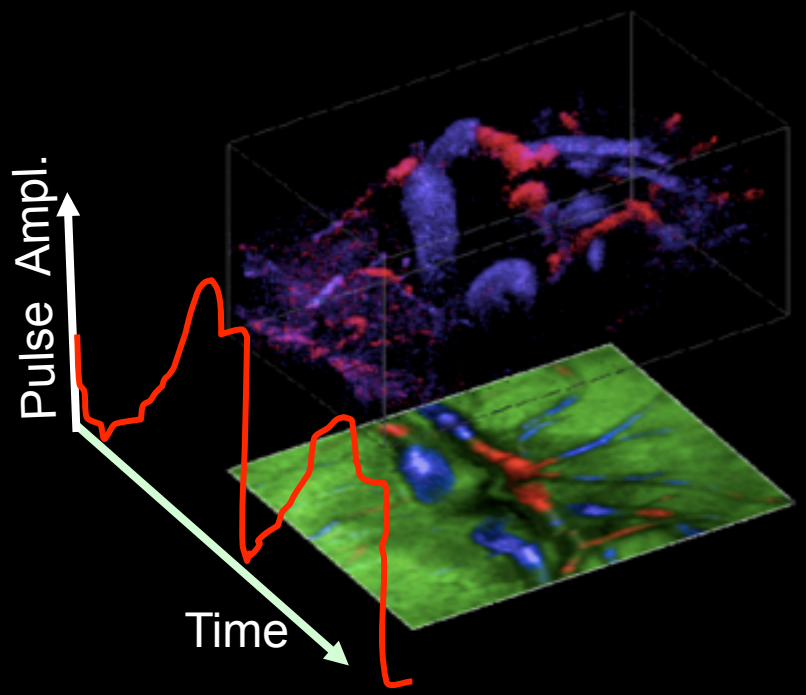


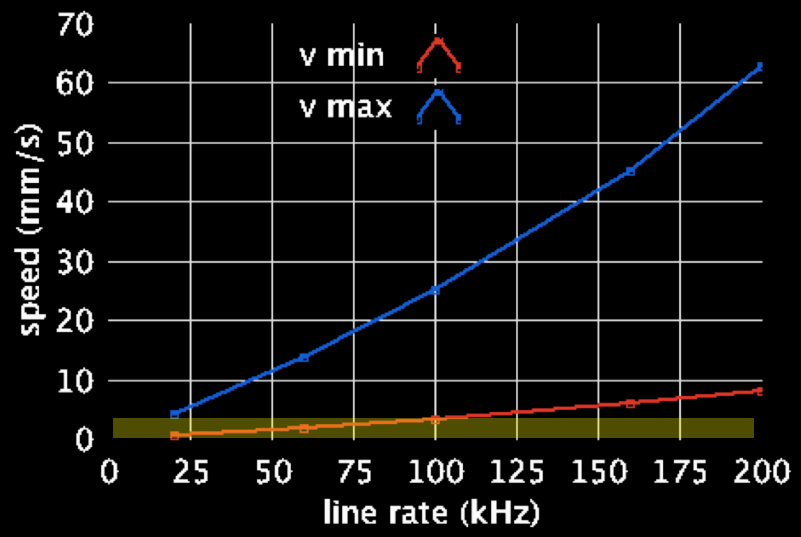






Pulse Coherent 4D Angiography

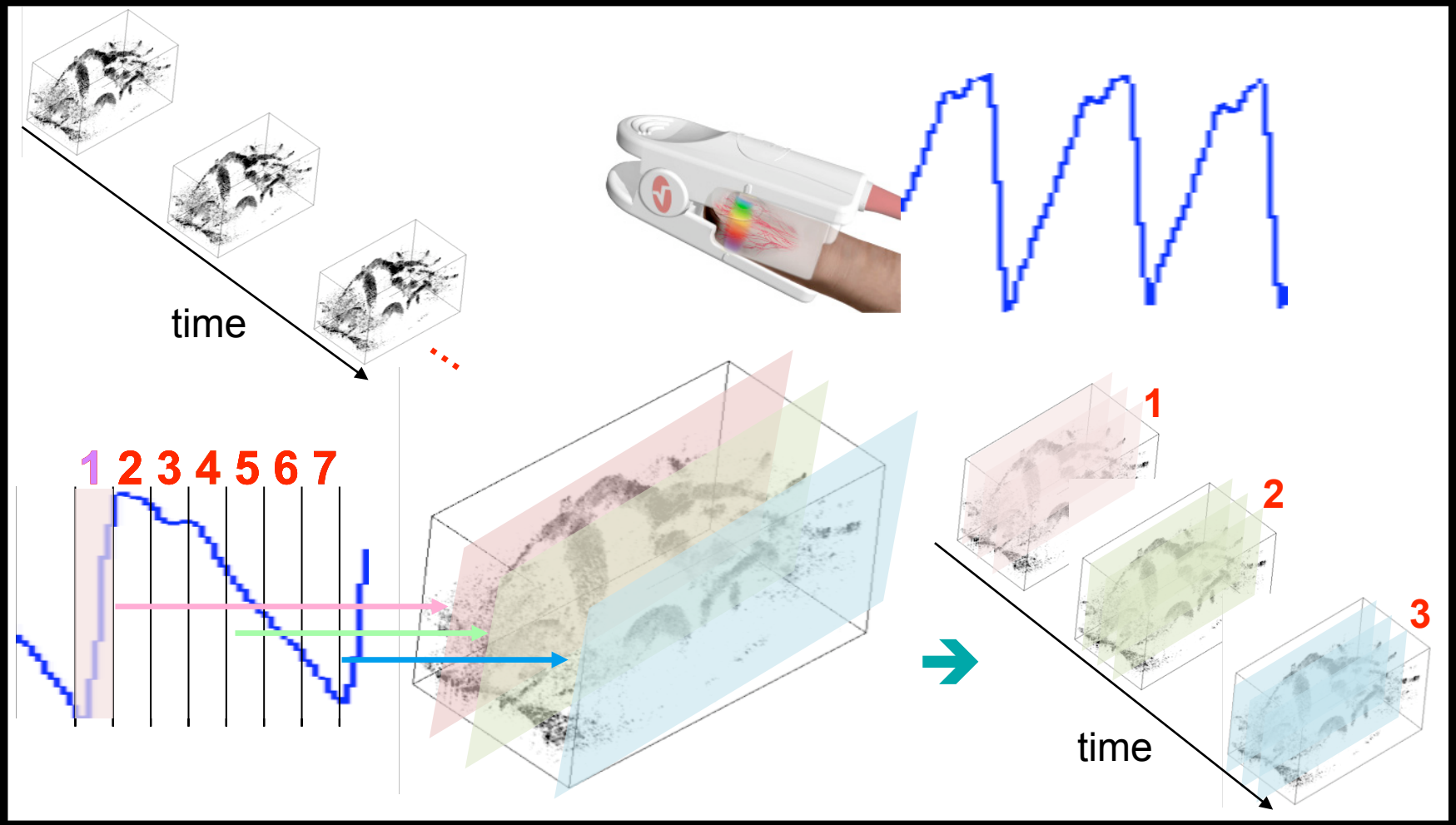




Acquisition time for a volume with sufficient sampling for quantitative analysis spans over several heart cycles.

➔ **difficult to observe quanitative retinal perfusion heartbeat phase coherently in 4D**

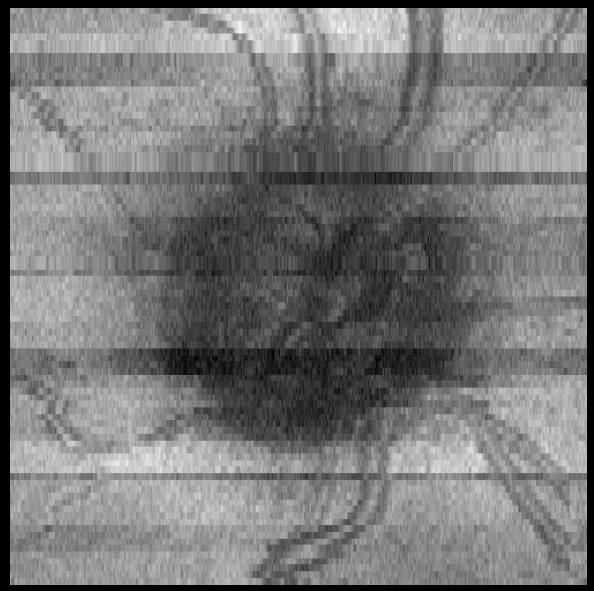
Cyclic Reconstruction of 4D Retinal Blood Flow



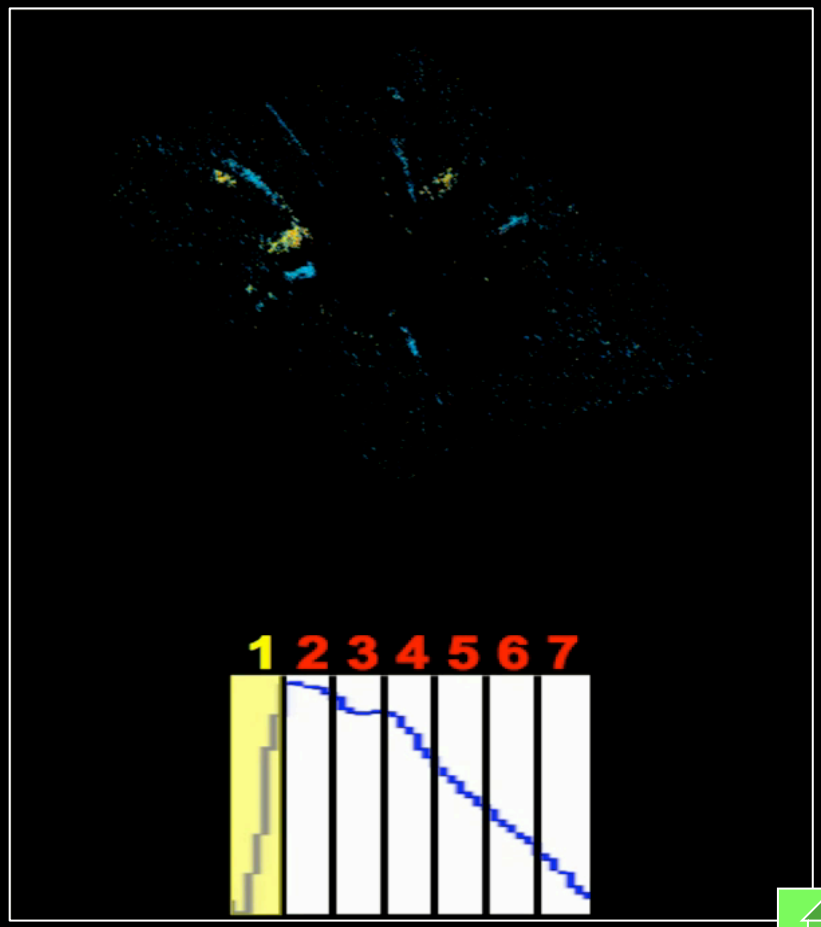
Results

Z-projections of 7 recombined phase coherent volumes:

OCT – fundus view



4D-pulse coherent Doppler - OCT

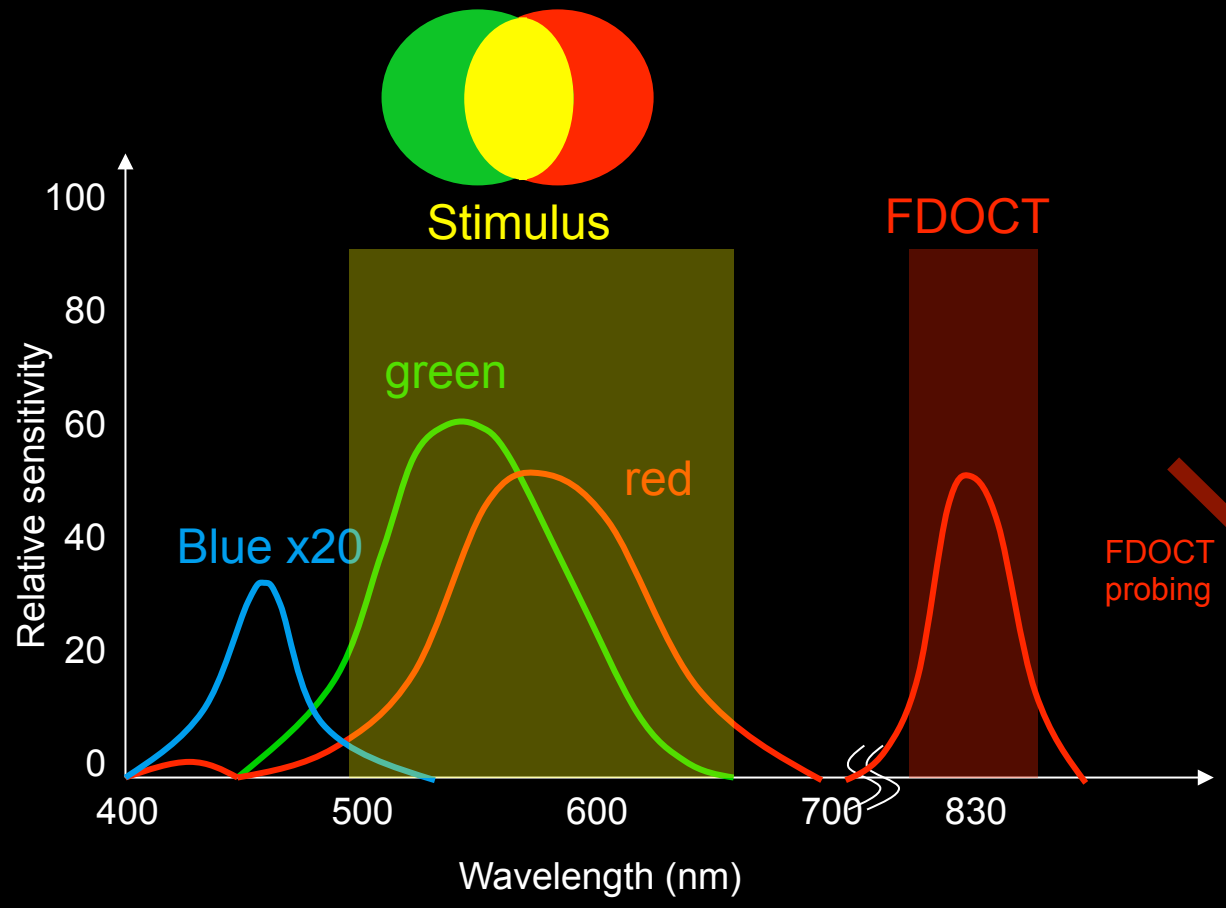


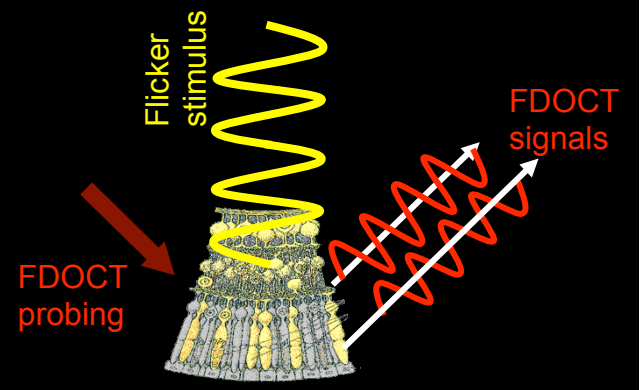
Motivation for optical Assessment of Neural Tissue Responses

Availability of Techniques to assess signaling pathways and photoreceptor functionality in-vivo are limited.

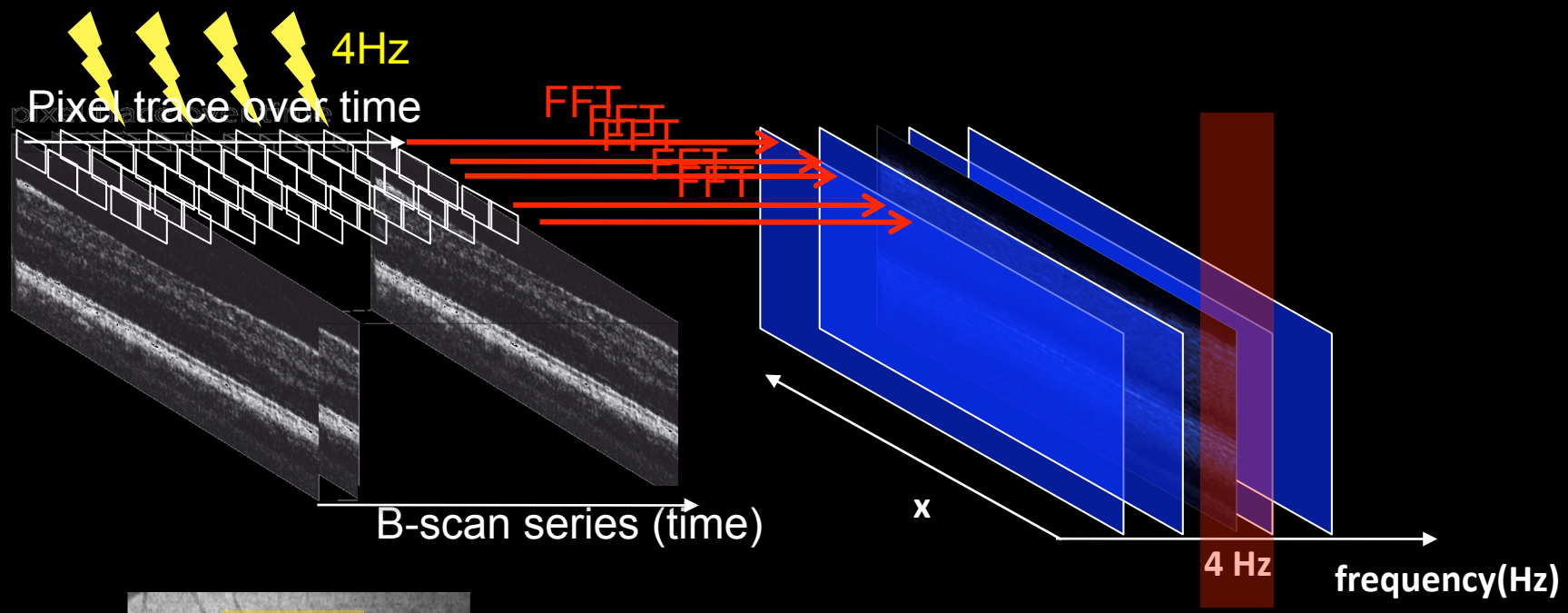
Optical methods that detect changes in retinal reflectivity as a response to flash stimuli indicate a direction for probing of retinal functionality depth resolved in a completely non-invasive way

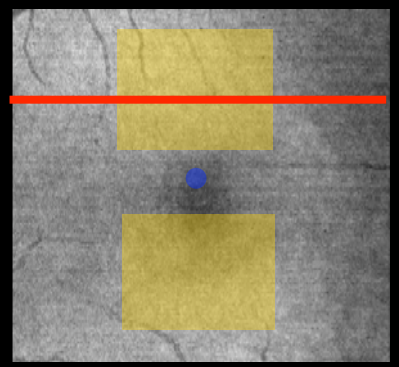
Stimulus / Probing Spectra





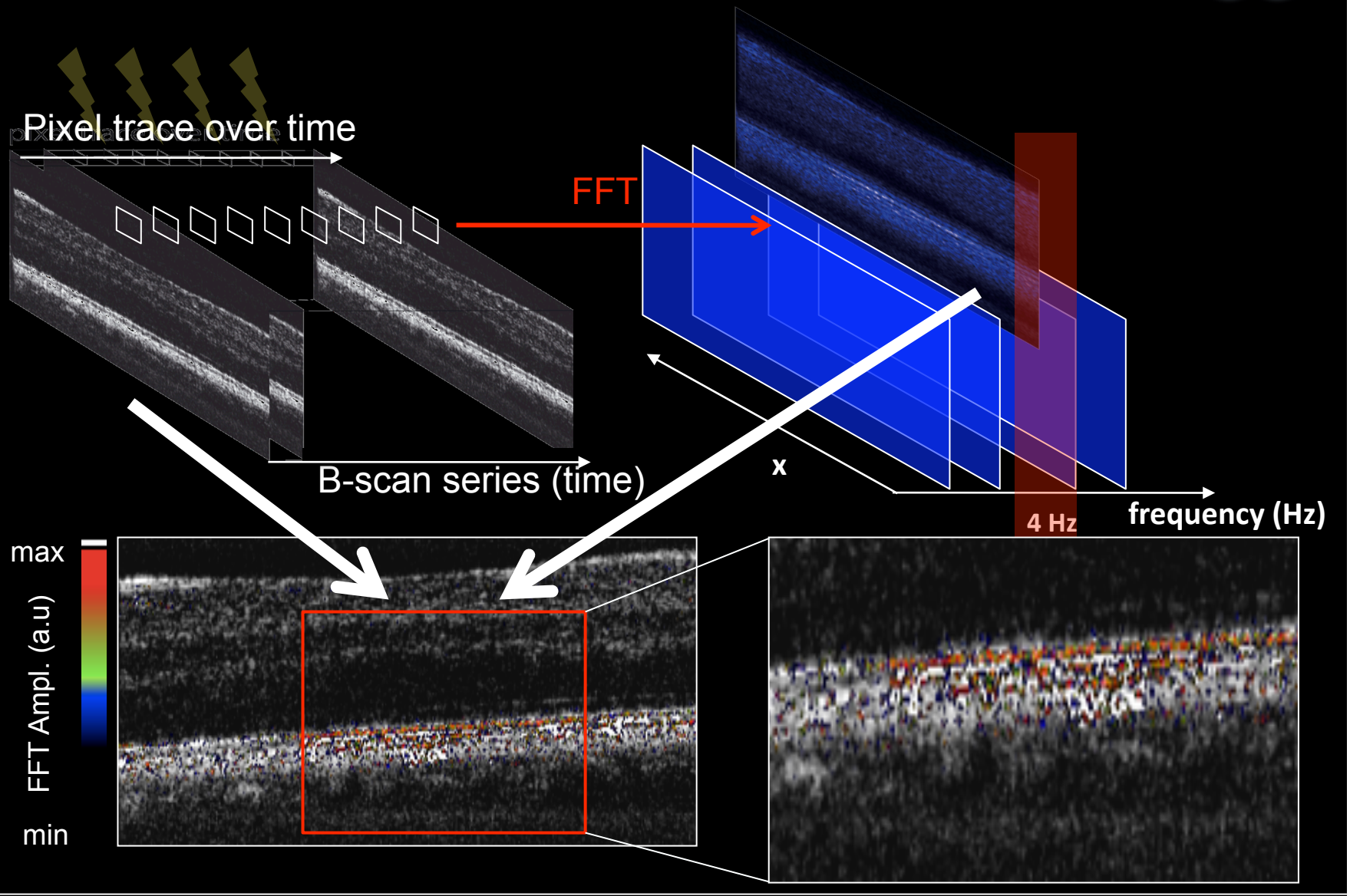
Data Processing





B-scan series at 60Hz (13ms / sample)
1000 scans/ B-scan at 60kHz (CMOS)
Flicker at 4Hz
30µW stimulus intensity at cornea
60µm spot size on the retina
B-scan series is registered prior to FFT !

fOCT Image


Pixel trace over time
FFT
B-scan series (time)
x
4 Hz
frequency (Hz)
max
FFT Ampl. (a.u)
min

Conclusion

- OCT does not only provide excellent resolution and high sensitivity it also profits from functional extensions that make use of the richness of information light carries.

- Novel light source and detector technology enable dynamic volumetric imaging opening new perspectives to understand tissue physiology and patho-physiology

- Novel developments will also focus on the delivery of OCT probing light to internal organs and in particular to the vascular system.

- Will OCT gain in molecular specificity ? Perhaps in combination with other techniques such as multi-photon microscopy.

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Thank you for your attention…

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