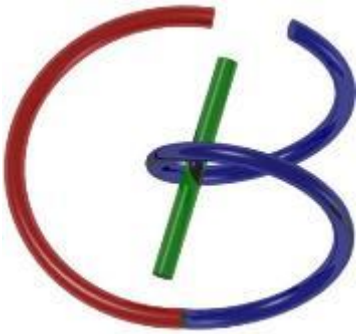
Rensselaer



38655 BMED-2300-02

Lecture 23: Optical Imaging

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April 20, 2018

BB Schedule for S18

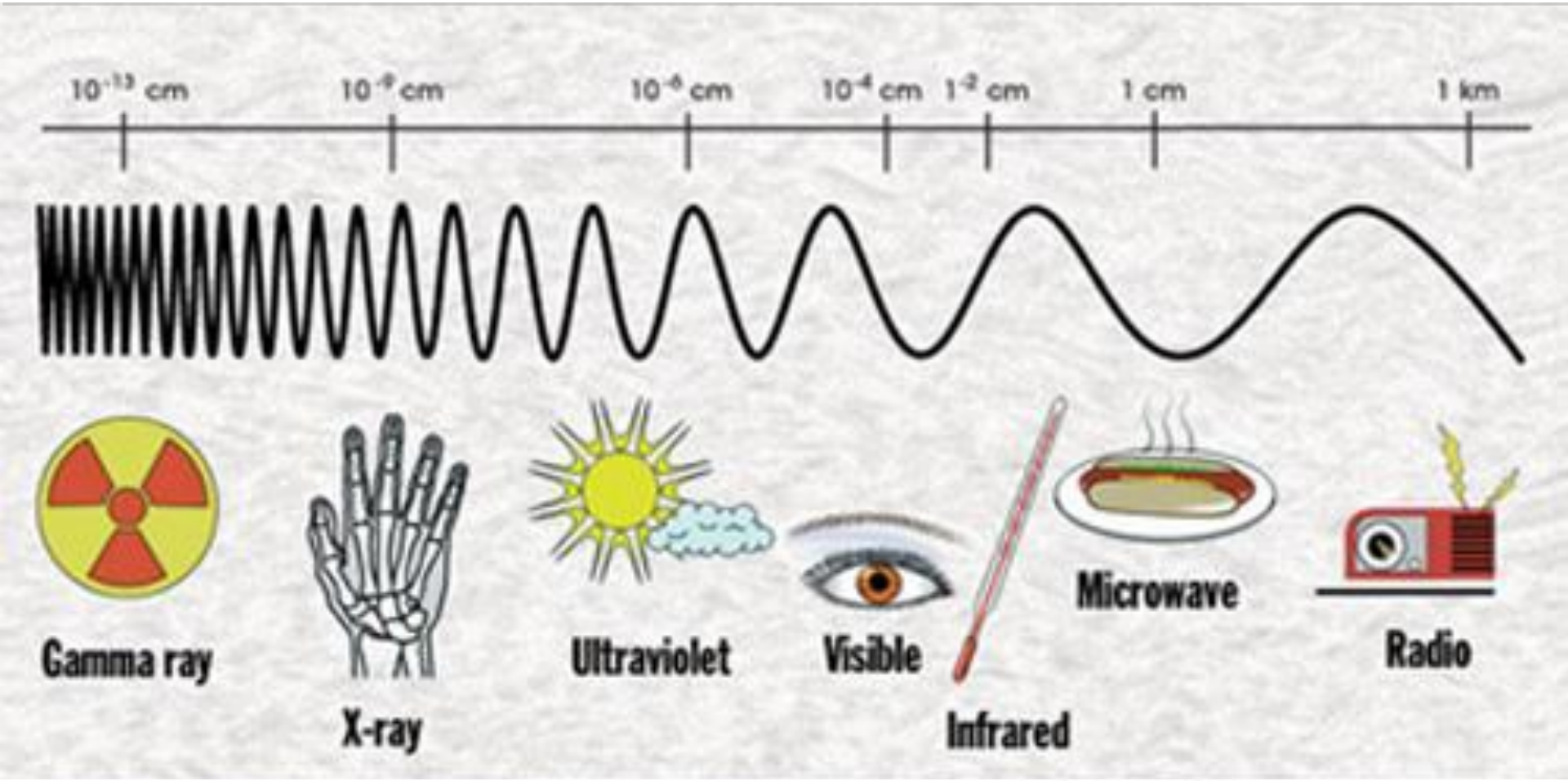
Tue	Topic	Fri	Topic
1/16	Introduction	1/19	MatLab I (Basics)
1/23	System	1/26	Convolution
1/30	Fourier Series	2/02	Fourier Transform
2/06	Signal Processing	2/09	Discrete FT & FFT
2/13	MatLab II (Homework)	2/16	Network
2/20	No Class	2/23	Exam I
2/27	Quality & Performance	3/02	X-ray & Radiography
3/06	CT Reconstruction	3/09	CT Scanner
3/20	MatLab III (CT)	3/23	Nuclear Physics
3/27	PET & SPECT	3/30	MRI I
4/03	Exam II	4/06	MRI II
4/10	MRI III	4/13	Ultrasound I
4/17	Ultrasound II	4/20	Optical Imaging
4/24	Machine Learning	4/27	Exam III

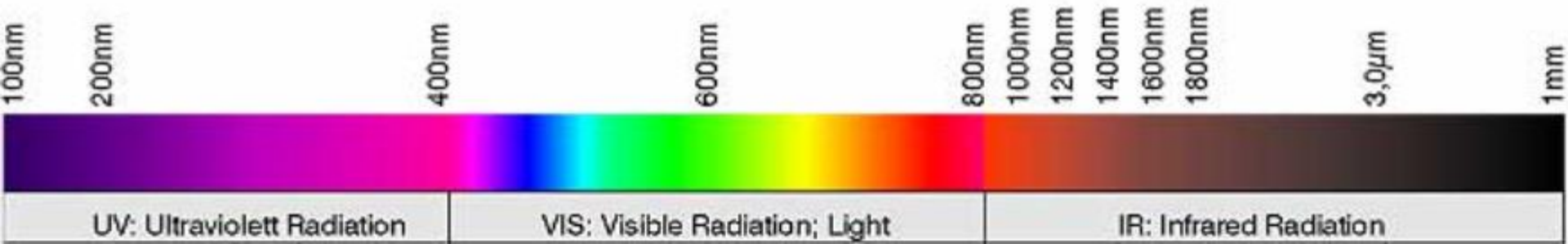
Office Hour: **Ge** **Tue & Fri 3-4 @ CBIS 3209** **|** wangg6@rpi.edu
Kathleen **Mon 4-5 & Thurs 4-5 @ JEC 7045** **|** chens18@rpi.edu

Optical Imaging

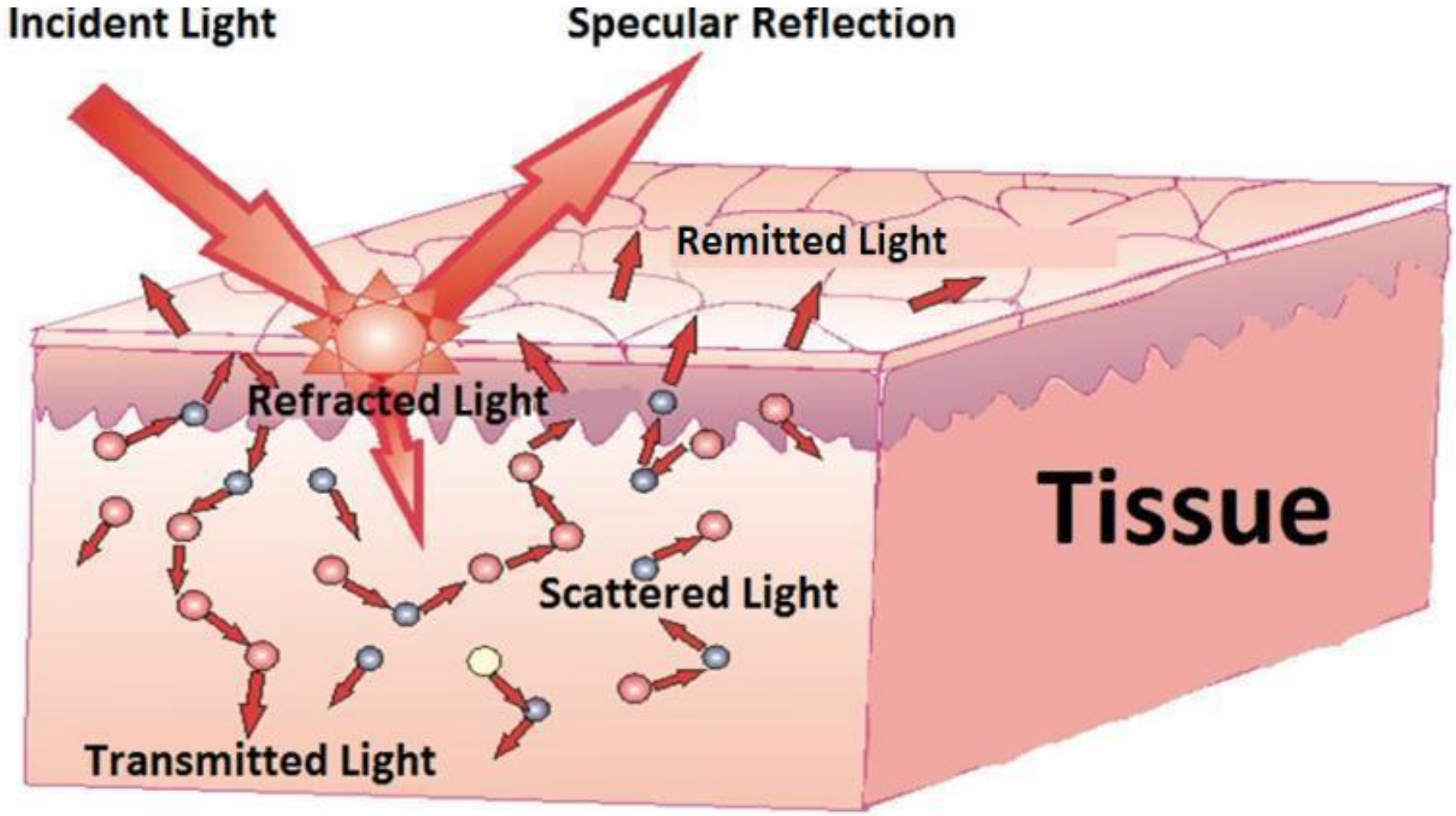
- **Optical Microscopy**
  - EM Wave
  - Optical-tissue Interaction
  - Microscopy
- **Optical Coherence Tomography**
  - Principle
  - Applications
- **Diffuse Optical Imaging**
  - DOS, DOT, FMT, BLT
- **X-ray Optical Coupling**
  - XLCT, XMLT

EM Wave / Light Spectrum



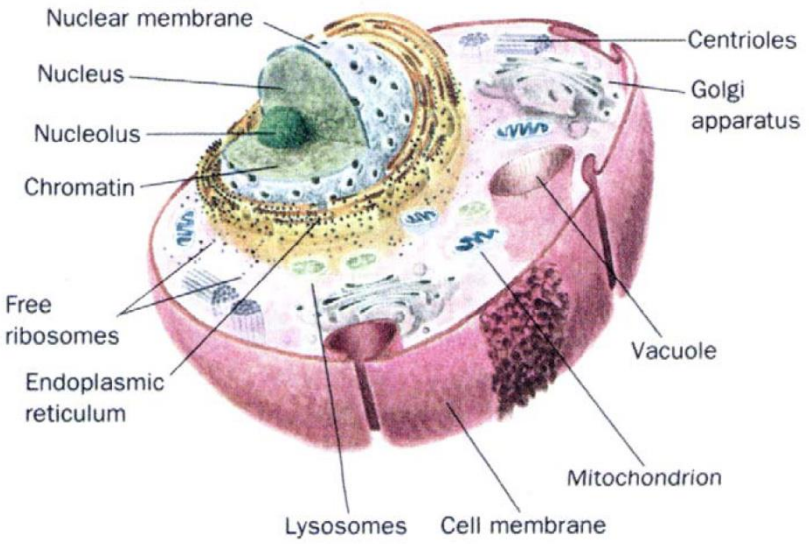


Light-tissue Interactions

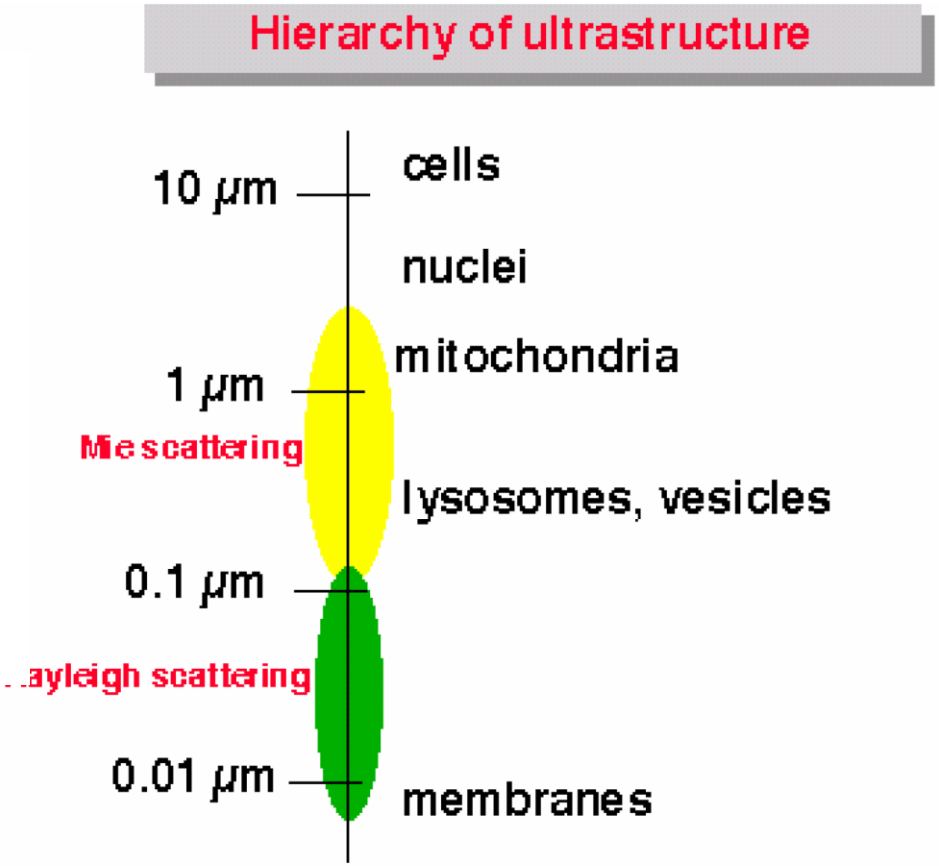


Scattering in Tissue

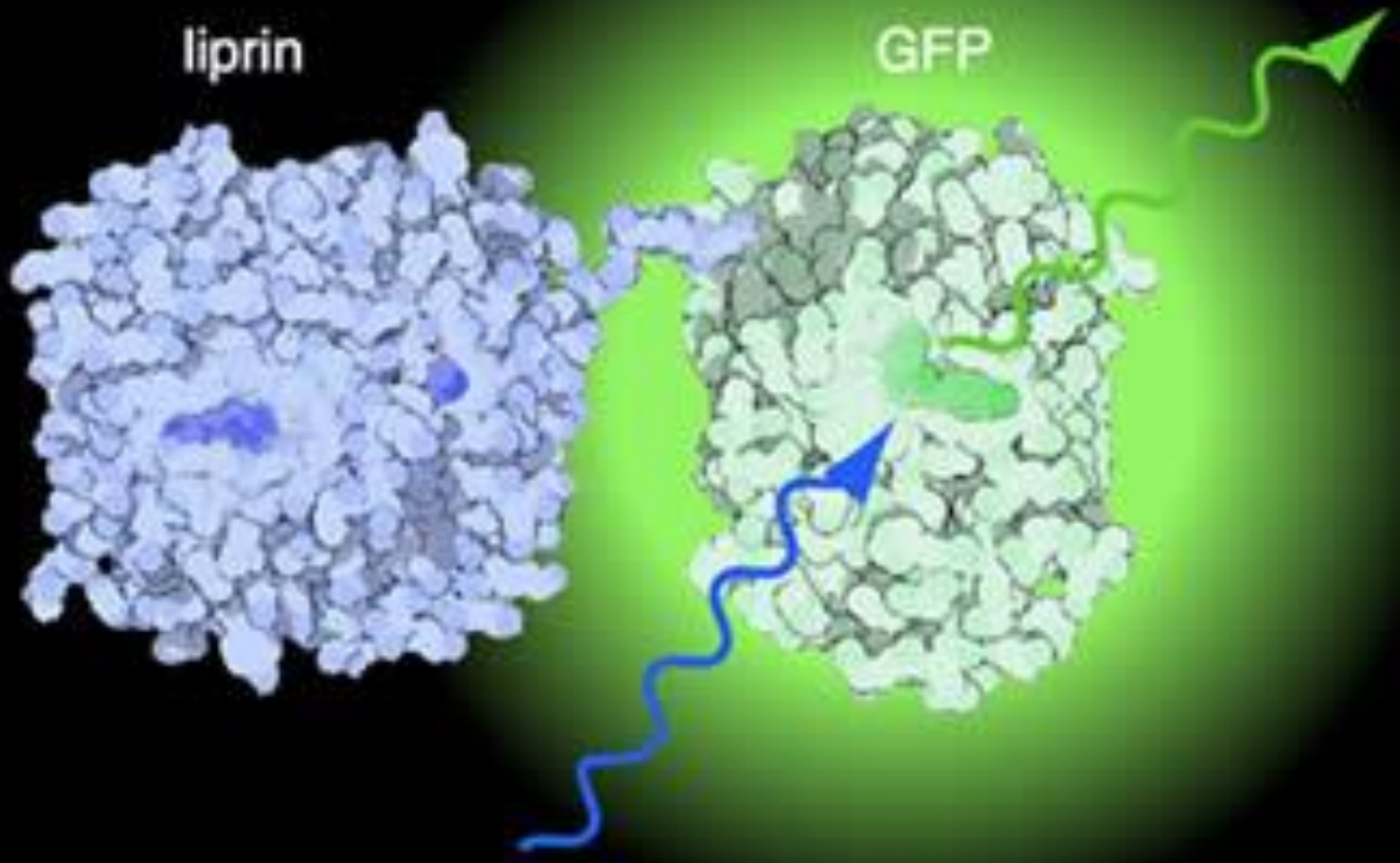
Cell Structure



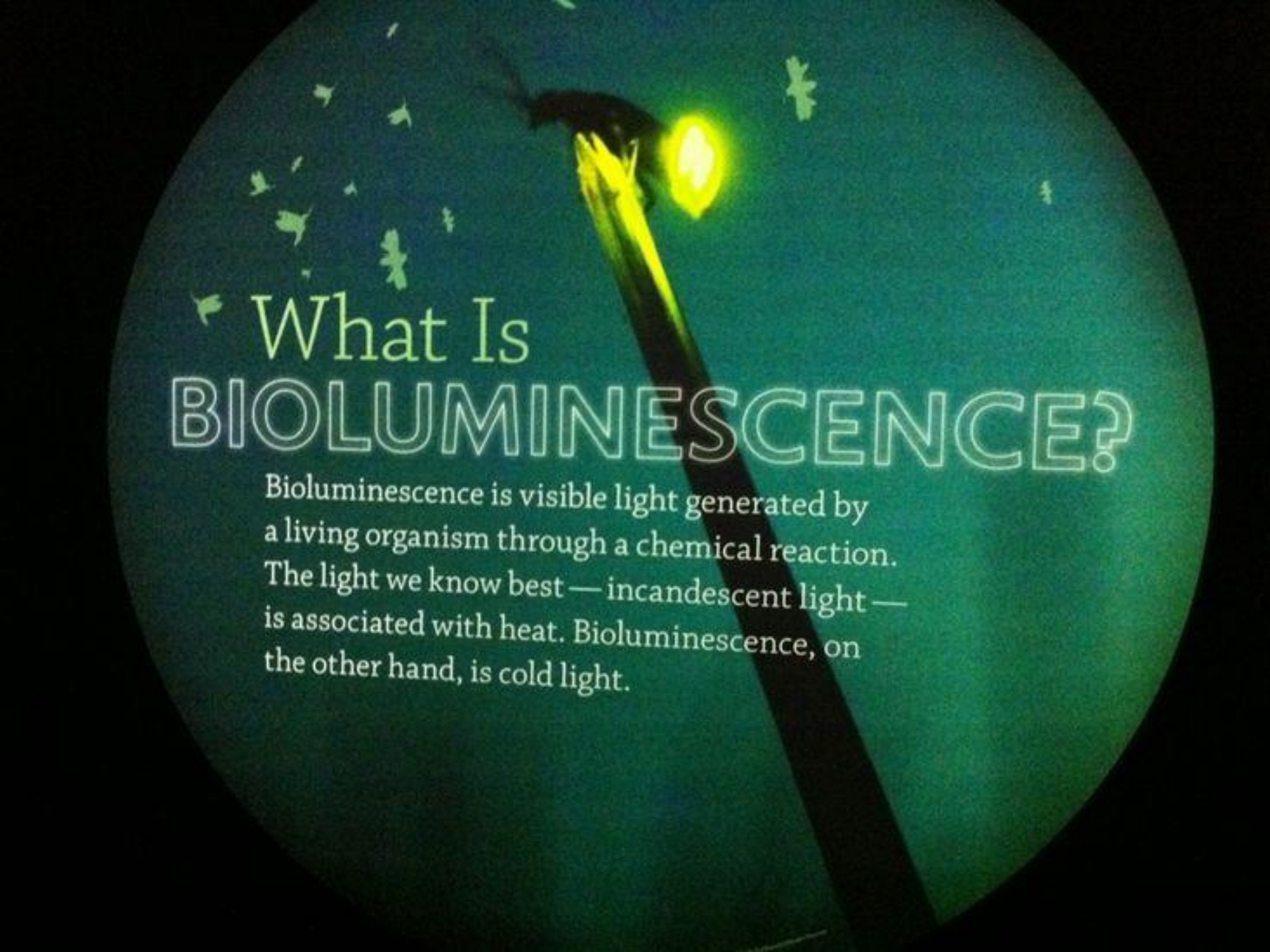
10-30μm
(1μm=10^{-6}m)



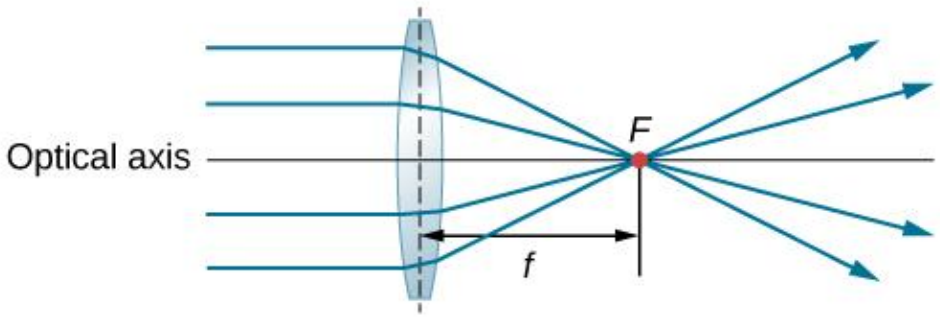
proteins can be tagged with fluorescent proteins



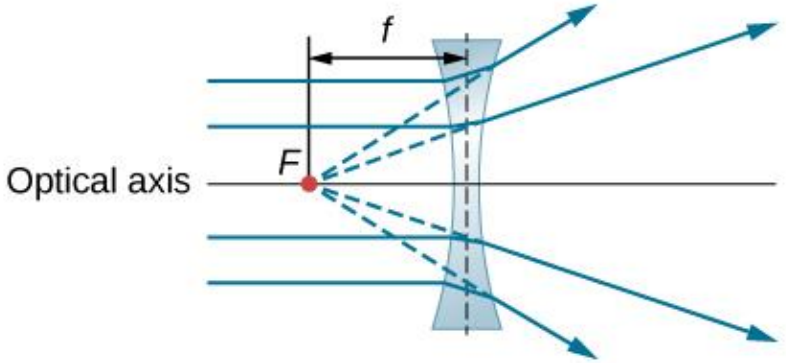
green fluorescent protein converts blue light (488nm) into green light


What Is
BIOLUMINESCENCE?
Bioluminescence is visible light generated by a living organism through a chemical reaction. The light we know best — incandescent light — is associated with heat. Bioluminescence, on the other hand, is cold light.

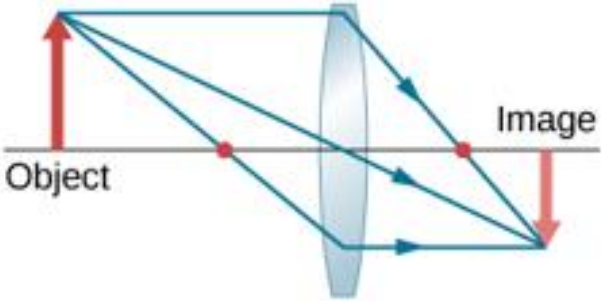
Thin Lens



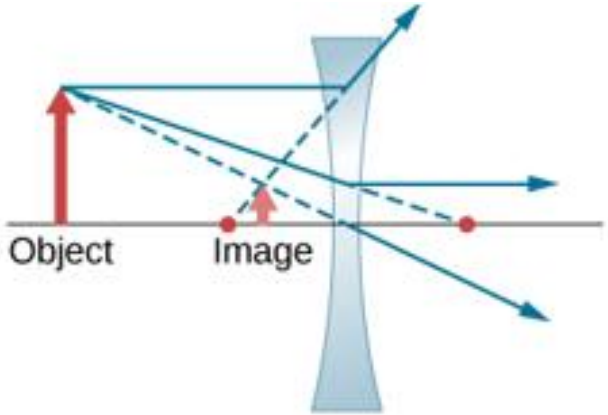
Converging lens



Diverging lens

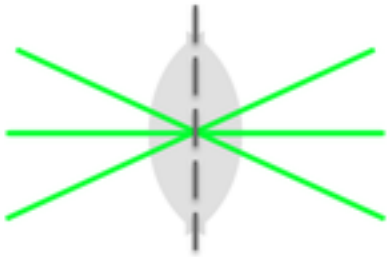


Converging lens
Real image

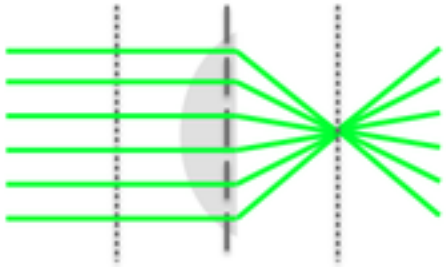


Diverging lens
Virtual image

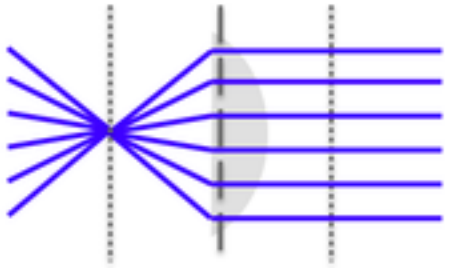
Rules for Ray Tracing

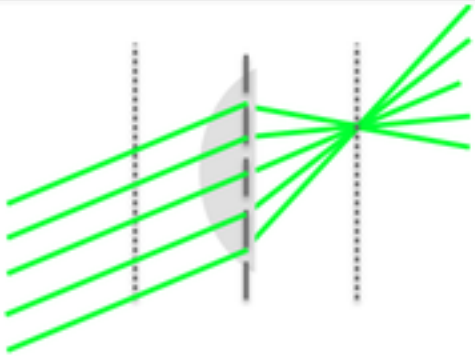


Rule 1: Rays passing through the center of a lens are unaffected by the lens.

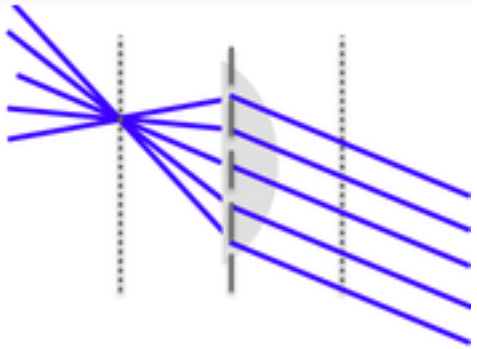


Rule2 : Rays that are parallel to the optical axis pass before hitting a lens pass through the focal point after the lens and vice versa.



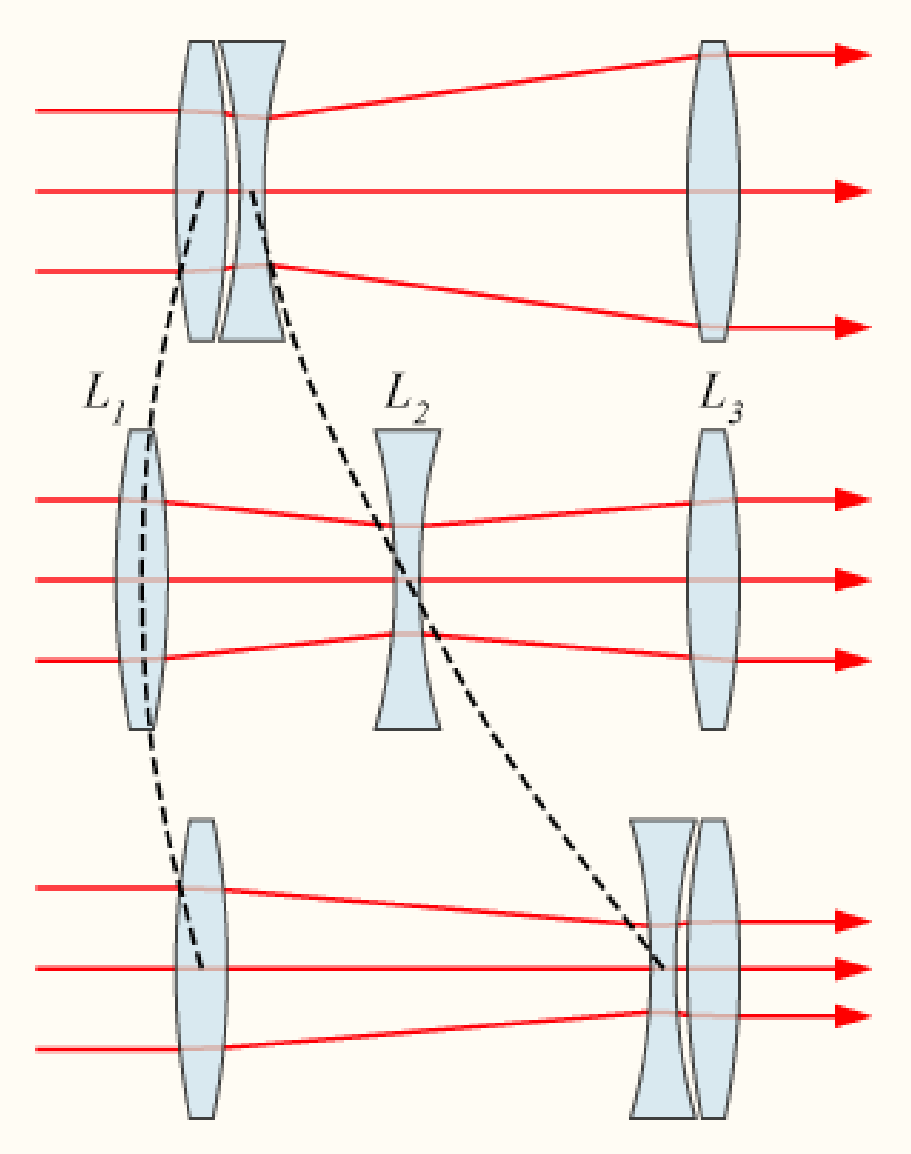


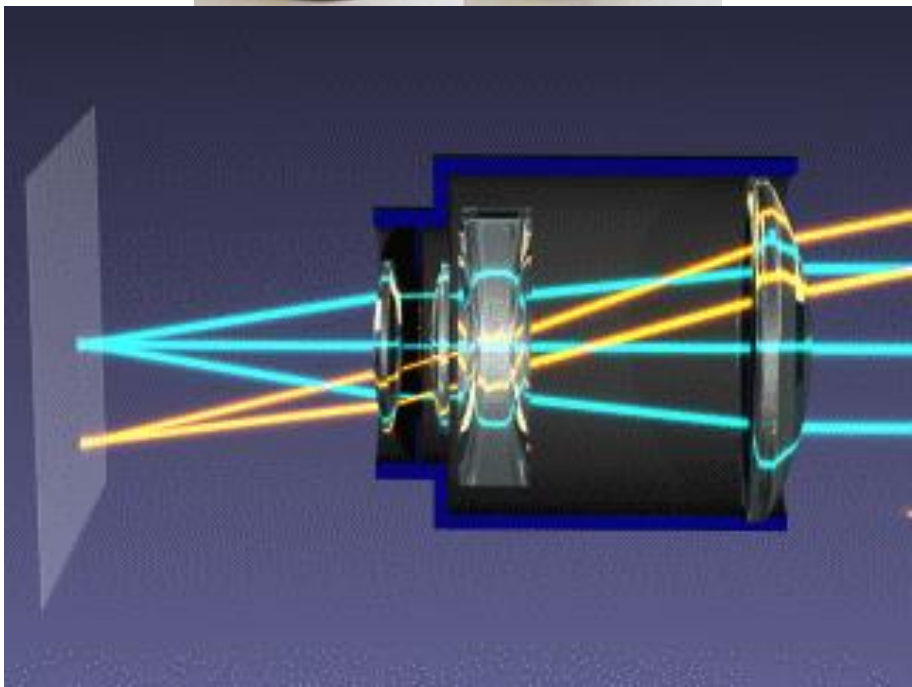
Rule 3: Parallel rays (any angle to optical axis) pass through the same point in the focal plane after refraction and vice versa



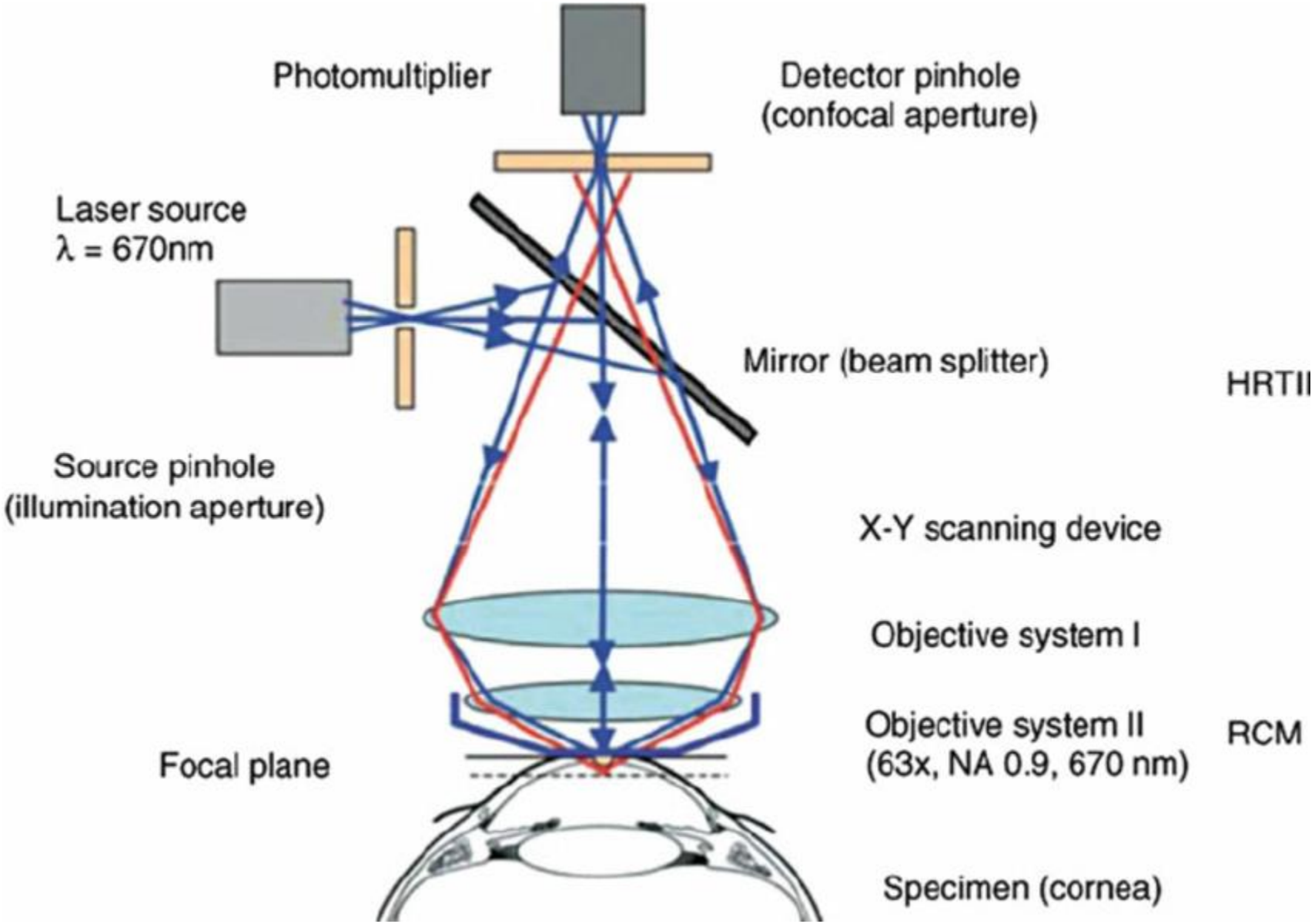
http://measurebiology.org/wiki/Geometrical_optics_and_ray_tracing

Zoom Lens





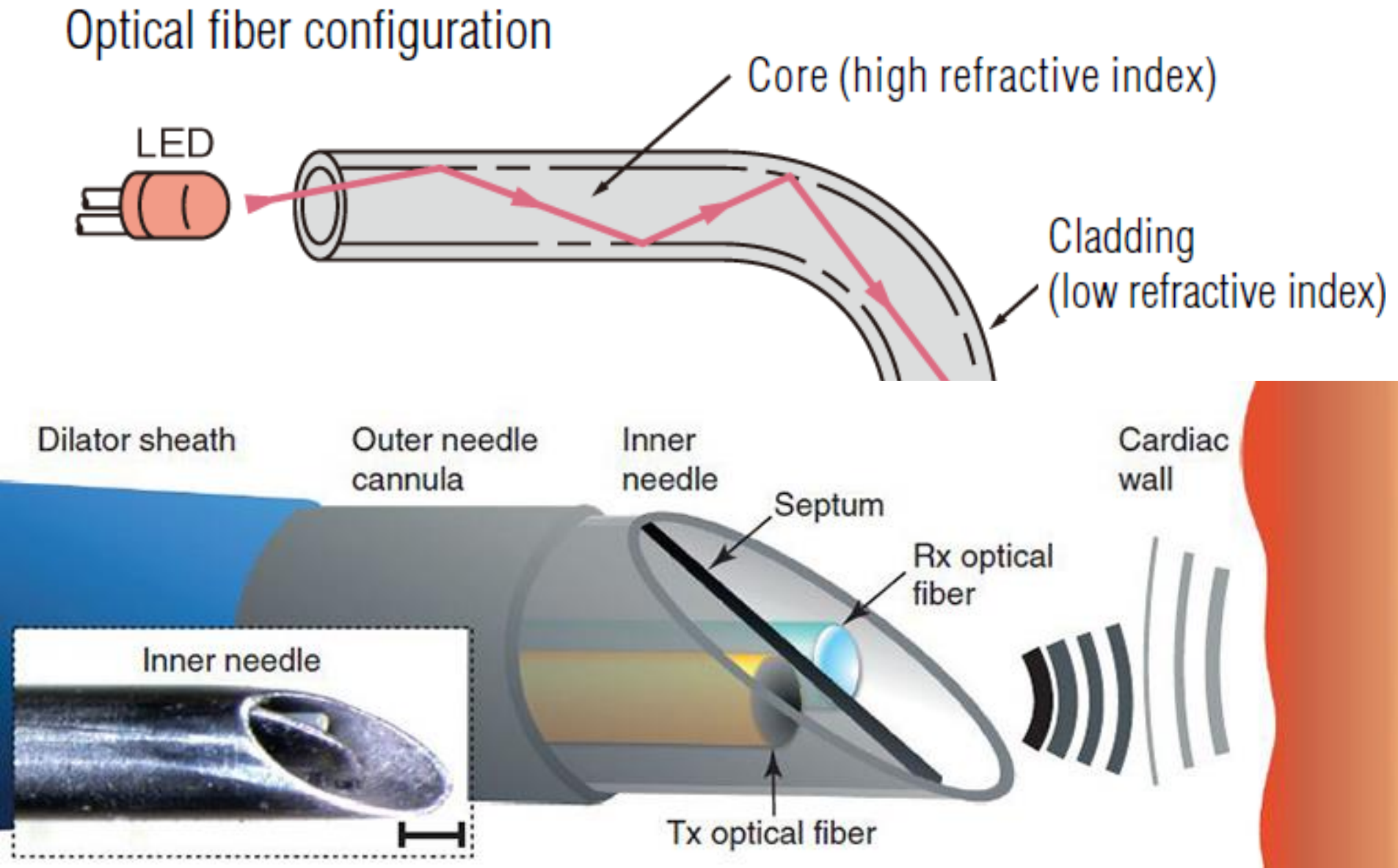
Confocal Optical Microscope



Cell Division

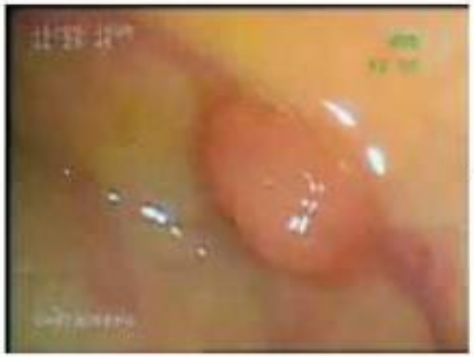
https://www.olympus-lifescience.com/en/microscope-resource/moviegallery/confocal/rk13cherryh2b/

Optical Fiber

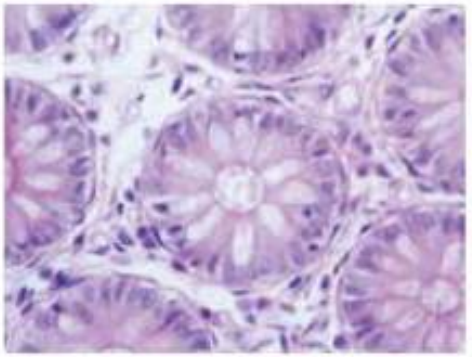


Optical Biopsy

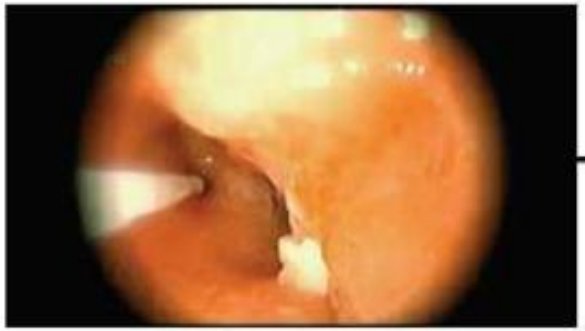
Biopsies
(Tens of millions every year)



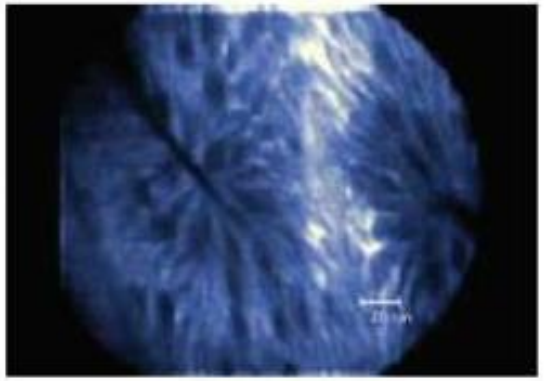
Days/Weeks



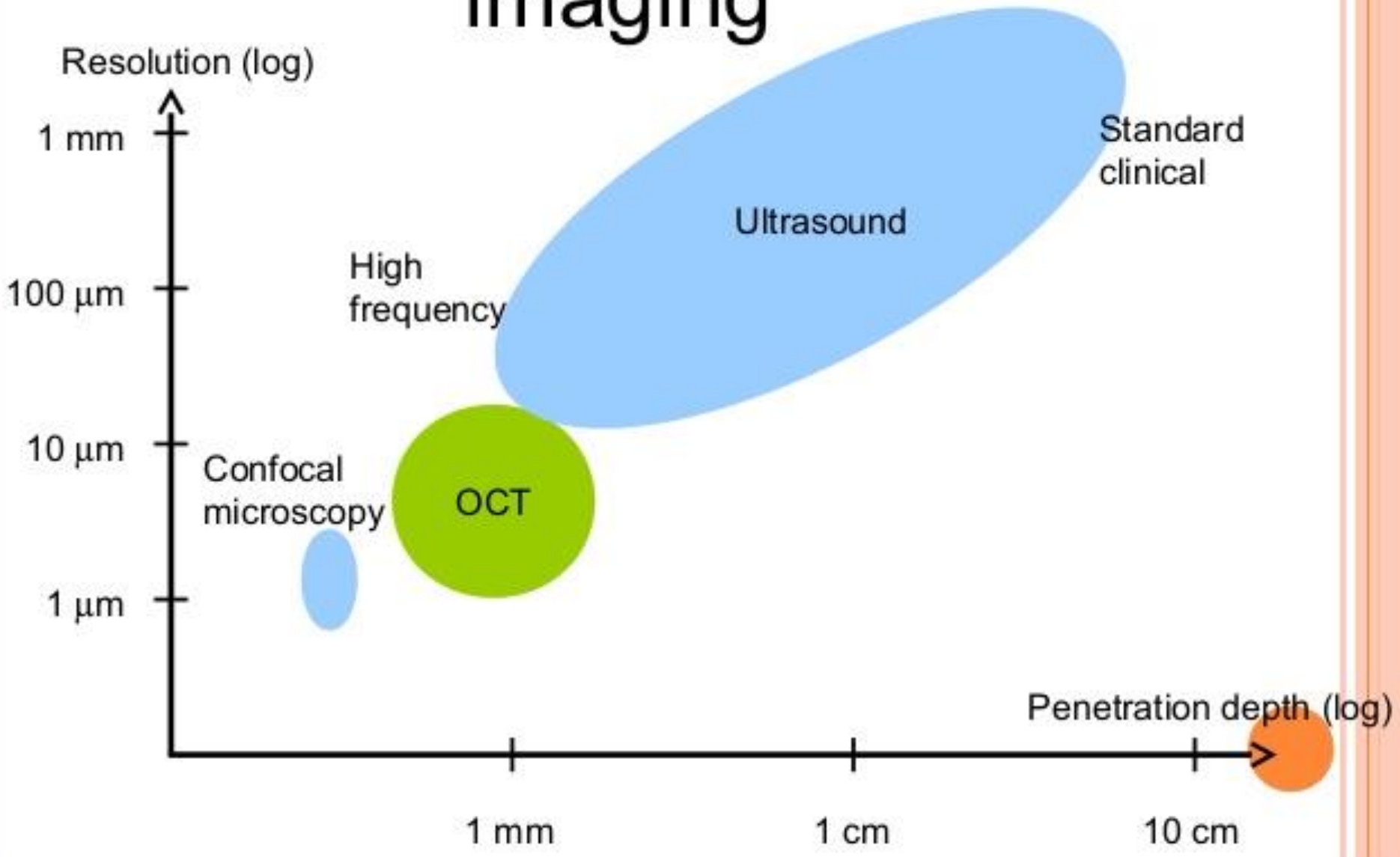
Non invasive procedure



Milliseconds



OCT vs. standard imaging



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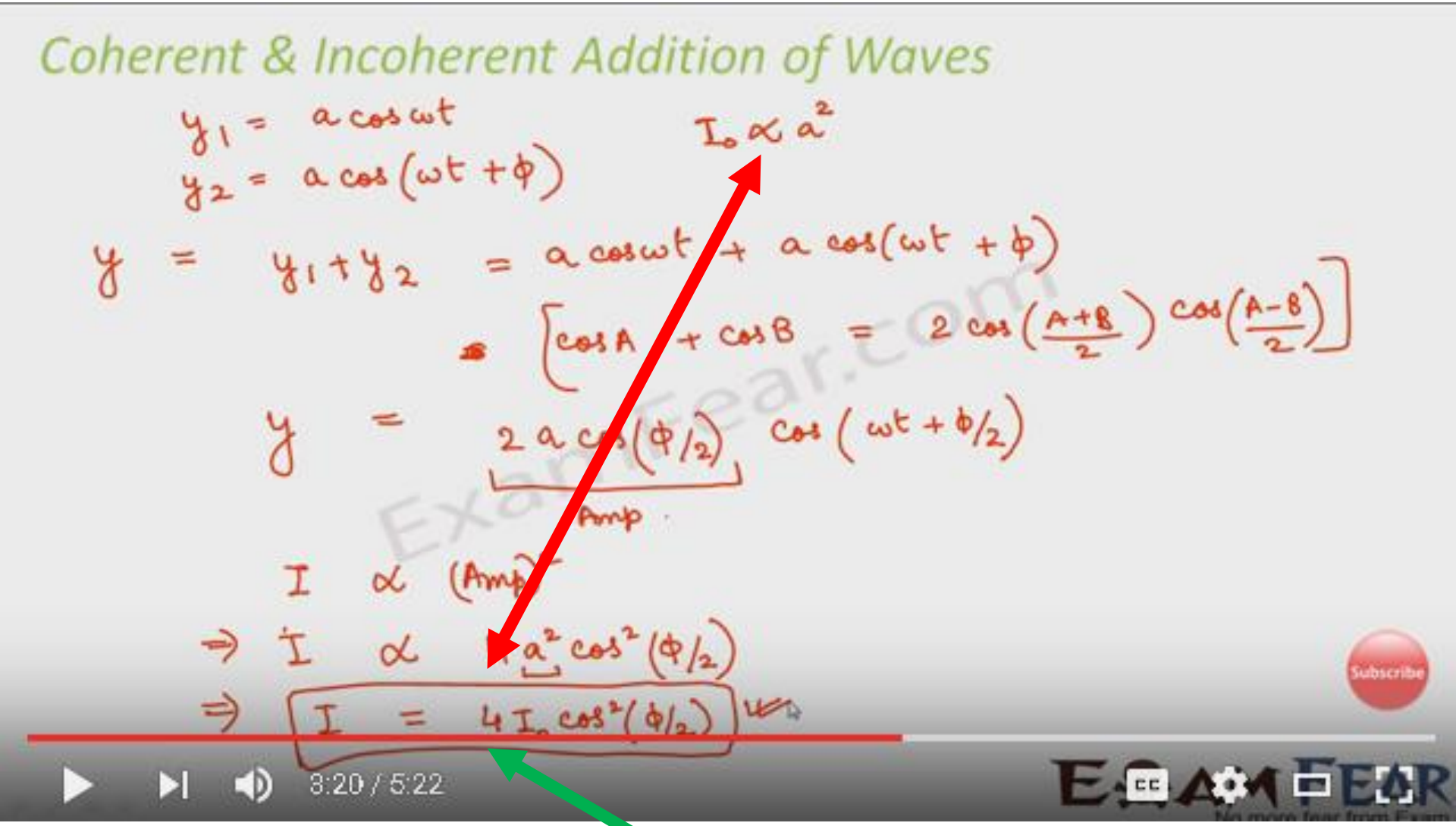
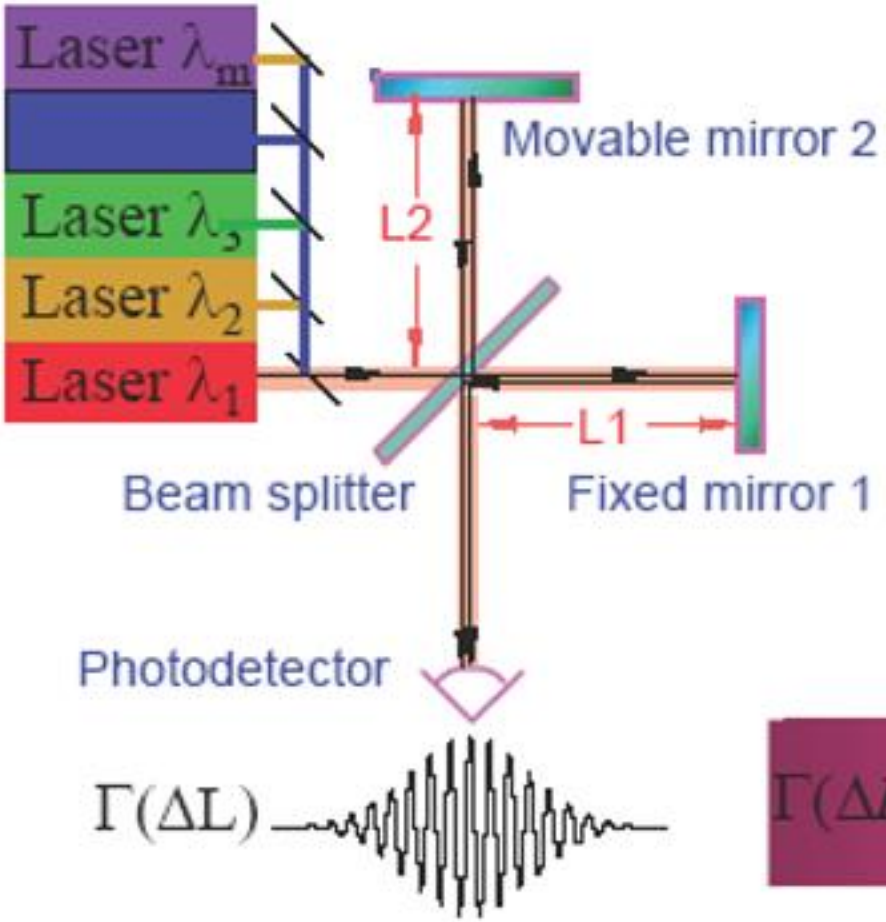
Change in Phase to Change in Amp



$$\cos^2 x = \frac{1}{2}\left(1+\cos(2x)\right)$$

Interference of Coherent Light



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

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

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

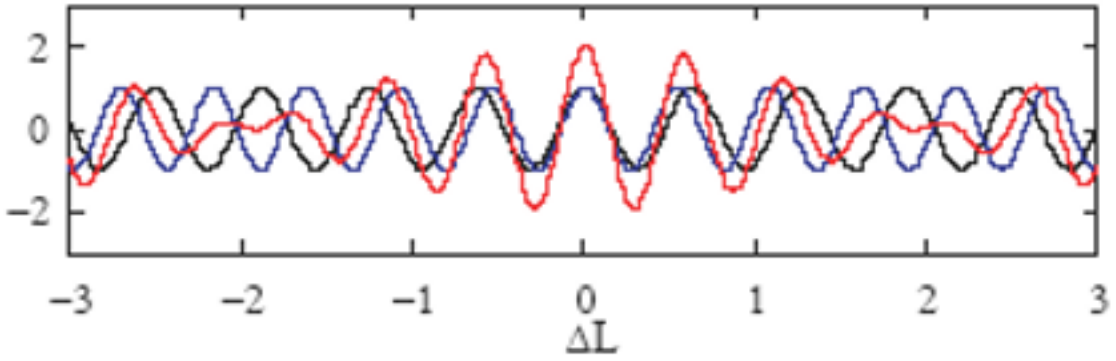
.....

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

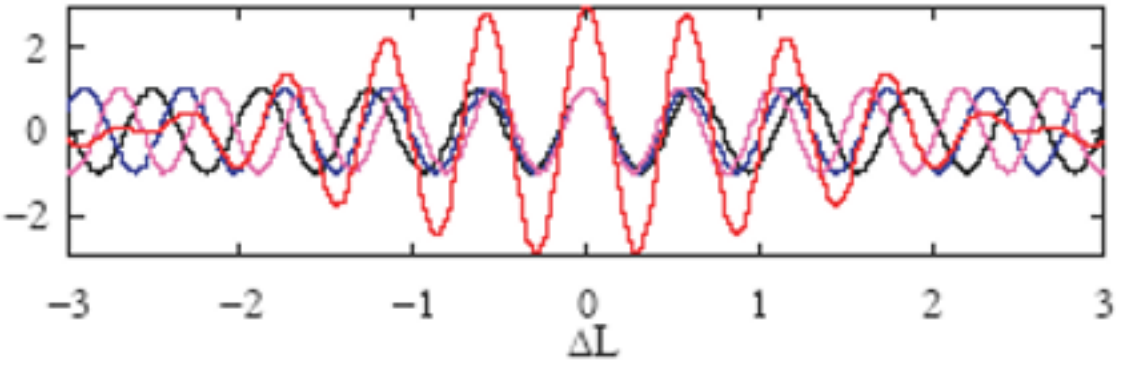
$$\Gamma(\Delta L,\nu_1,\nu_2..\nu_m)=2\sum_1^m I_0(\nu_i)\cos(2\pi\Delta L\nu_i)$$

Case of Partially Coherent Light

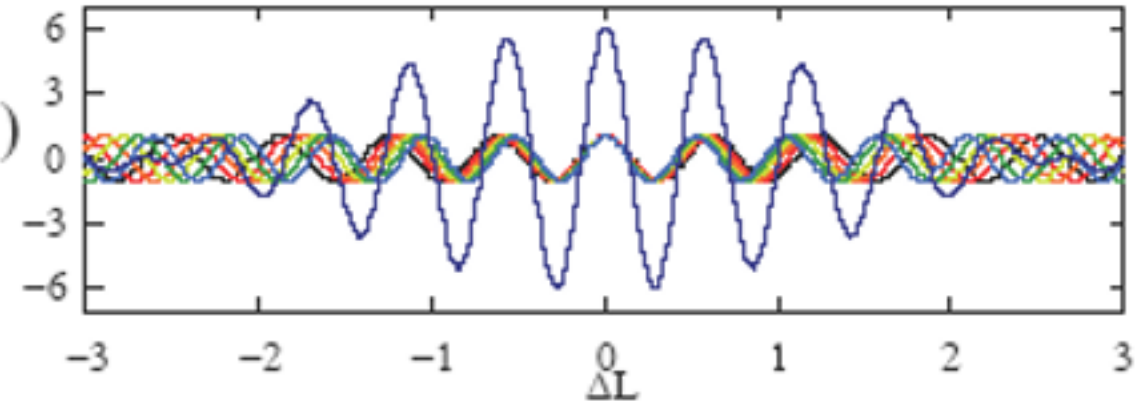
$\Gamma(\Delta L, \nu_1, \nu_2)$



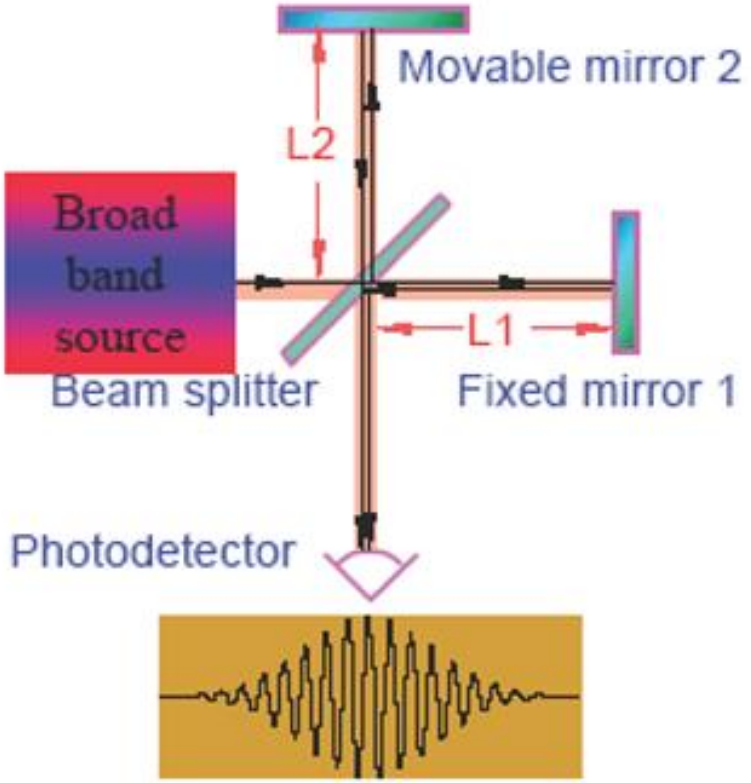
$\Gamma(\Delta L, \nu_1, \nu_2, \nu_3)$



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



Limiting Case

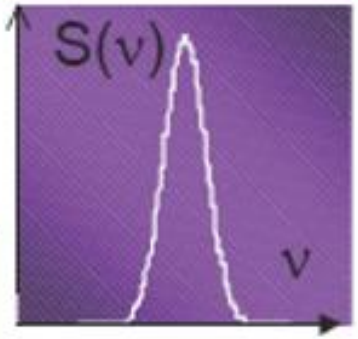


For discrete light with different wavelength

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

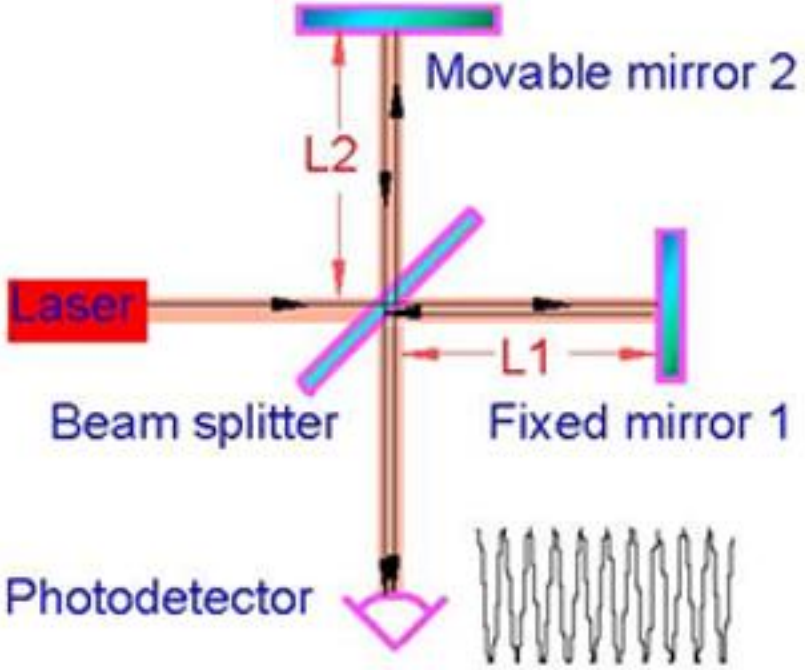
For continuous spectra with spectral density of S(ν):

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



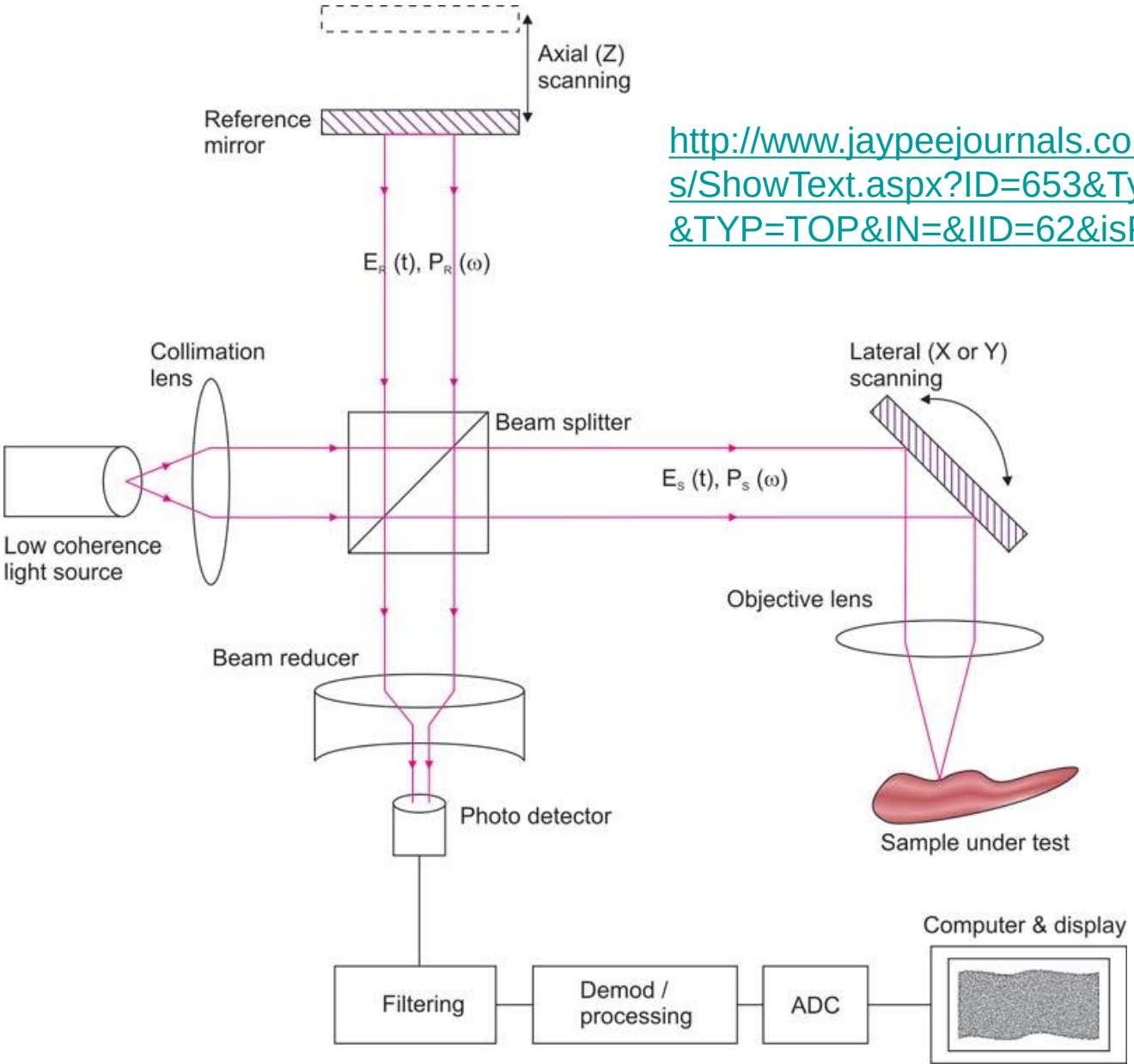
Interference fringes observed only when optical path lengths are matched within coherence length of the source

Michelson Interferometer



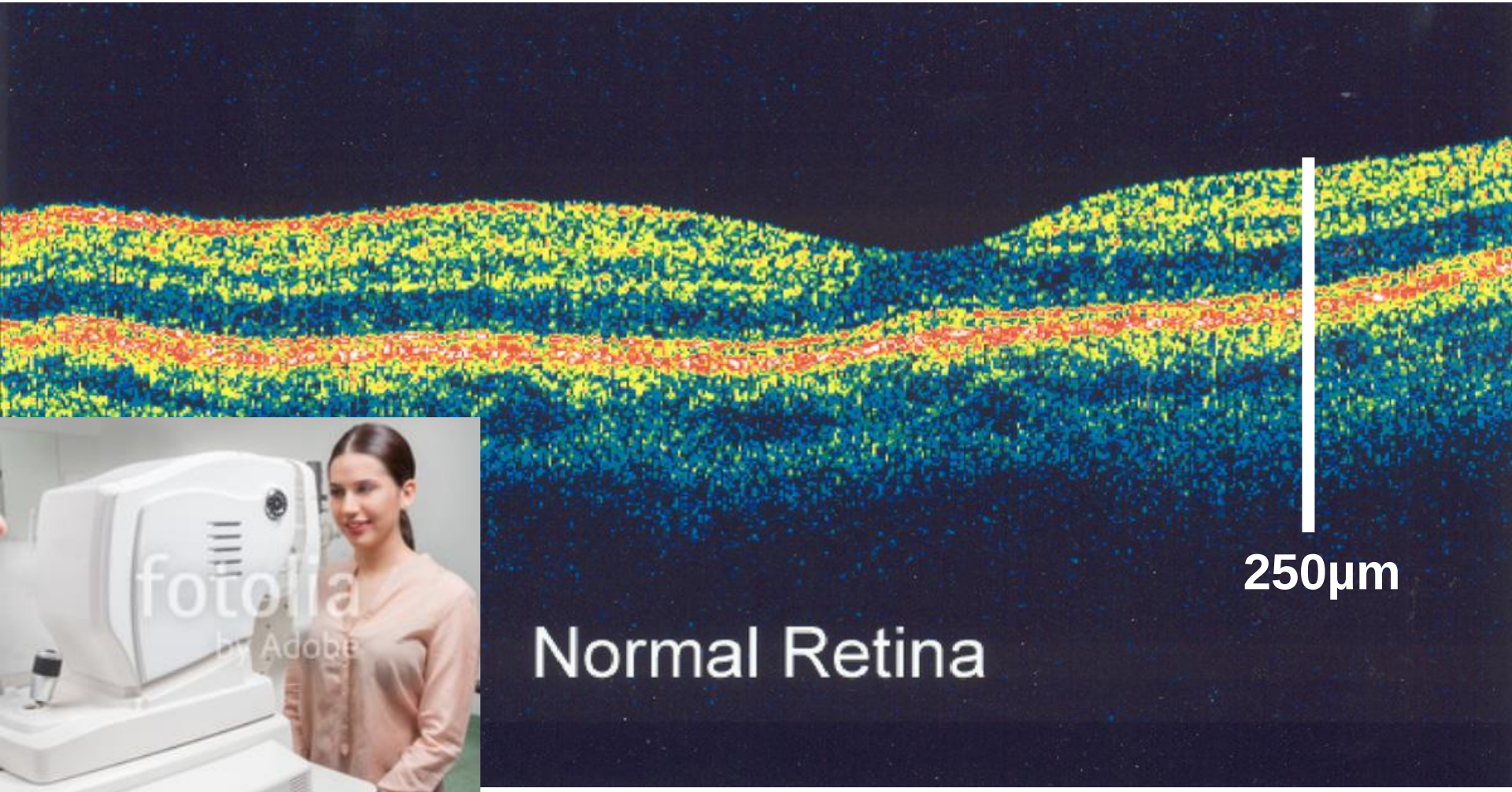
- **Optical path length difference:**
  $\Delta L = 2(L_2 - L_1)$
- **Phase difference:** $\phi = 2\pi\Delta L/\lambda$
- **Detected Light Intensity:**
  $$I = I_1 + I_2 + 2\sqrt{I_1 I_2}\cos(\phi)$$
- **Constructive interference:**
  $2\pi\Delta L/\lambda = 2m\pi$
  $\Delta L = m\lambda$
  $m = 0,1,2,.....$
- **Destructive interference:**
  $2\pi\Delta L/\lambda = (2m+1)\pi$
  $\Delta L = (m+1/2)\lambda$
  $m = 0,1,2,3,..$

OCT Principle

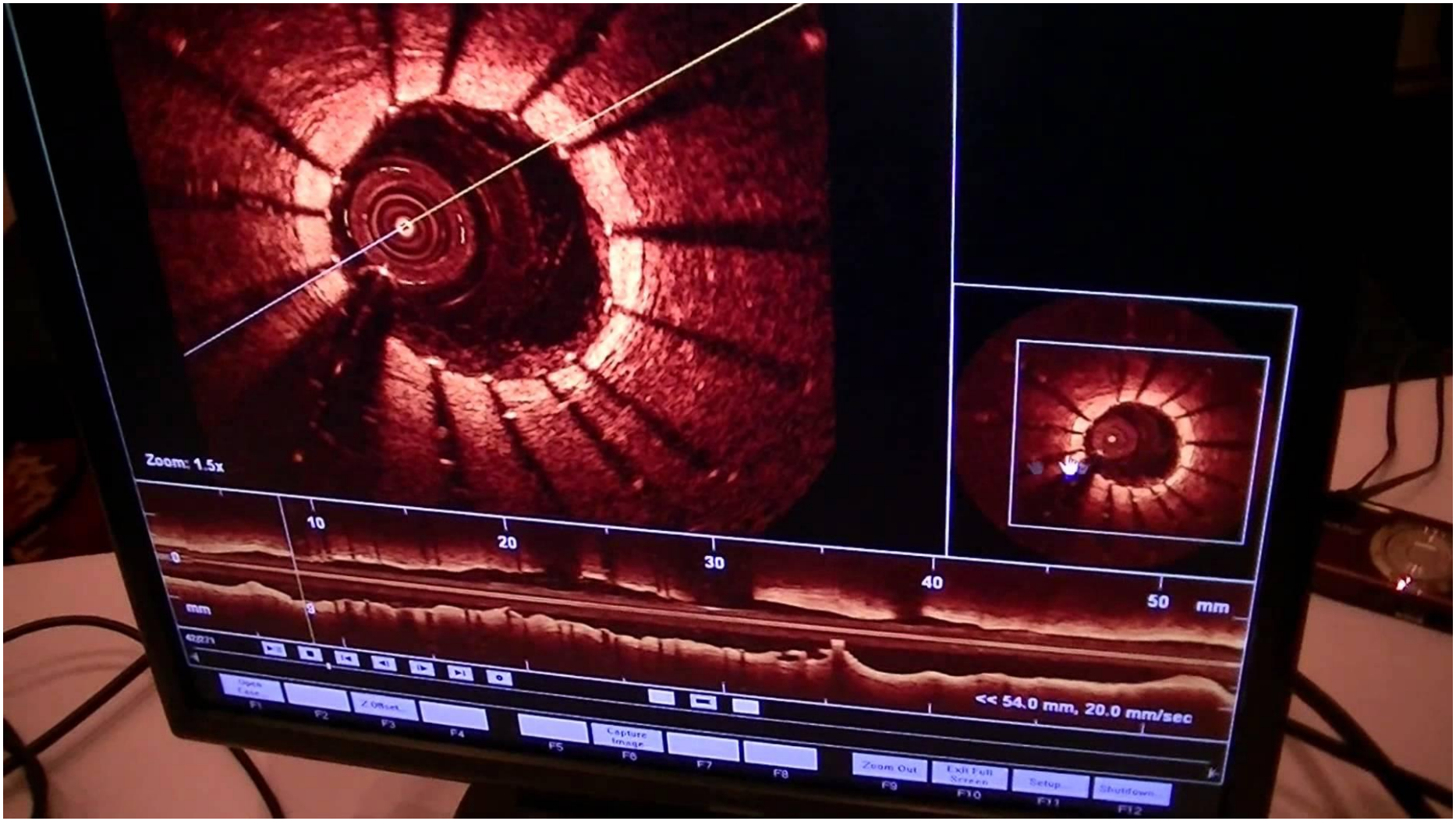


http://www.jaypeejournals.com/eJournals/ShowText.aspx?ID=653&Type=FREE&TYP=TOP&IN=&IID=62&isPDF=NO

Eye Exam with OCT



Cardiac Study with OCT



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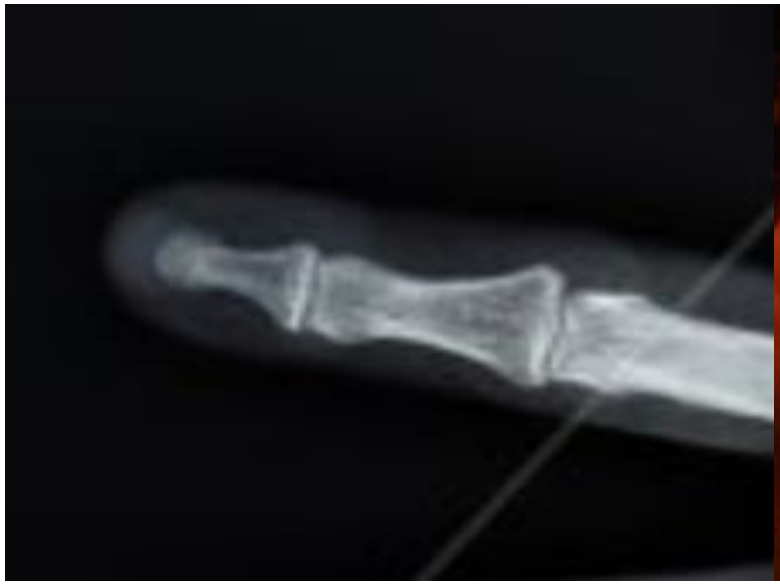
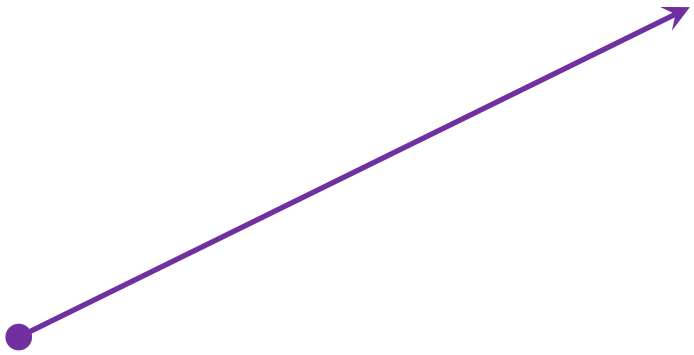
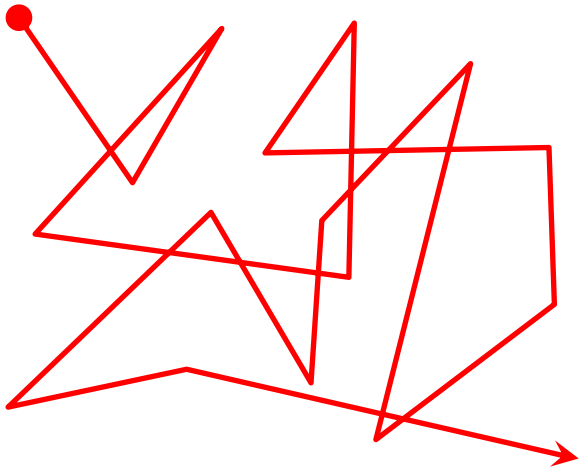
Light Diffusion

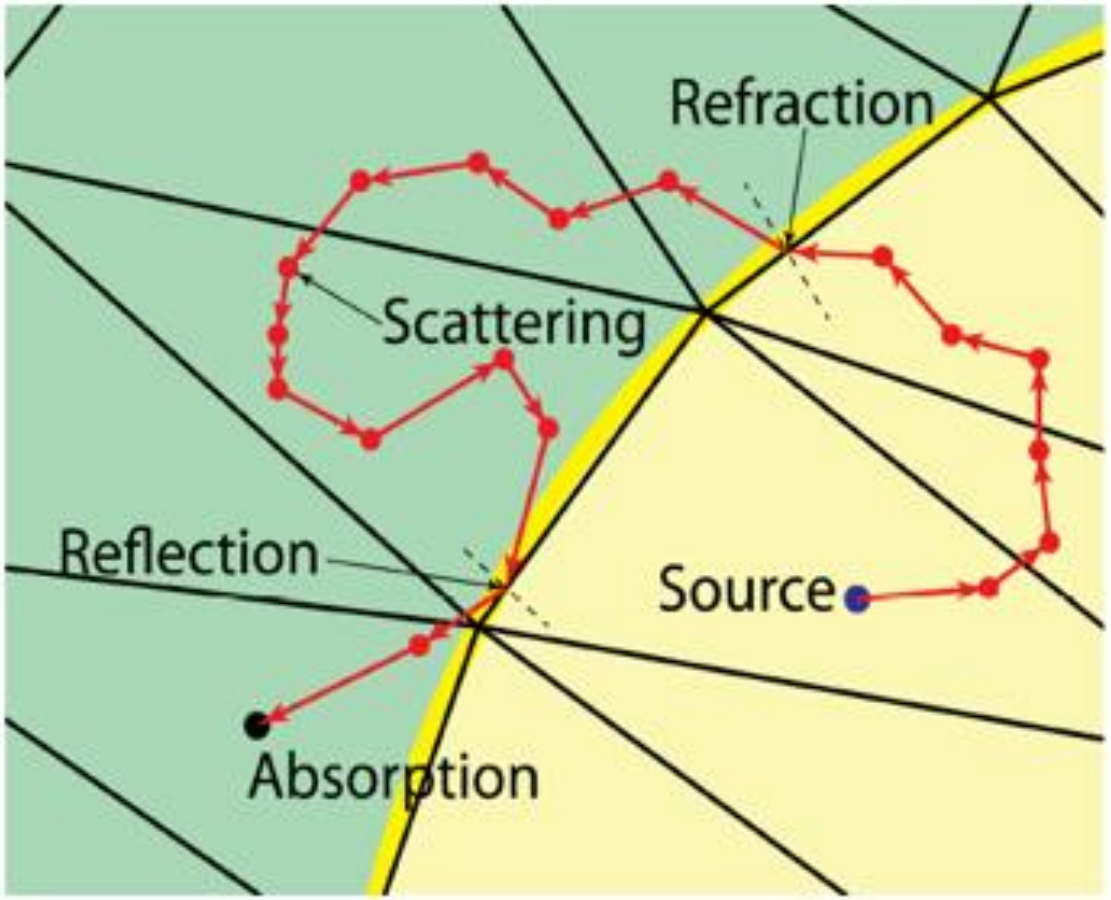




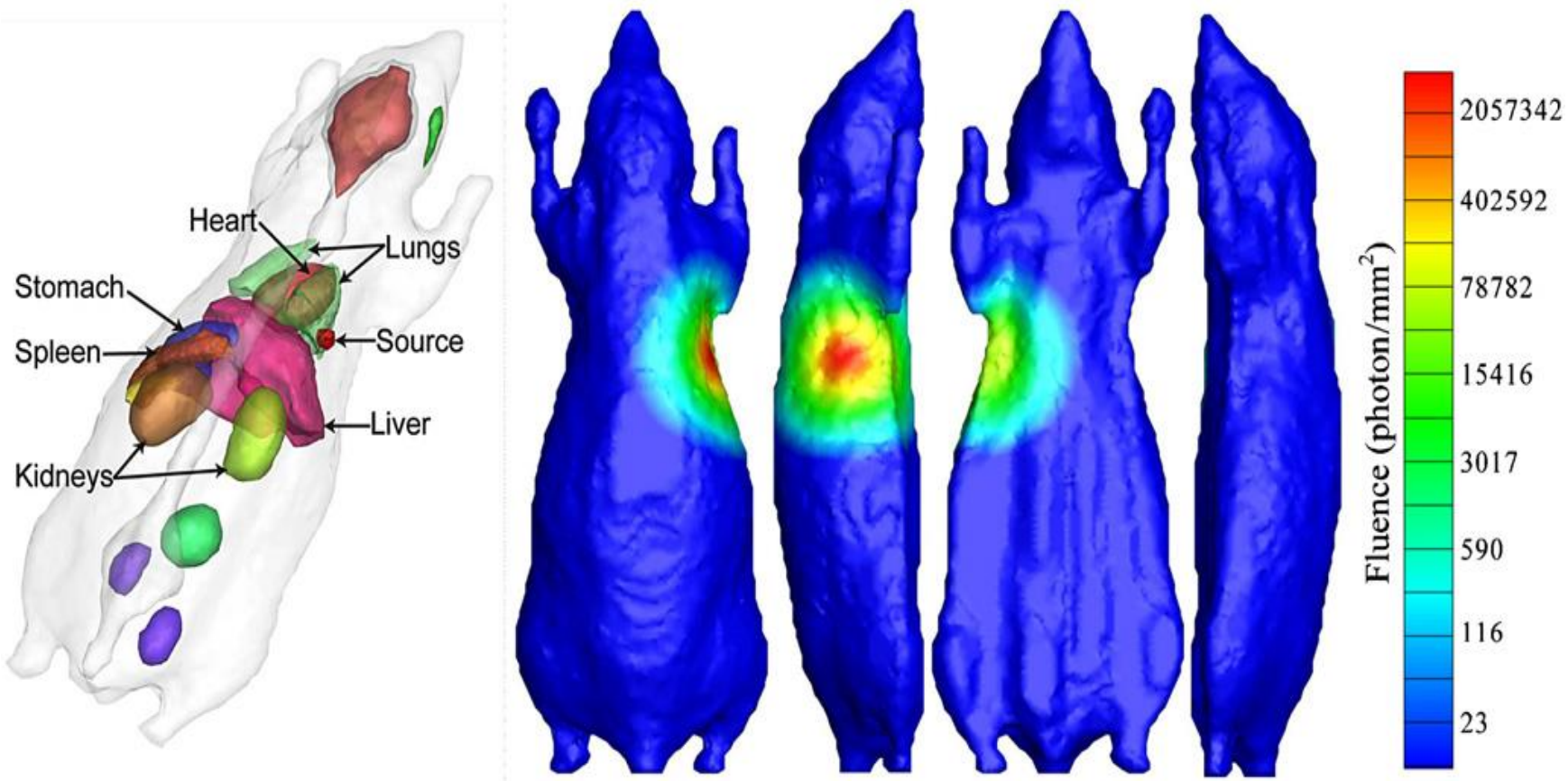


Monte-Carlo Simulation

An object is put as a finite element mesh with heterogeneous properties. Photons are traced according to light-tissue interactions.



Simulated Mouse



Shen HO, Wang G: A tetrahedron-based inhomogeneous Monte Carlo optical simulator. *Phys. Med. Biol.* 55:947, 2010

Mean Free Path (MFP) & Transport Mean Free Path (TMFP)

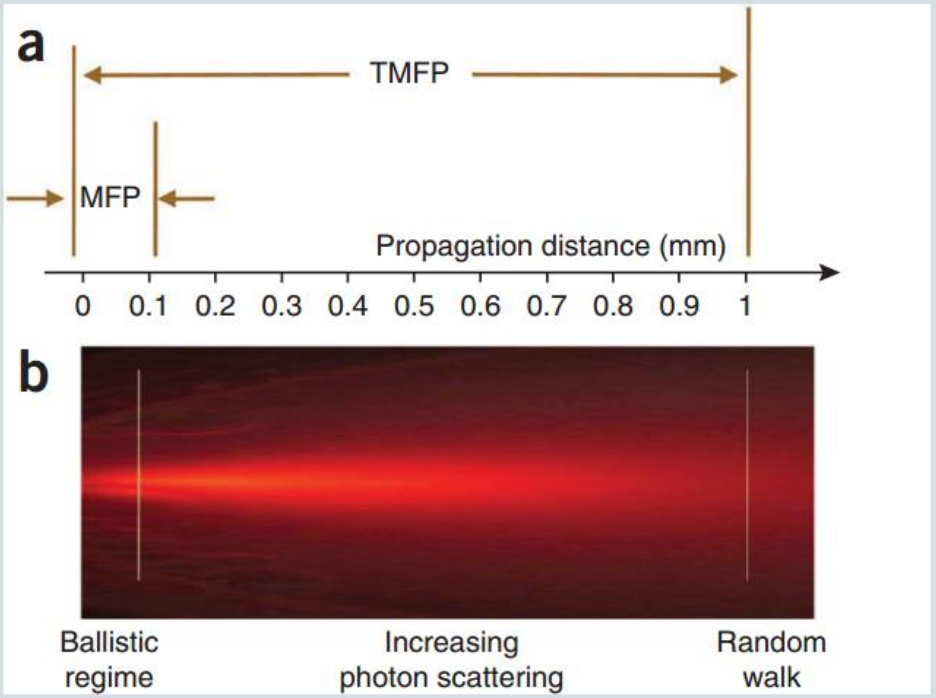
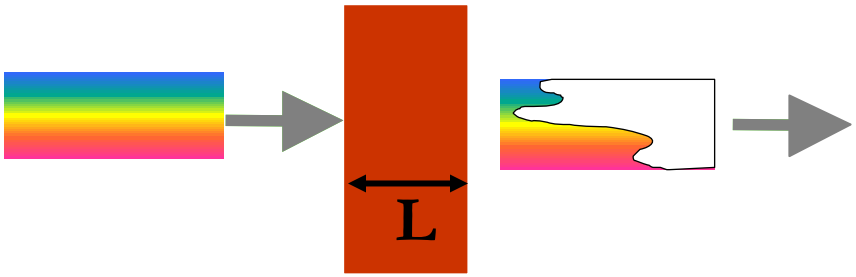


Figure 1 | Simplified metrics of photon propagation in tissue. (**a**,**b**) Schematic depiction of MFP and TMFP (**a**) and of photon propagation (**b**). The scale in physical dimensions is indicative of an average tissue with a reduced scattering coefficient of 10 cm^{-1}. This scale will vary depending on the tissue and the wavelength used.

http://www.nature.com/nmeth/journal/v7/n8/pdf/nmeth.1483.pdf

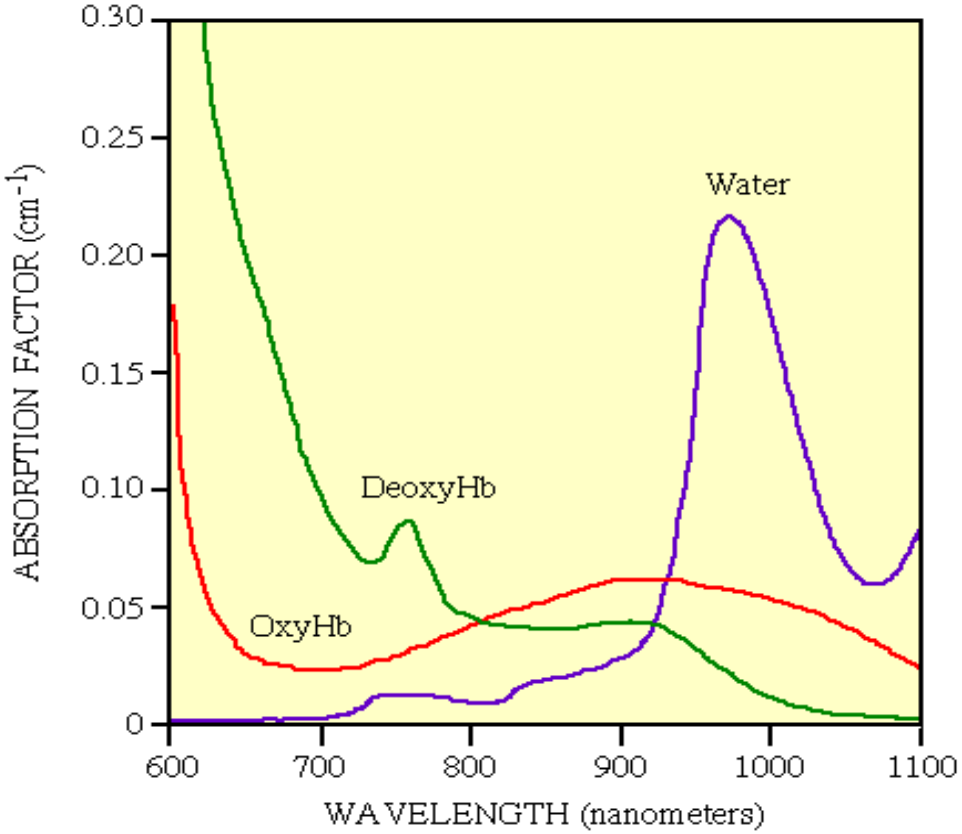
Diffuse Optical Spectroscopy (DOS)



$$\mu_a^{\lambda_1} = \varepsilon_{Hb}^{\lambda_1} \times [Hb] + \varepsilon_{HbO_2}^{\lambda_1} \times [HbO_2] + \mu_B^{\lambda_1}$$

$$\mu_a^{\lambda_2} = \varepsilon_{Hb}^{\lambda_2} \times [Hb] + \varepsilon_{HbO_2}^{\lambda_2} \times [HbO_2] + \mu_B^{\lambda_2}$$

$$I(\lambda) = I0(\lambda)\exp(-\mu_a L)$$

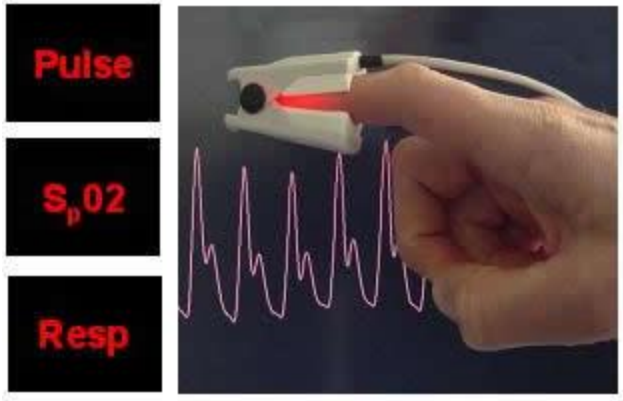


Hemoglobin Concentration

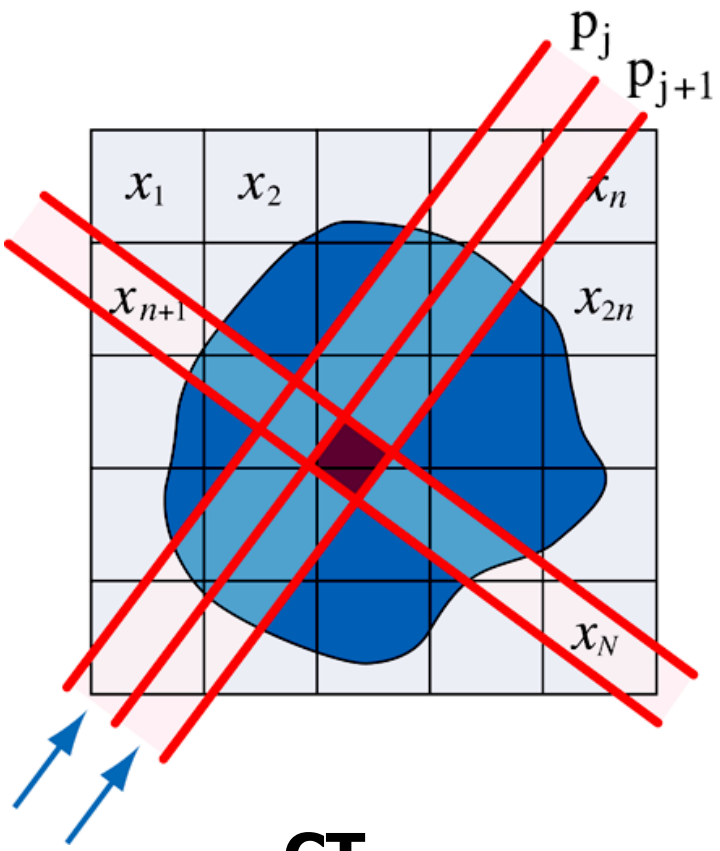
$$[THb] = [Hb] + [HbO_2]$$

Oxygen Saturation

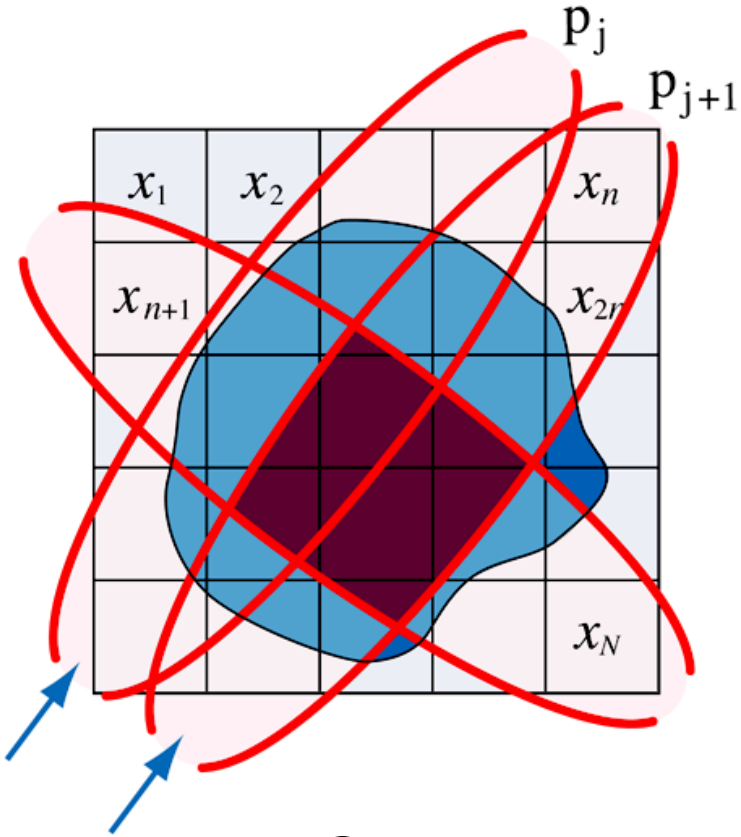
$$Y = \frac{[HbO_2]}{[Hb] + [HbO_2]} \times 100\ \%$$



Diffuse Optical Tomography (DOT)



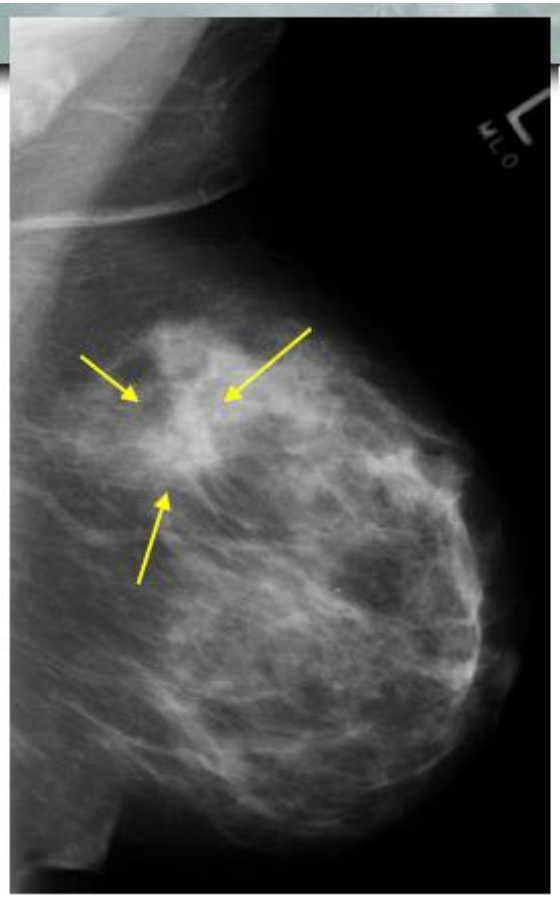
CT

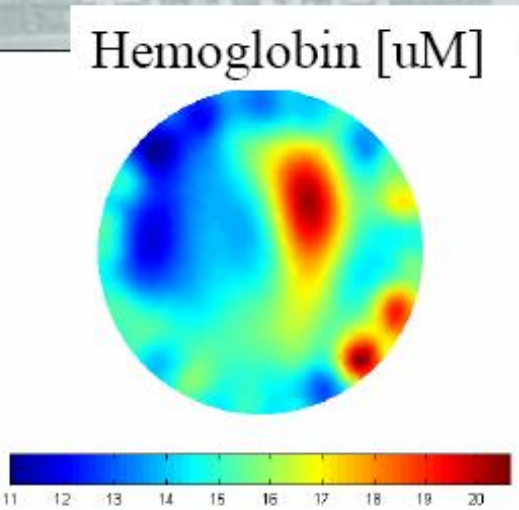


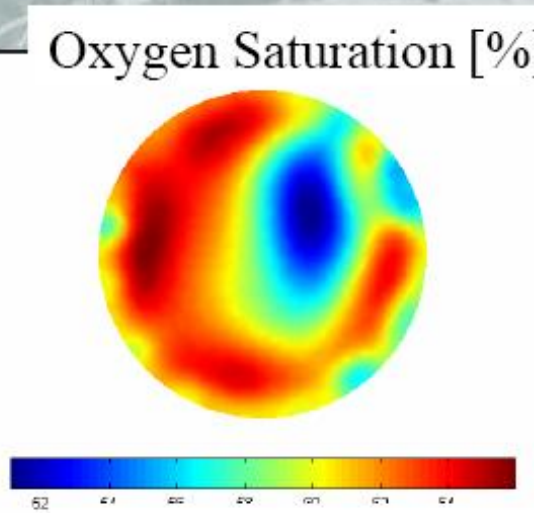
DOT

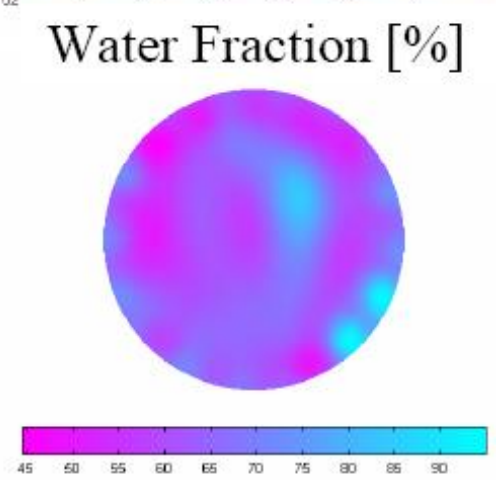
X. Intes, V. Ntziachristos, J. Culver, et al., Phys. Med. Biol., 47:N1 (1998)

DOT of Breast Cancer





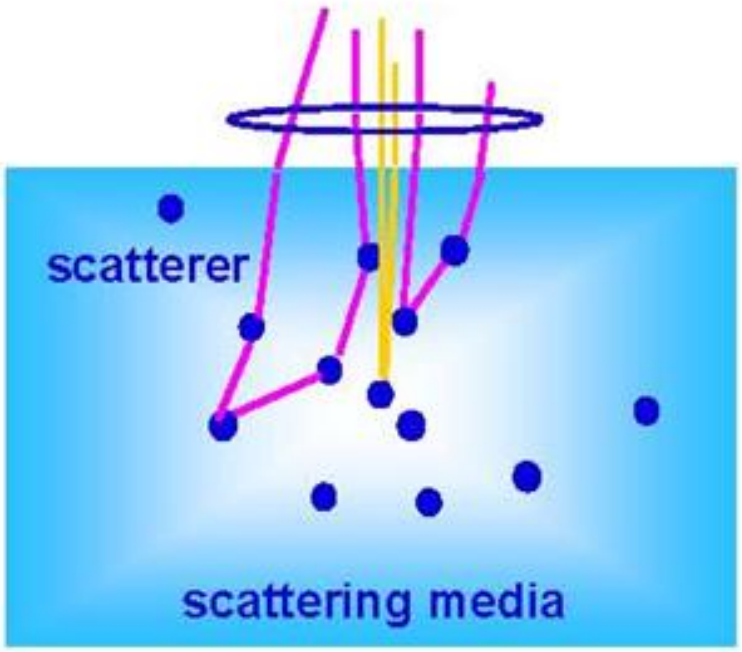


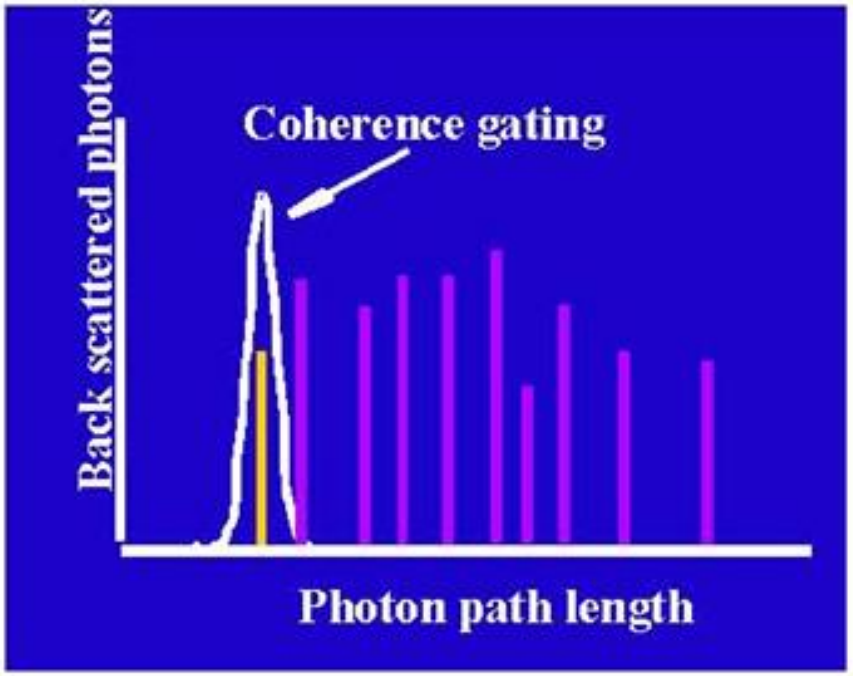


1) increased hemoglobin
2) decreased oxygen saturation
3) increased water

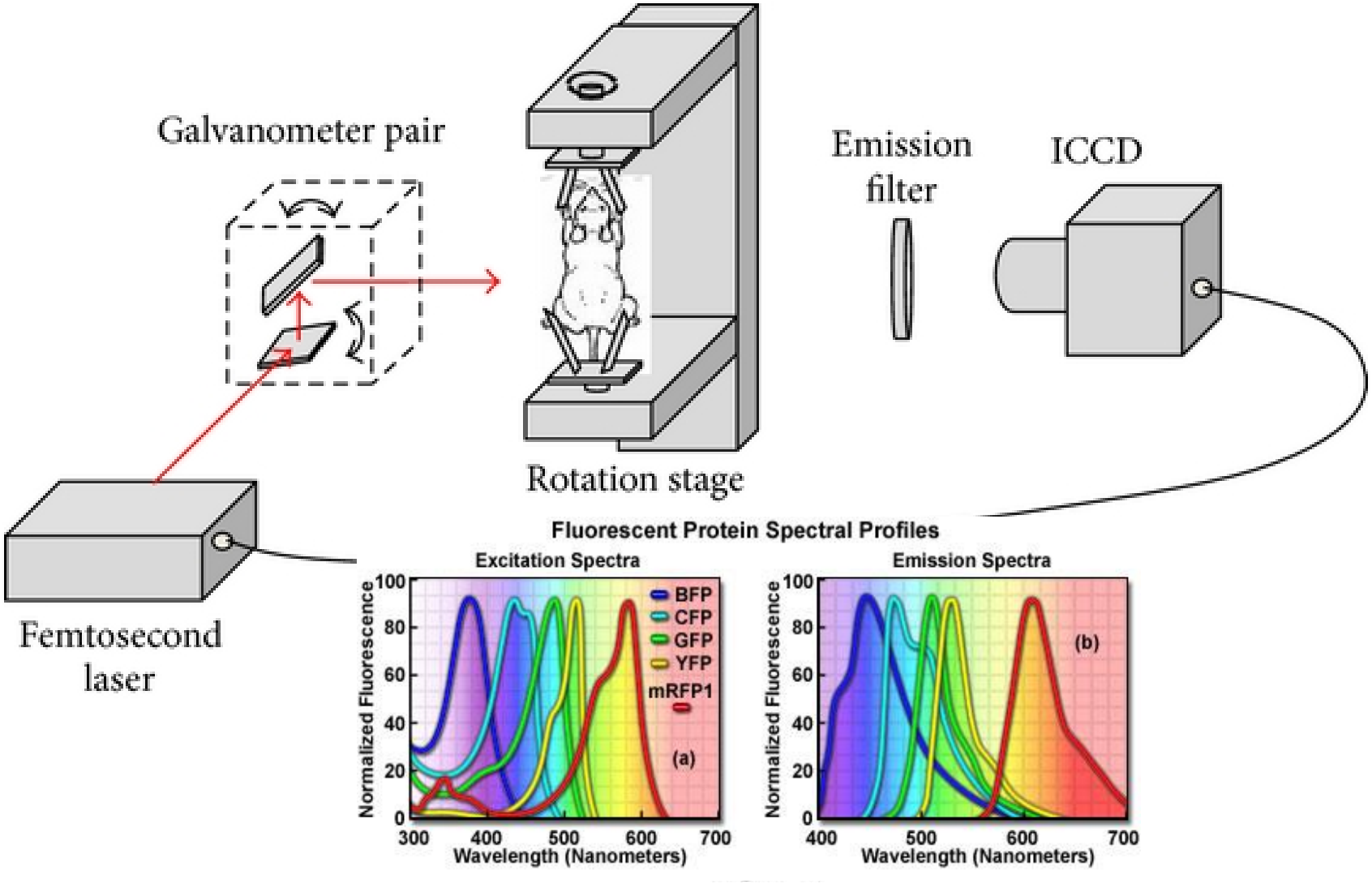
Dr. Brian Pogue, Dartmouth College

Temporal Gating





Fluorescence Molecular Tomography



Fluorescence Molecular Tomography

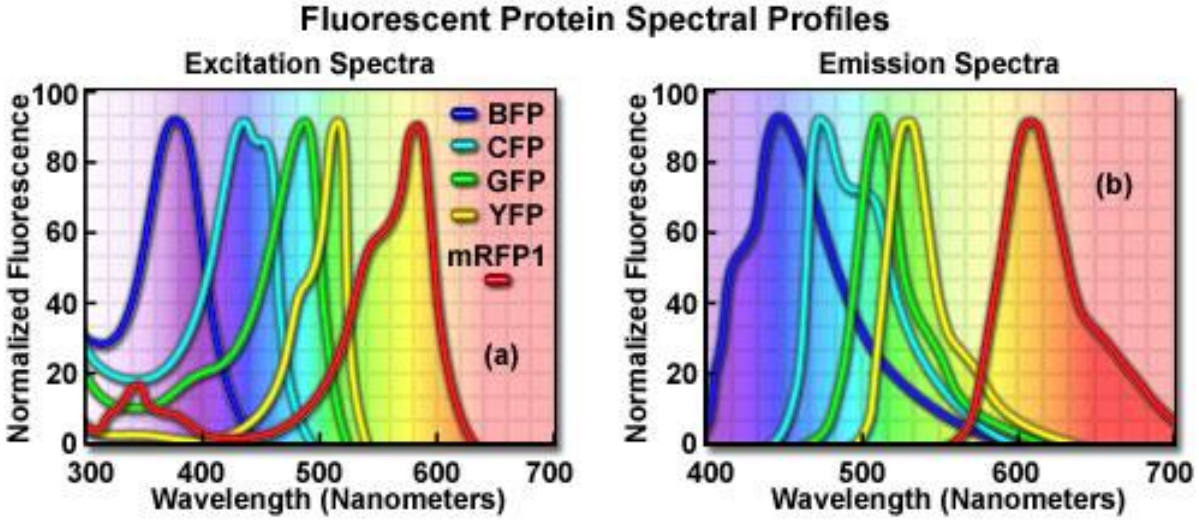
Fluorescent protein

Genetic expression

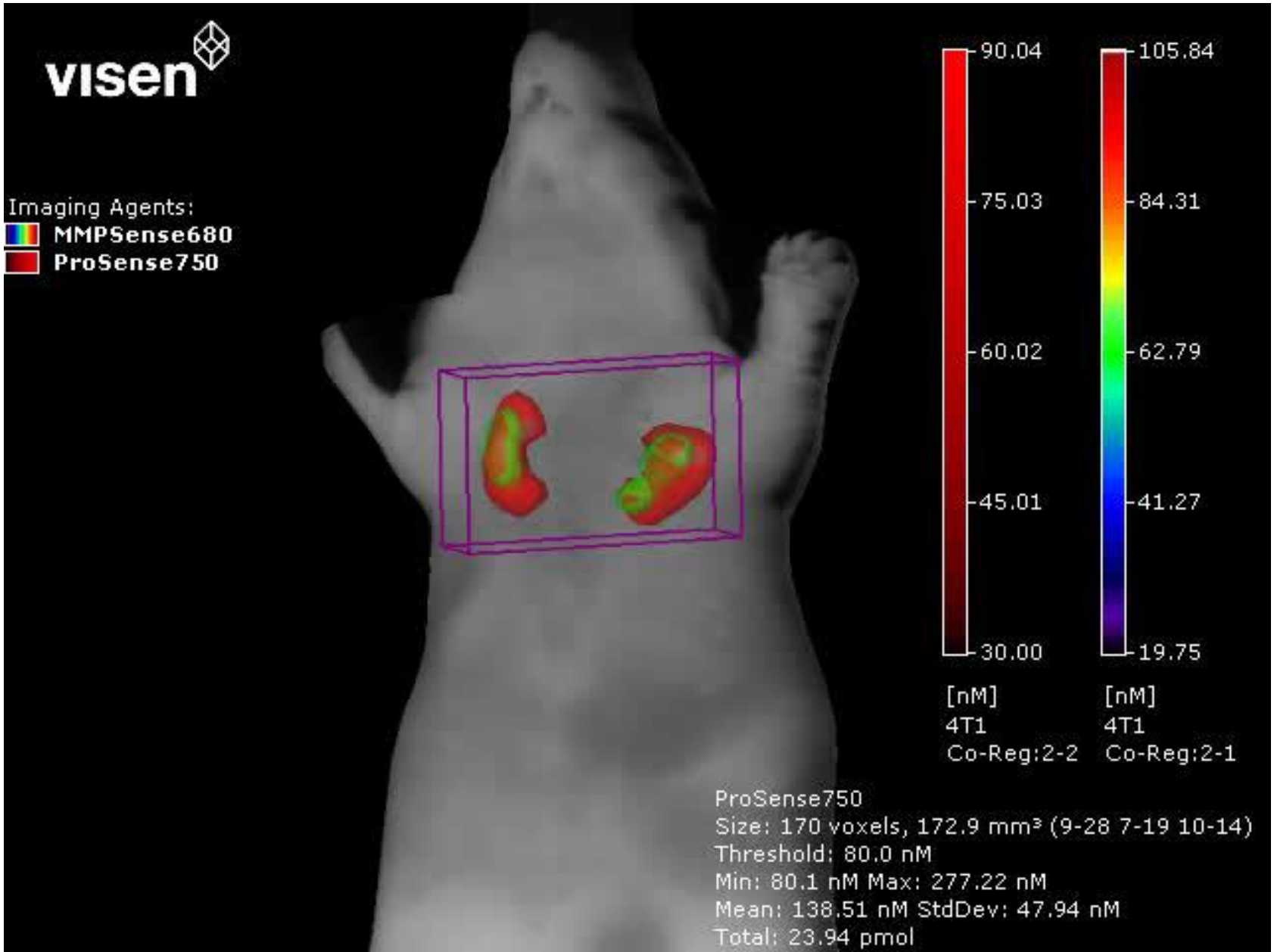
Green fluorescent protein from photogenic cells of jellyfish

Endogenous-Exogenous fluorophore

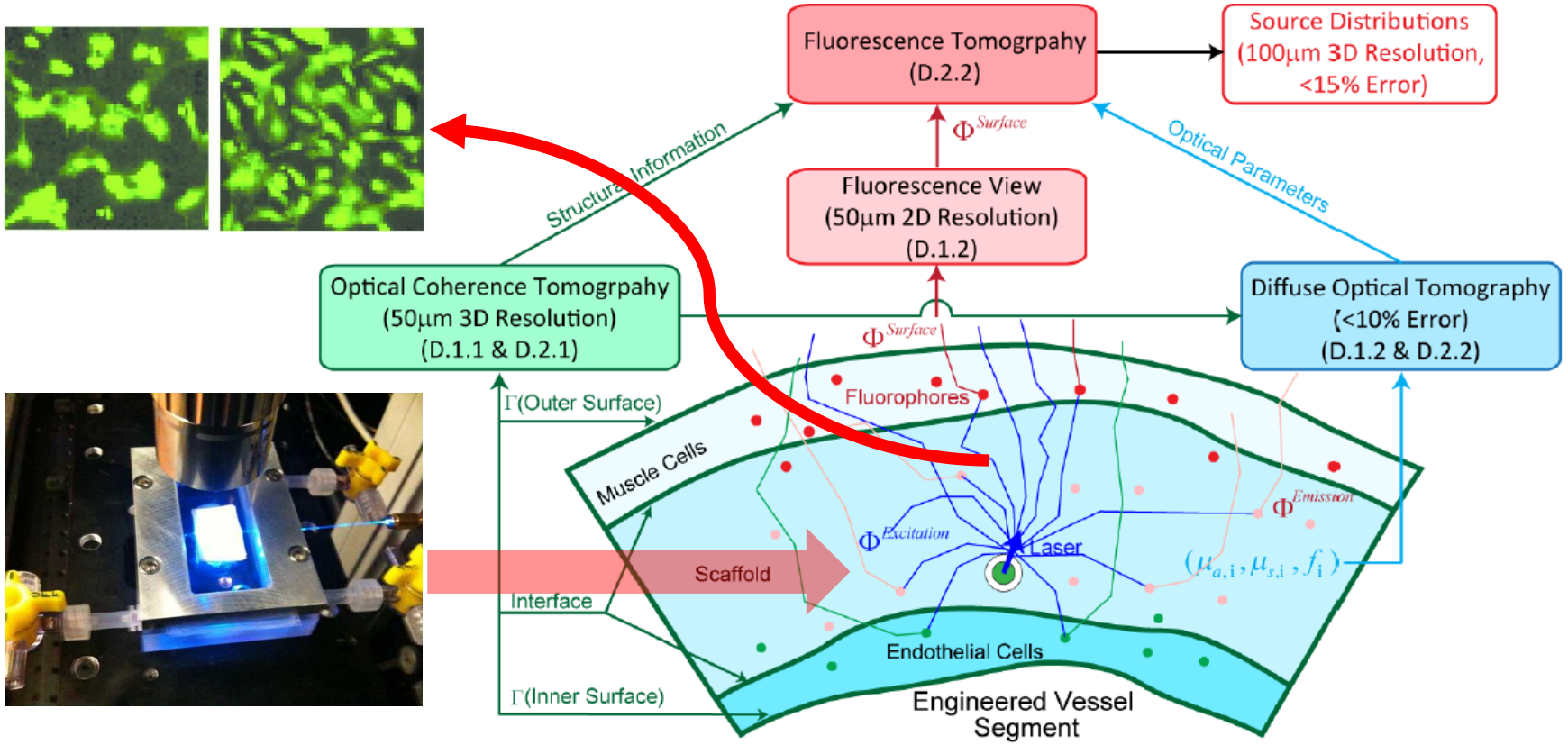
Not naturally occurring/expressed in cells



FMT Reconstruction



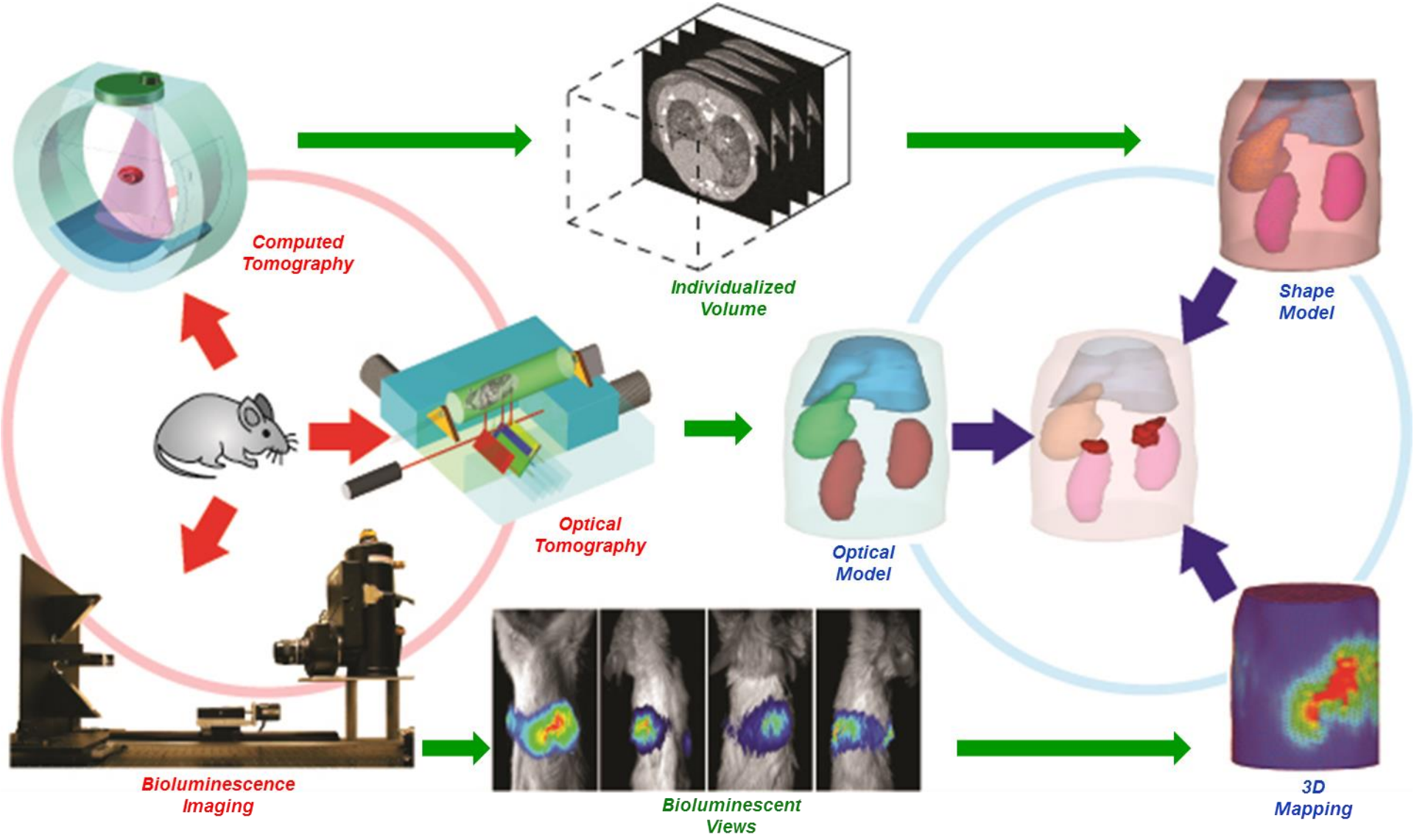
Optical Molecular Tomography for Regenerative Medicine (with Wake)



The goal is to develop a multi-probe multi-modal optical molecular tomography system for visualization of bioengineered blood vessels in bioreactors and after implantation into living animals.

Multi-PIs: Ge Wang & Shay Soker, NIH R01/BRP HL098912, 02/10-11/14

Bioluminescence Tomography



X-ray Optical Fusion

FMT-PCCT: Hybrid fluorescence molecular tomography - X-ray phase-contrast CT imaging of mouse models

Article (PDF Available) *in* IEEE Transactions on Medical Imaging 33(7) · March 2014 *with* 134 Reads
DOI: 10.1109/TMI.2014.2313405 · Source: PubMed


1st Pouyan Mohajerani
23.82 · Helmholtz Zentrum München

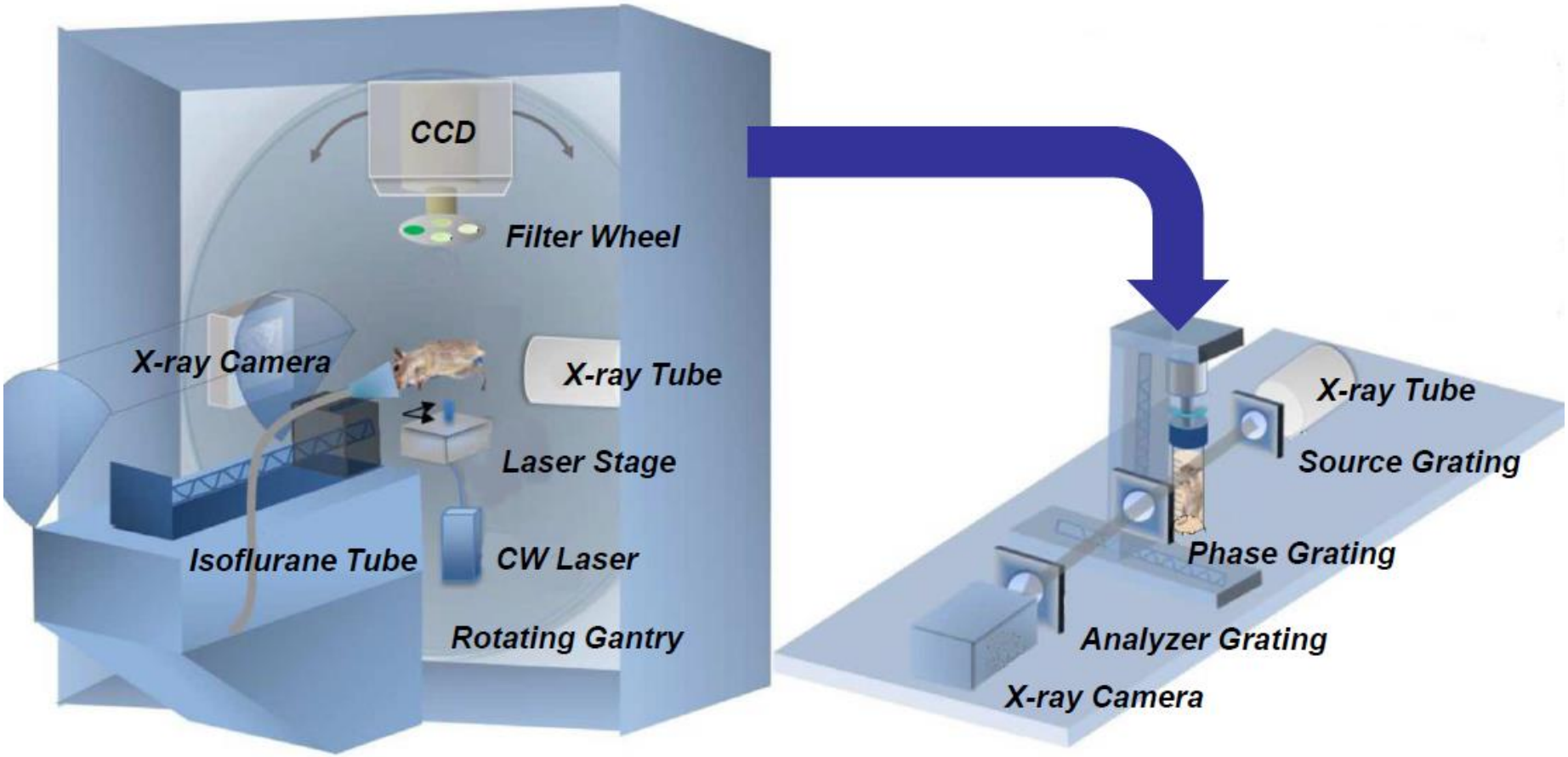

2nd Alexander Hipp
23.84 · Helmholtz-Zentrum Geesthacht


3rd Marian Willner
31.21 · Technische Universität ...

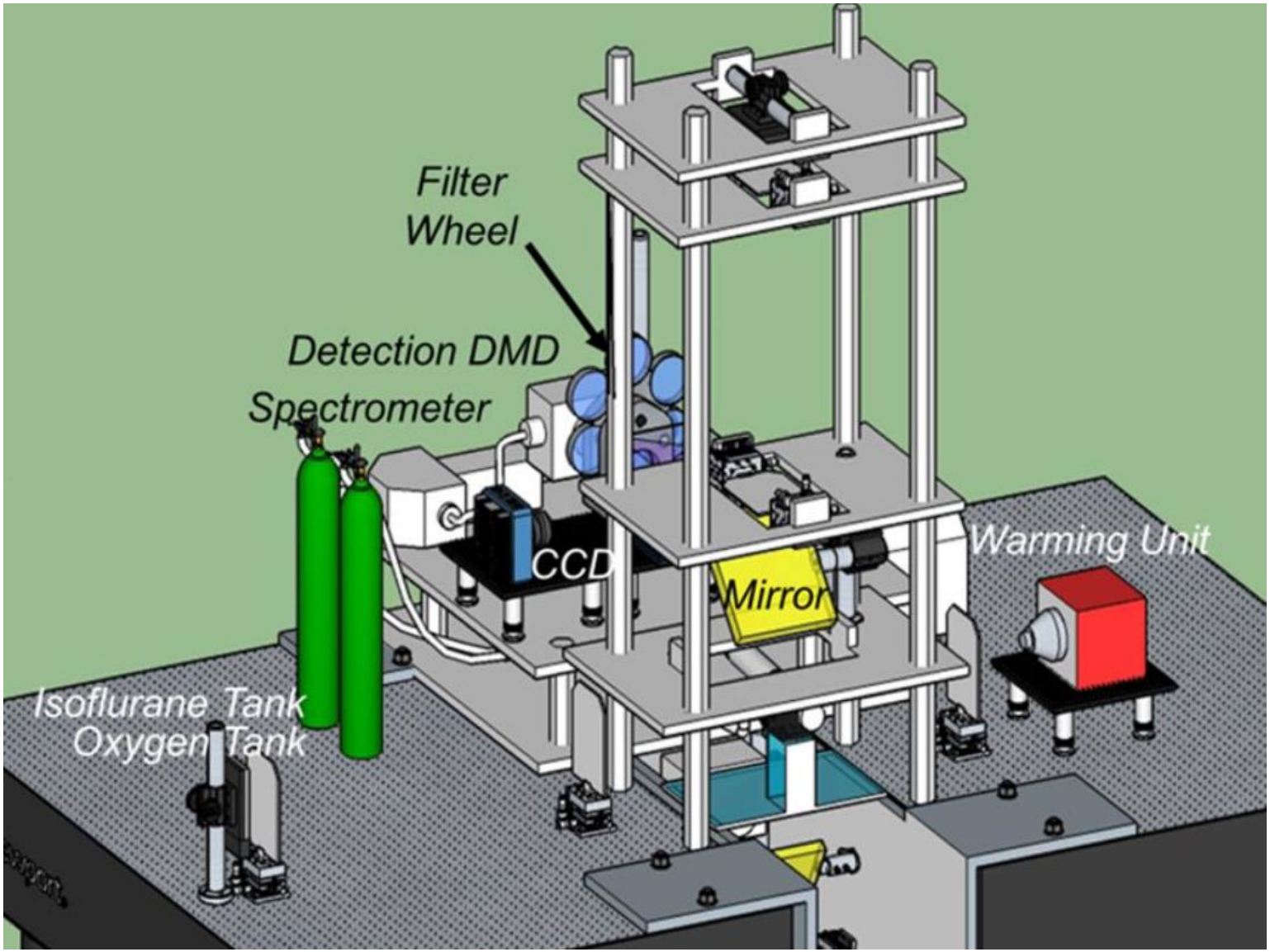
+ 7


Last Vasilis Ntziachristos

Ex Vivo Study



Tighter Integration at RPI



Optical Imaging

- **Optical Microscopy**
  - EM Wave
  - Optical-tissue Interaction
  - Microscopy
- **Optical Coherence Tomography**
  - Principle
  - Applications
- **Diffuse Optical Imaging**
  - DOS, DOT, FMT, BLT
- **X-ray Optical Coupling**
  - XLCT, XMLT

Coupling via Stimulated Emission

SCIENTIFIC REPORTS

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SUBJECT AREAS:
CONDENSED-MATTER PHYSICS
OPTICAL MATERIALS AND STRUCTURES
OPTICAL PHYSICS
NANOSCALE MATERIALS

Photostimulated near-infrared persistent luminescence as a new optical read-out from Cr^{3+}-doped $LiGa_5O_8$

Feng Liu[1,2], Wuzhao Yan[1,2], Yen-Jun Chuang[1], Zipeng Zhen[3], Jin Xie[3] & Zhengwei Pan[1,2]

[1]College of Engineering, University of Georgia, Athens, GA 30602, USA, [2]Department of Physics and Astronomy, University of Georgia, Athens, GA 30602, USA, [3]Department of Chemistry, University of Georgia, Athens, GA 30602, USA.

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6 March 2013

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8 March 2013

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27 March 2013

In conventional photostimulable storage phosphors, the optical information written by x-ray or ultraviolet irradiation is usually read out as a visible photostimulated luminescence (PSL) signal under the stimulation of a low-energy light with appropriate wavelength. Unlike the transient PSL, here we report a new optical read-out form, photostimulated persistent luminescence (PSPL) in the near-infrared (NIR), from a Cr^{3+}-doped $LiGa_5O_8$ NIR persistent phosphor exhibiting a super-long NIR persistent luminescence of more than 1,000 h. An intense PSPL signal peaking at 716 nm can be repeatedly obtained in a period of more than 1,000 h when an ultraviolet-light (250–360 nm) pre-irradiated $LiGa_5O_8:Cr^{3+}$ phosphor is repeatedly stimulated with a visible light or a NIR light. The $LiGa_5O_8:Cr^{3+}$ phosphor has promising applications in optical information storage, night-vision surveillance, and *in vivo* bio-imaging.

X-ray Luminescence CT

Simultaneous Anatomical and Molecular Tomographic Imaging using X-Ray-Excitable Nanoparticles - Internet Explorer

http://www.wmis.org/abstracts/2010/forSystemUse/papers/0110.html

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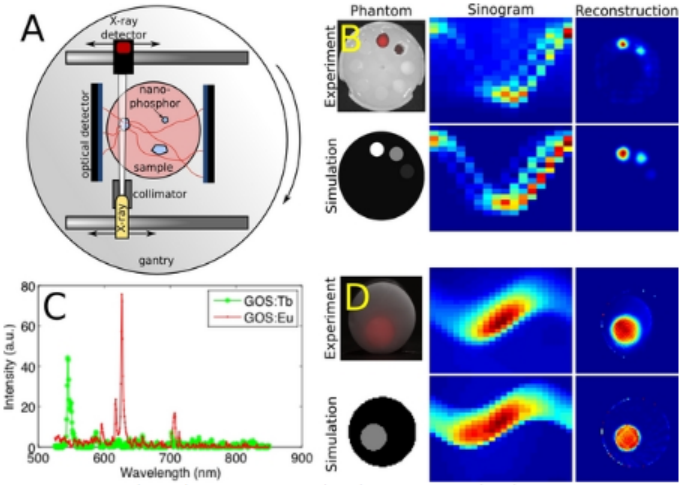
Presentation Number **0110**
Scientific Session 12: Novel Hybrid Molecular Imaging Technology
September 10, 2010 / 09:15-09:30 / Room: A

Simultaneous Anatomical and Molecular Tomographic Imaging using X-Ray-Excitable Nanoparticles

Guillem Pratx[1], *Colin M. Carpenter*[1], *Conroy Sun*[1], *Padmanabha R. Ravilisetty*[2], *Lei Xing*[1], [1]*Radiation Oncology, Stanford University School of Medicine, Stanford, CA, USA;* [2]*SRI International, Menlo Park, CA, USA. Contact e-mail: pratx@stanford.edu*

X-ray luminescence computed tomography (XLCT) is proposed as a new molecular imaging modality for imaging X-ray-excitable phosphorescent nanoparticles three-dimensionally, in small animals. Some of these nano-sized particles can emit near-infrared (NIR) light when excited with X-rays and be functionalized to target specific biological processes in vivo. XLCT enables anatomical images to be acquired simultaneously with molecular images via standard X-ray computed tomography (CT). The imaging mechanism used in XLCT consists in irradiating the subject using a sequence of X-ray beams while sensitive photo-detectors measure the light diffusing out of the subject. For each beam position, the production of light is constrained to the narrow volume of the beam, hence, the collection of optical measurements forms parallel-beam projections. An XLCT system was simulated using Monte-Carlo. Preliminary experiments were also conducted in phantoms using a 50 kvP treatment X-ray generator and an EM-CCD camera. Images were reconstructed using a maximum-likelihood iterative algorithm. From simulations, tracer uptake in 2 mm-diameter targets can be detected and quantified with sub-picomolar sensitivity with less than 1 cGy of average radiation dose. Provided sufficient signal-to-noise ratio, the spatial resolution of the system can be made arbitrarily small by narrowing the beam aperture. In particular, 1 mm uniform spatial resolution was achieved for a 1 mm-wide X-ray beam. Images reconstructed from experimental XLCT measurements showed good agreement with the simulation model. In particular, the reconstructed signal was linear with phosphor concentration. Preliminary simulations and experiments show that XLCT is a feasible approach for imaging small animals or dedicated organs. With the next version of our experimental set-up, we expect improved spatial resolution and molecular sensitivity.



A: Proposed design for an XLCT system. B: Gradient phantom. C: Nanophosphor X-ray-stimulated emission spectrum. D: Optically diffusive phantom.

Disclosure of author financial interest or relationships:
G. Pratx, None; **C.M. Carpenter**, None; **C. Sun**, None; **P.R. Ravilisetty**, None; **L. Xing**, Varian Medical Systems, Grant/research support .

Start | 11:41 PM 1/9/2014

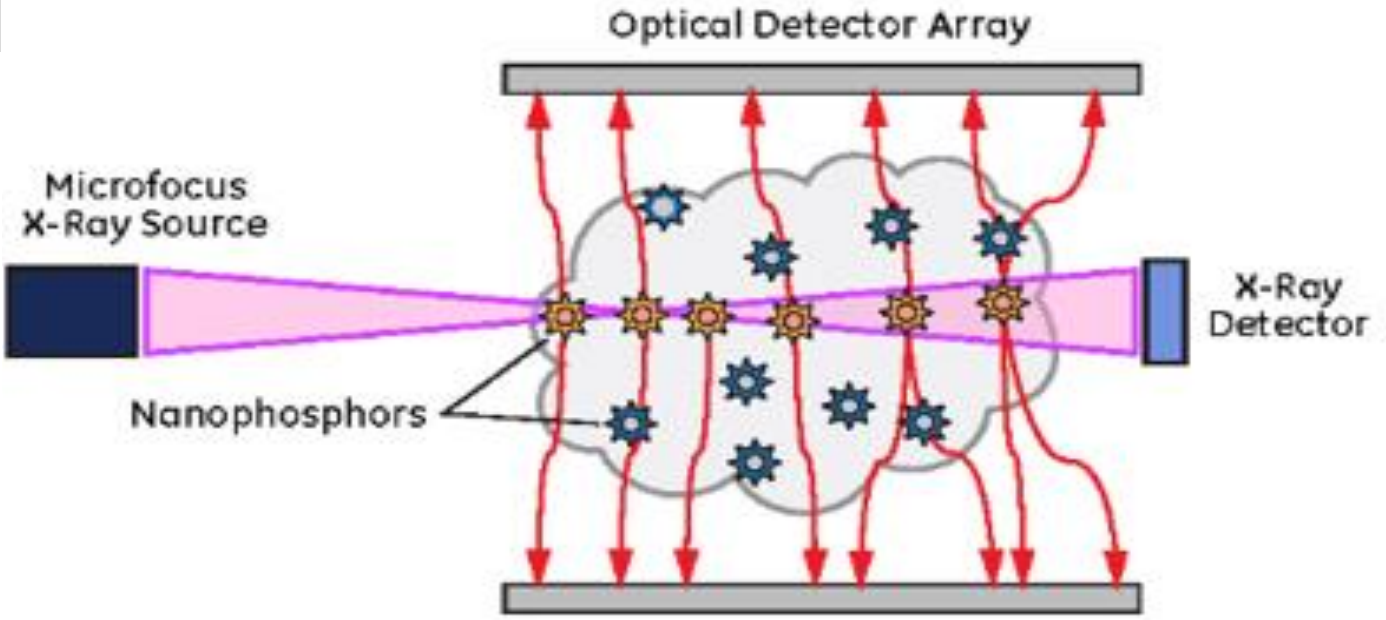
X-ray Micro-modulated Luminescence Tomography

Optics EXPRESS THE INTERNATIONAL ONLINE JOURNAL OF OPTICS
Editor: Andrew M. Weiner Vol. 22, Iss. 5 — Mar. 10, 2014 pp: 5572–5580

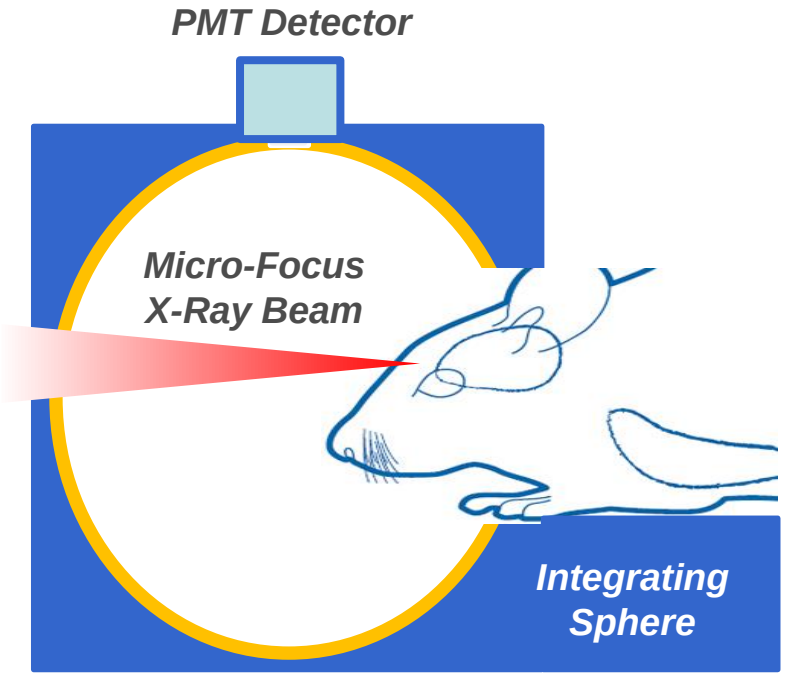
X-ray micro-modulated luminescence tomography (XMLT)

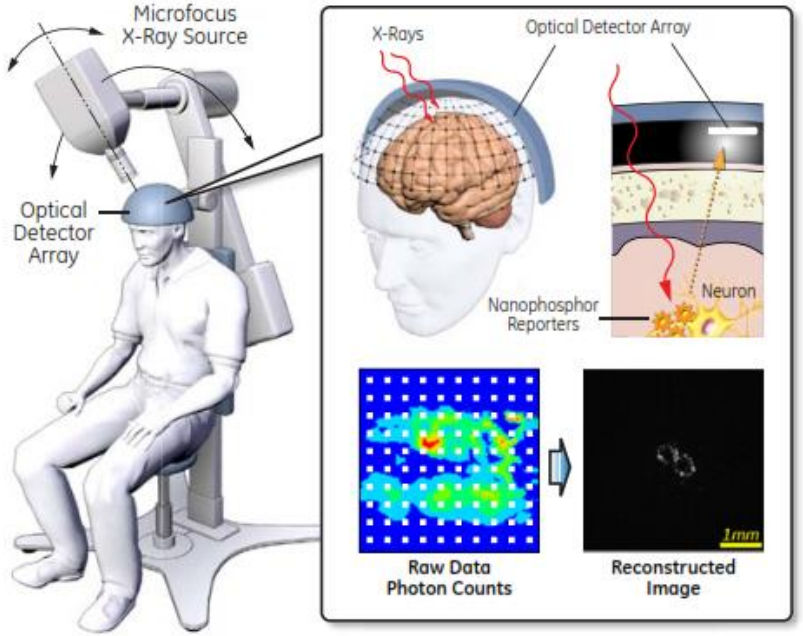
Author Affiliations

Wenxiang Cong,[1] Fenglin Liu,[1,2] Chao Wang,[1] and Ge Wang[1,*]



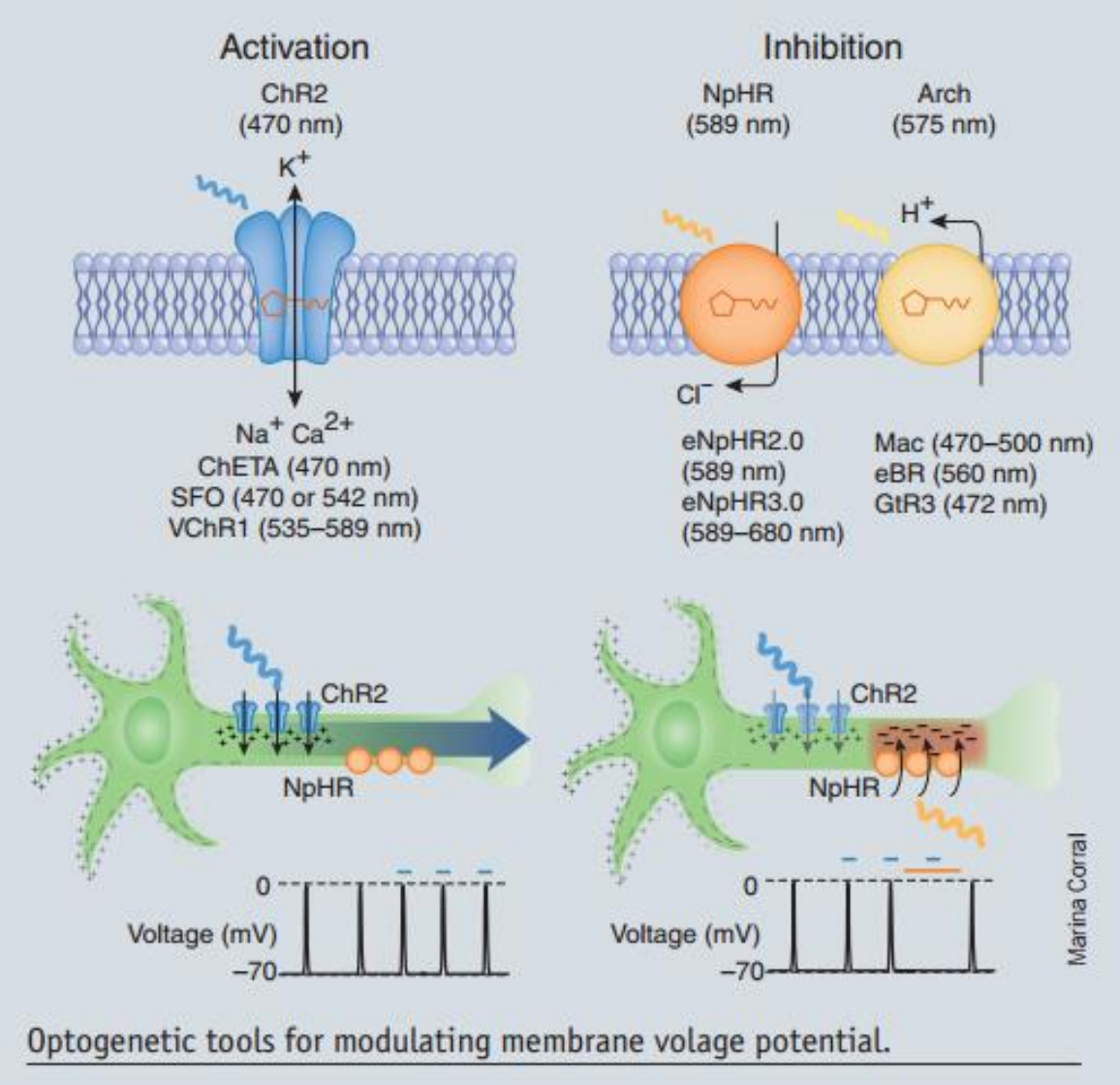
XMLT in Collaboration with GE





X-ray Micro-modulated Luminescence Tomography (XMLT) uses focused x-ray for nanophosphor excitation deeply into the neocortex and other tissue types. The nanophosphors may be functionalized to have specificity similar to μPET, resolution superior to μMRI, contrast comparable with optical imaging, and performance beyond typical μCT.

Optogenetics



Optogenetic tools for modulating membrane volage potential.

http://www.nature.com/nmeth/journal/v8/n1/full/nmeth.f.323.html

X-optogenetics

Photonics **2015**, *2*(1), 23-39; doi:10.3390/photonics2010023

Open Access

Article

X-Optogenetics and U-Optogenetics: Feasibility and Possibilities

Rachel Berry [†] ✉, **Matthew Getzin** [†] ✉, **Lars Gjesteby** ✉ **and Ge Wang** [*] ✉

Authors' affiliations

Received: 22 November 2014 / Accepted: 30 December 2014 / Published: 7 January 2015

(This article belongs to the Special Issue Biomedical Optics and Optical Imaging)

Abstract: Optogenetics is an established technique that uses visible light to modulate membrane voltage in neural cells. Although optogenetics allows researchers to study parts of the brain like never before, it is limited because it is invasive, and visible light cannot travel very deeply into tissue. This paper proposes two new techniques that remedy these challenges. The first is x-optogenetics, which uses visible light-emitting nanophosphors stimulated by focused x-rays. X-rays can penetrate much more deeply than infrared light and allow for nerve cell stimulation in any part of the brain. The second is u-optogenetics, which is an application of sonoluminescence to optogenetics. Such a technique uses ultrasound waves instead of x-rays to induce light emission, so there would be no introduction of radiation. However, the tradeoff is that the penetration depth of ultrasound is less than that of x-ray. The key issues affecting feasibility are laid out for further investigation into both x-optogenetics and u-optogenetics.

Keywords: Optogenetics; x-rays; ultrasound; nanophosphors; penetration depth

Homework

1. Review this lecture to summary key ideas/points.

2. Transcribe the 1st part, 2nd part, or the last two parts of this lecture.

3. If we make a smart phone send and receive light anyway you want, what medical imaging applications could you imagine?