

# Micro- and Nano- Tomography of Biological Tissues

Marco Stampanoni and Kevin Mader

Swiss Light Source, Paul Scherrer Institut  
Institute for Biomedical Engineering, University and ETH Zürich

ETH-227-0965-00 L



# Contacts

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ETH Zürich, ETZ F 85

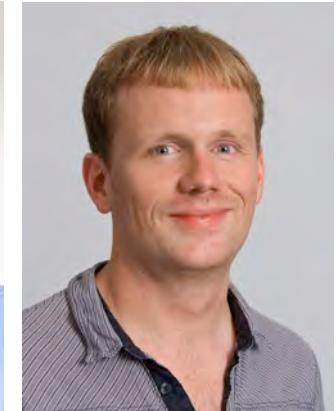
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# Assistant - Exercises

**Mr Ioannis Vogiatzis-Oikonomidis**

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IBT, ETZ H75 , Gloriastrasse 35, 8092 Zürich

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Filippo Arcadu



Maria Büchner



# Course logistic

Date	Topic	Lecturer	Room
14.09	Lectures Start HS 2015		
21.09	<b>L: X-ray physics: generation, interactions with matter</b> E: Papers distribution	Stampanoni	ETZ-E9
28.09	<b>L: Image formation: from 2D to 3D</b> E: Exe 1-2	Stampanoni Vogiatzis	ETZ-E9
05.10	<b>P : Practical "Reconstruction"</b>	Arcadu/Büchner Vogiatzis	TbD
12.10	<b>L: Synchrotron light: imaging at the micron scale</b> E : Exe 3-4	Stampanoni Vogiatzis	ETZ-E9
19.10	<b>L : Imaging beamlines, in-situ experiments</b> E : Exe 5-6	Stampanoni Vogiatzis	ETZ-E9
26.10	<b>L: Visualizing soft tissue: X-ray phase contrast</b> E: Exe 7-8	Stampanoni Vogiatzis	ETZ-E9
02.11	<b>P: Practical "Quantification"</b>	Arcadu/Büchner Vogiatzis	TbD
9.11.	<b>L: Pushing the limits : Microimaging</b> E: Exe 9-10	Stampanoni Vogiatzis	ETZ-E9
16.11	<b>L: Pushing the limits: Nanoimaging</b> E: Exe 11-12	Stampanoni Vogiatzis	ETZ-E9
23.11	<b>L: Preprocessing: from measurements to images</b> E: Student presentation 10min per pair (if needed)	Mader Stampanoni/Mader	ETZ-E9
30.11	<b>L: Segmentation: from images to features</b> E: Student presentation 10min per pair	Mader Stampanoni/Mader	ETZ-E9
7.12	<b>L: Segmentation: from features to statistics</b> E: Student presentation 10min per pair	Mader Stampanoni/Mader	ETZ-E9
14.12	<b>E: Visit @ Swiss Light Source</b>	Stampanoni	SLS (!)

Documents will be put online (polybox) at latest the day before the lecture as PDF  
Download at: you will get an email with details (via myStudies)

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- **Basics of X-ray imaging**

- X-ray generation and interaction with matter
- Projection and tomographic imaging, image reconstruction
- Image quality, noise and dose issues.

- **Imaging at the micron scale**

- Synchrotron light and its properties
- Imaging beamlines and related instrumentation
- Sample environments
- In-situ experiments

- **Soft-tissue imaging - Phase contrast imaging**

- Crystal interferometry
- Transport of Intensity
- Grating interferometry

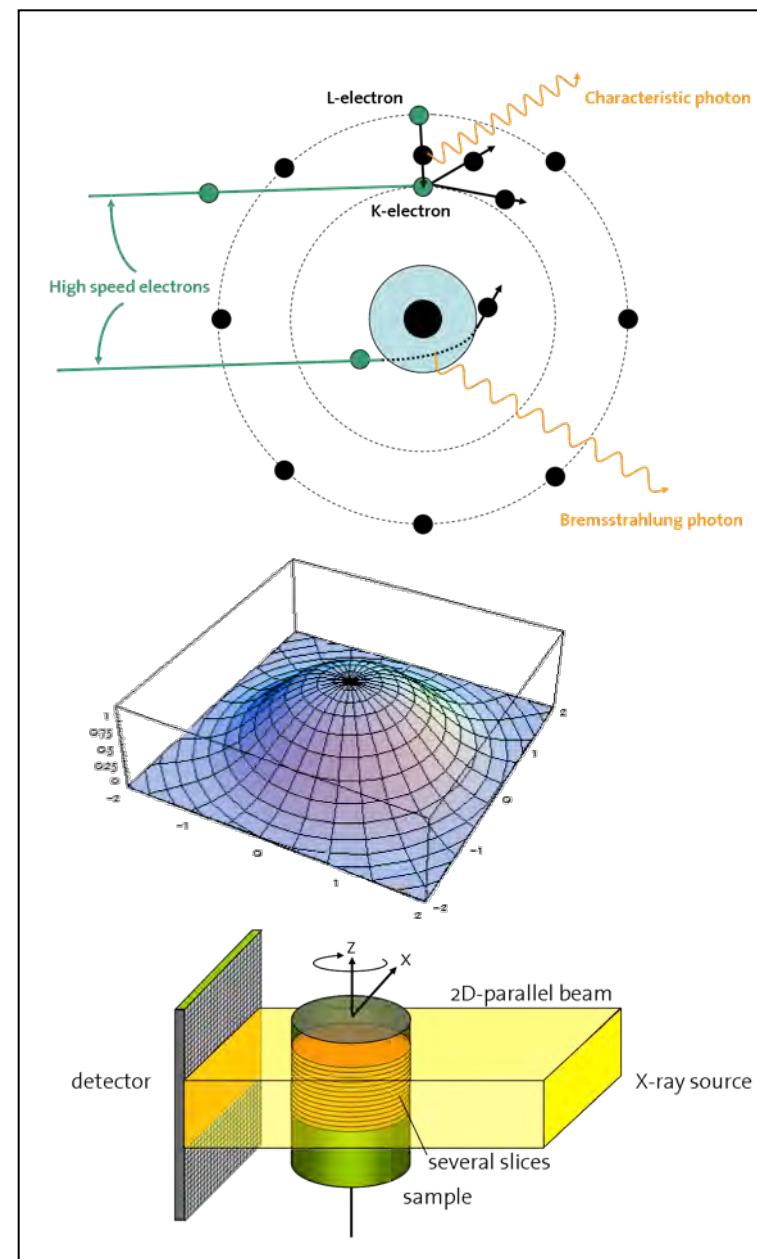
- **From micro- to nano-tomographic imaging**

- Full Field Microscopes
- Fresnel Zone Plates / KB Systems / CR lenses
- Scanning Transmission X-ray Microscopy
- Hard X-rays Microscopes vs Water window
- Realtime imaging

- **Extracting quantitative information from 3D data**

- Filtering and Segmentation
- Morphometrical Analysis
- Statistics
- Applications to bio-imaging

- **Experiment at the Swiss Light Source**



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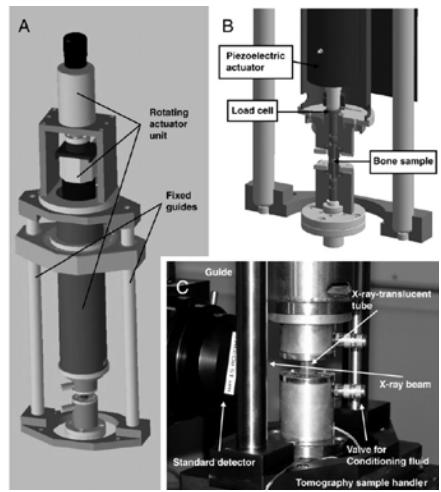
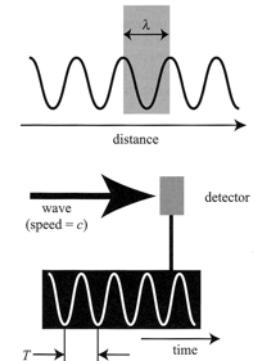
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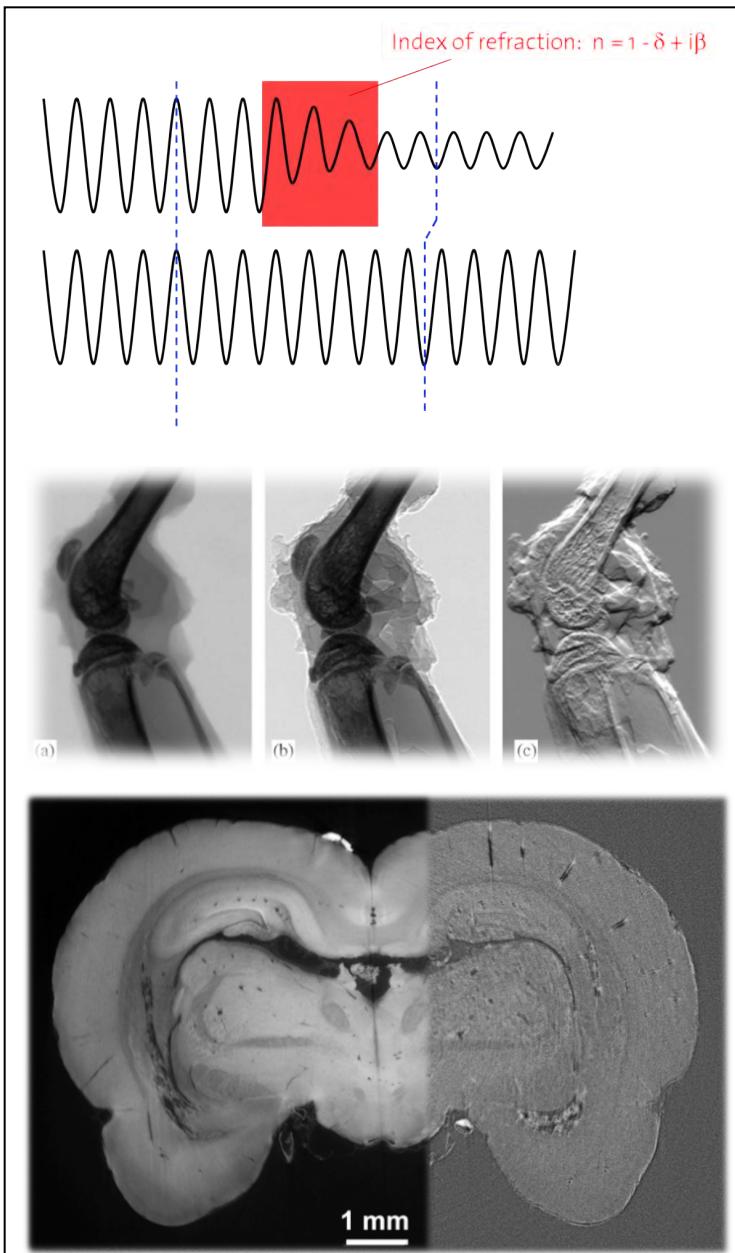
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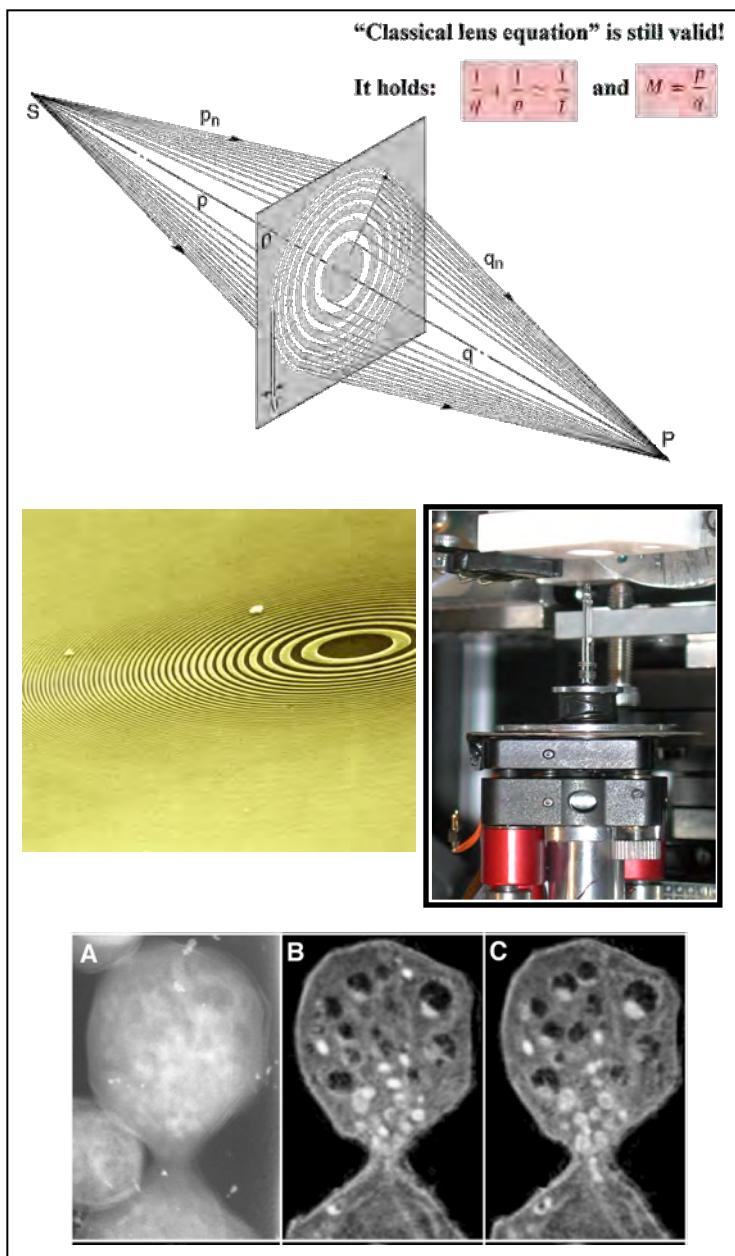
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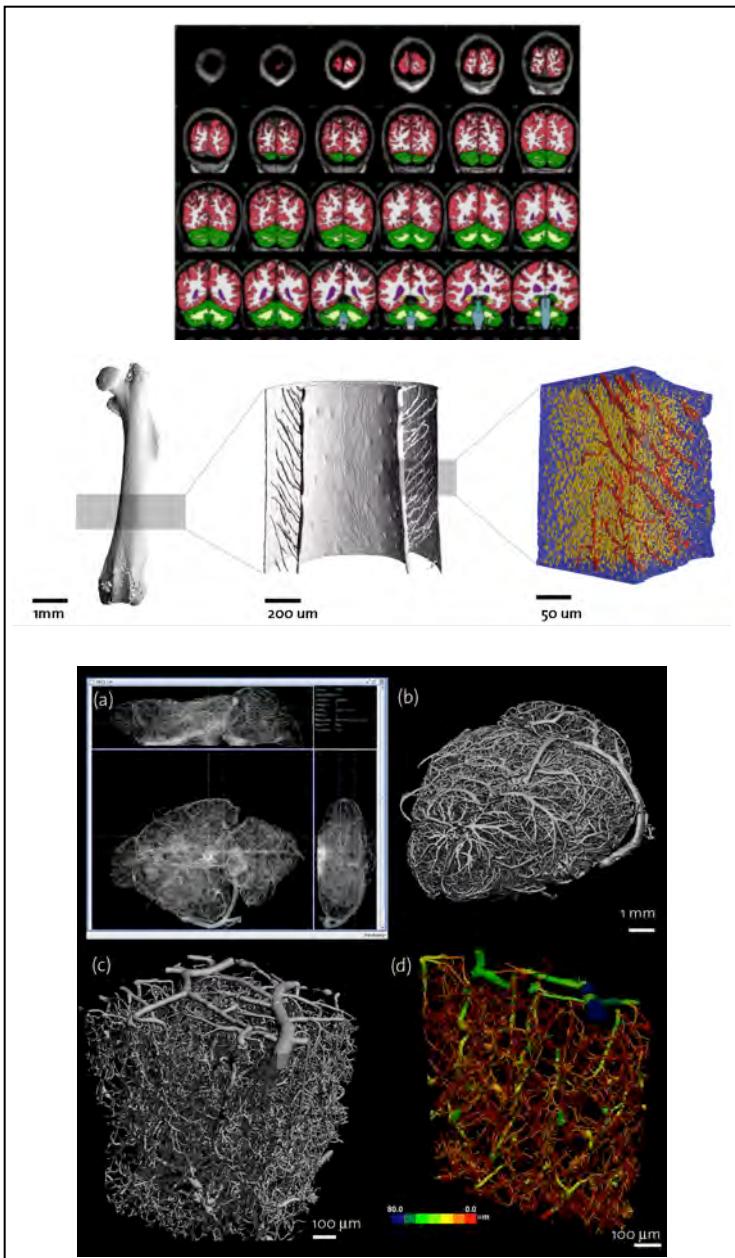
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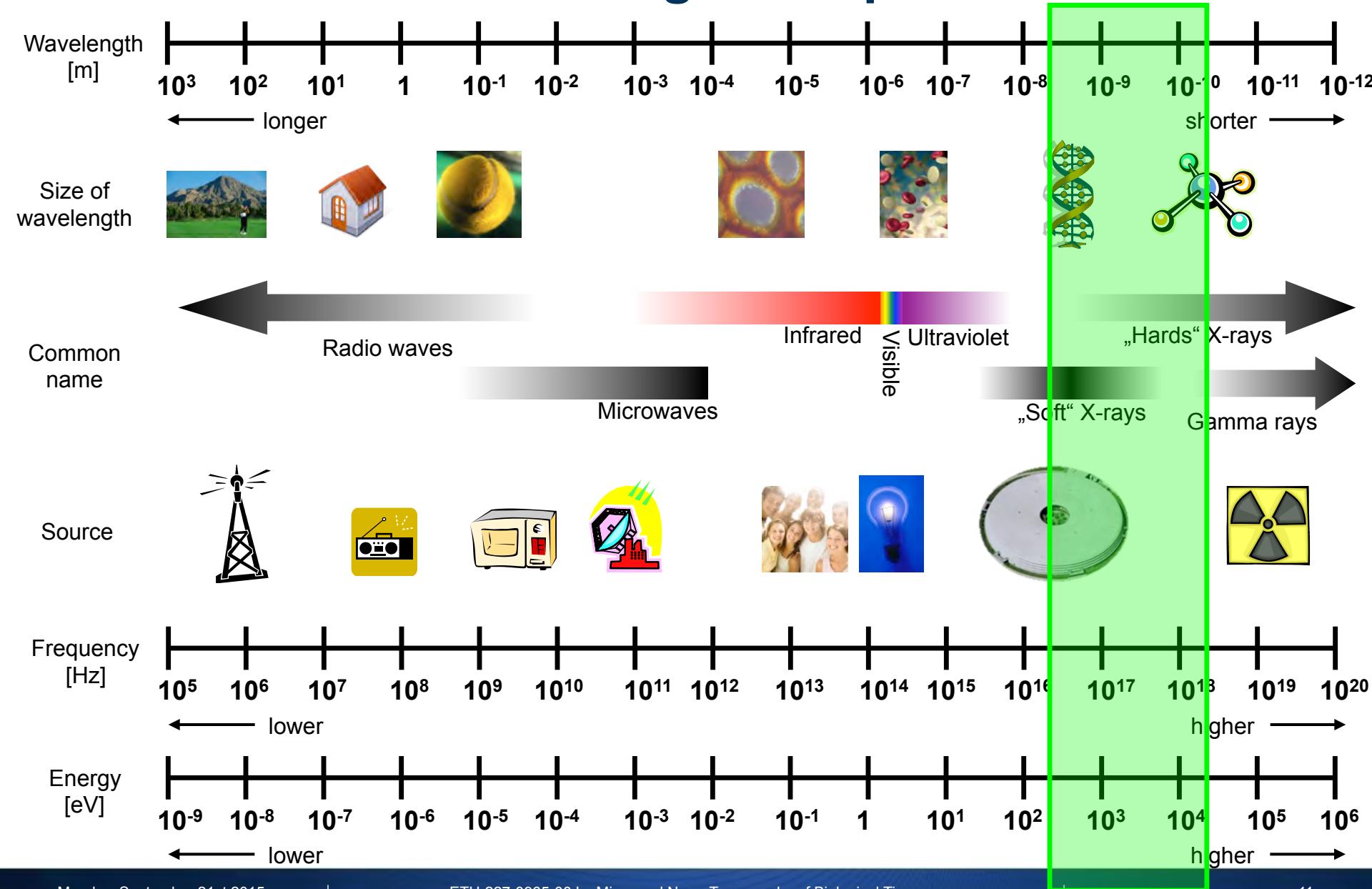
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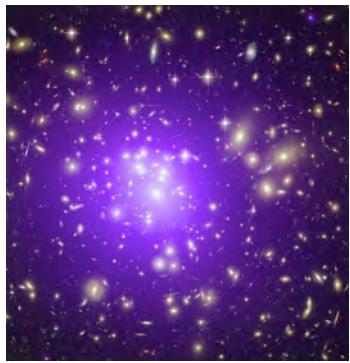
- **Experiment at the Swiss Light Source**



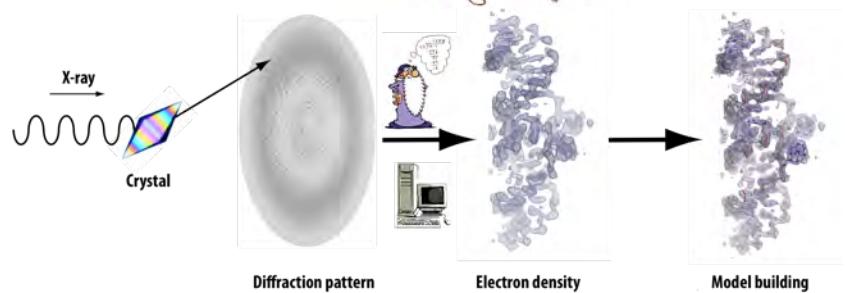
# The electromagnetic spectrum



# What can X-rays tell you ?



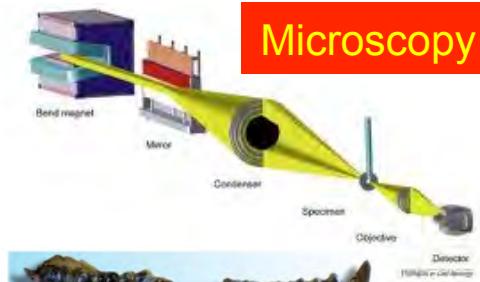
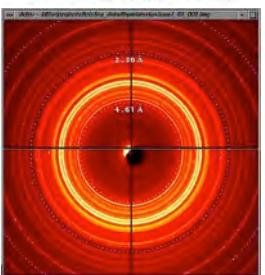
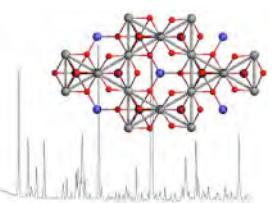
Astronomy



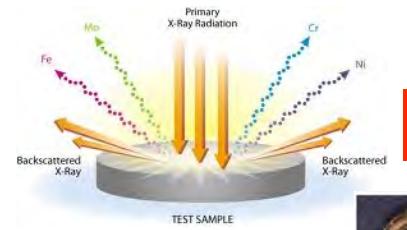
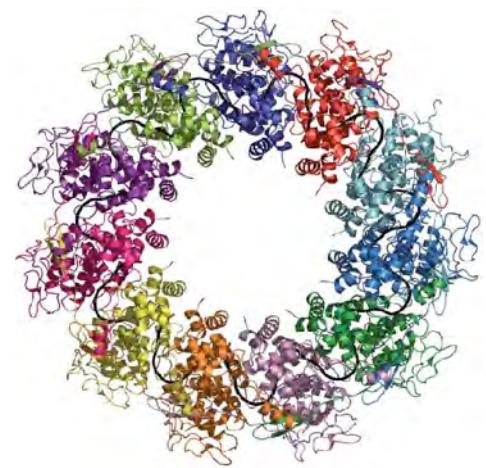
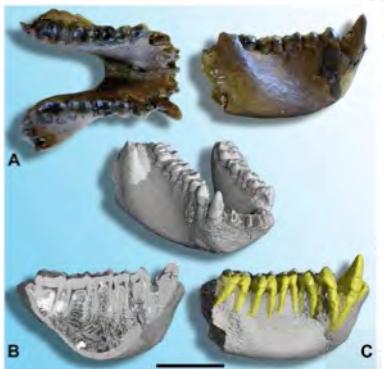
Protein cristallography



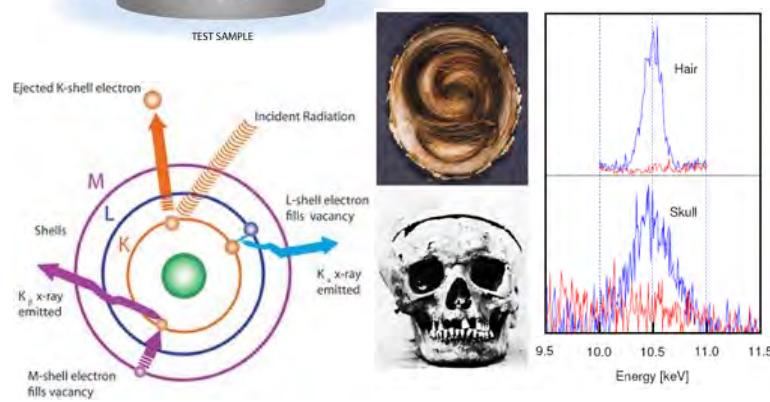
Powder diffraction



Microscopy



Fluorescence



# A short “nobel” story

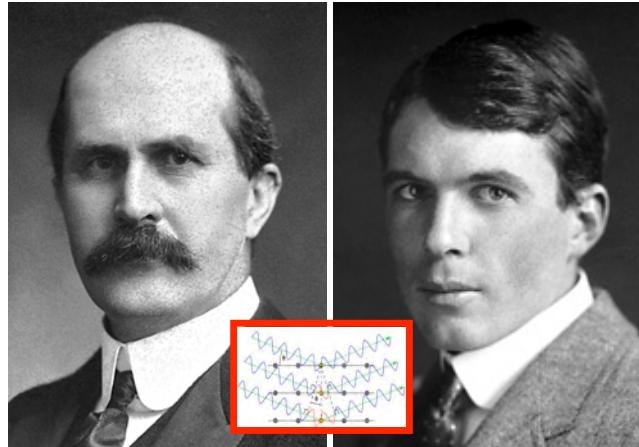
W. Röntgen, 1901



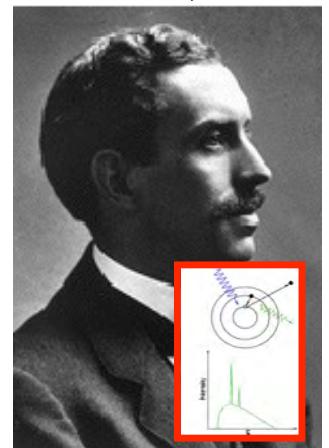
M. von Laue, 1914



W. H. Bragg, W. L. Bragg, 1915



C. Barkla, 1917



F. Crick, J. Watson, M. Wilkins, 1962



G. Hounsfield, A. Cormack, 1979



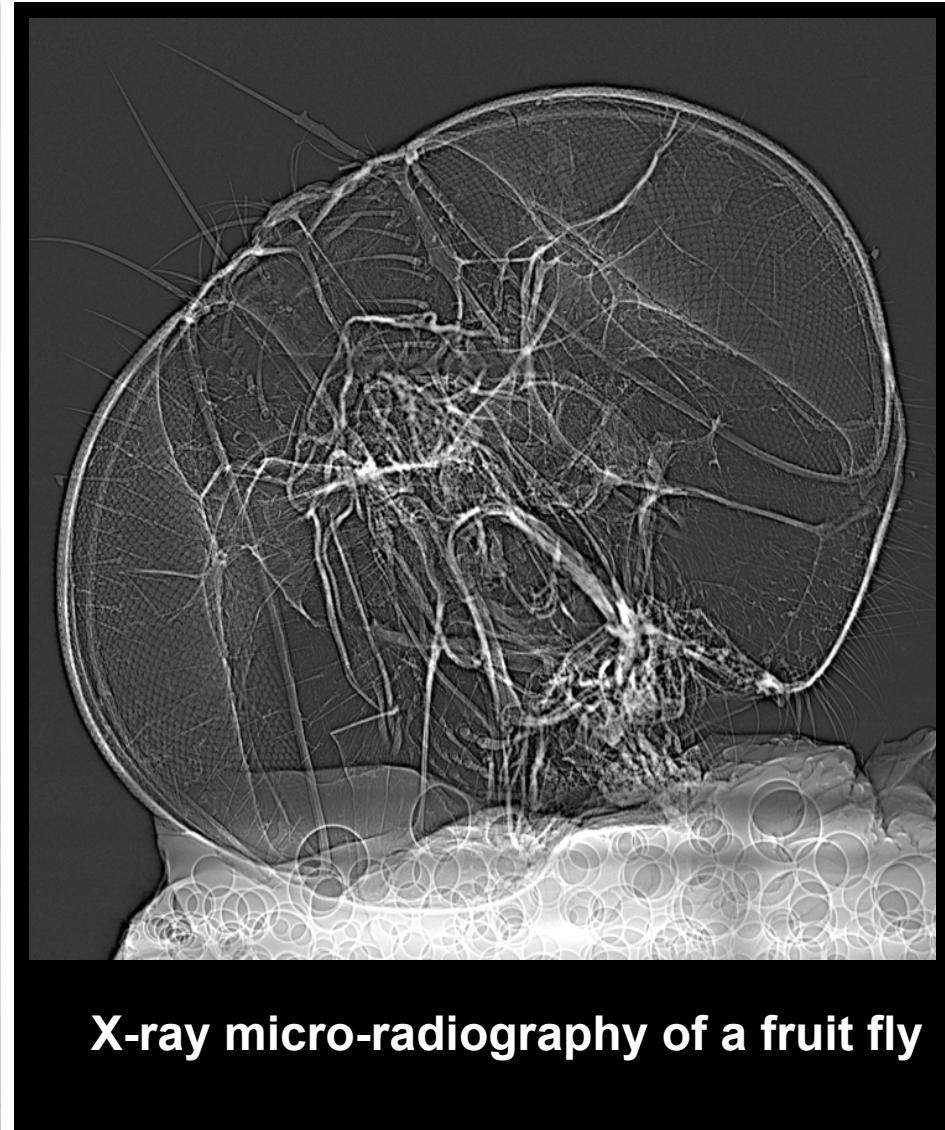
A. Yonath, V. Ramakrishnan, T. Steitz, 2009



<http://www.nobelprize.org>

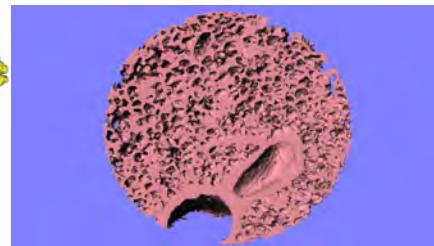
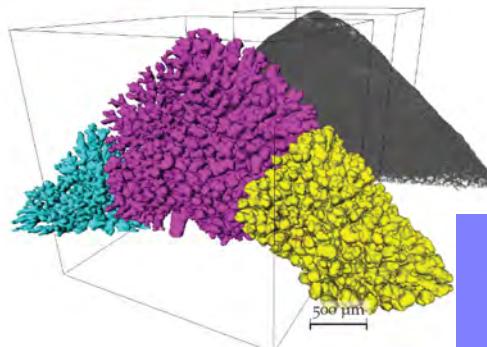
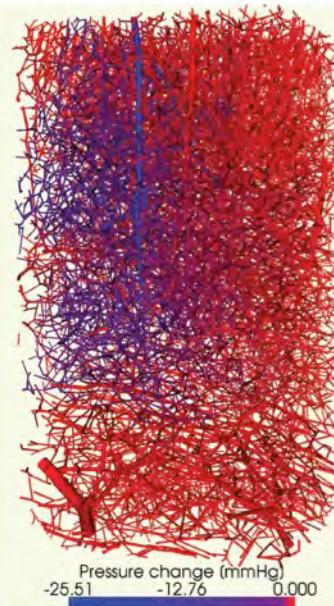
# X-ray imaging yesterday...

First X-ray image, 1896



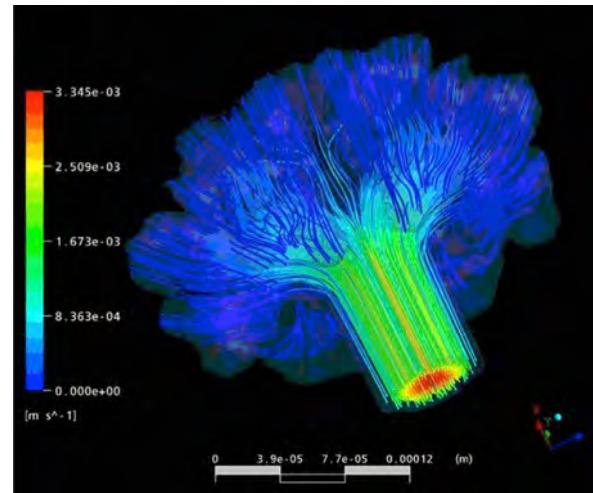
X-ray micro-radiography of a fruit fly

# Absorption-based tomographic microscopy



## Morphology of lung acini

Haberthür et al., Journal of Synchrotron Radiation, 17(5), 2010  
Schittny et al., American Journal of Physiology 294 (L246), 2008

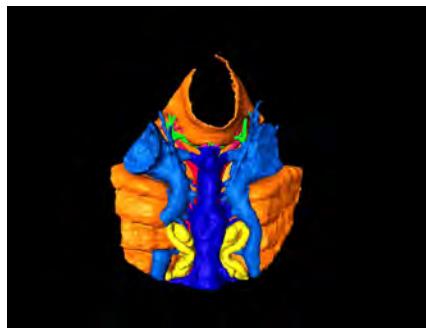
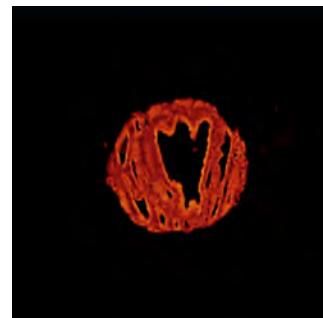


## Air-flow simulation in terminal alveoli

Sznitman et al., Journal of Visualization, Online Version, June 2010

## Simulation of blood flow in brain micro-vasculature

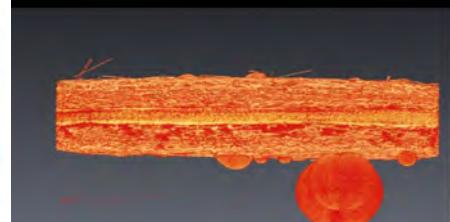
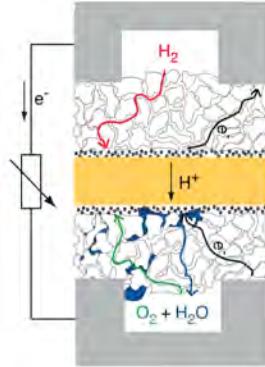
Reichold et al., Journal of Cerebral Blood Flow and Metabolism, 29(8), 1429-1443 (2009)



## Tomographic microscopy of fossil materials

P. Donoghue et al., Nature 442, Aug. 2006  
W. Hagadorn et al., Science 314, Oct. 2006

Z. Gai, Nature 476, Aug. 2011  
T. Huldgren, Science 334, Dec. 2011

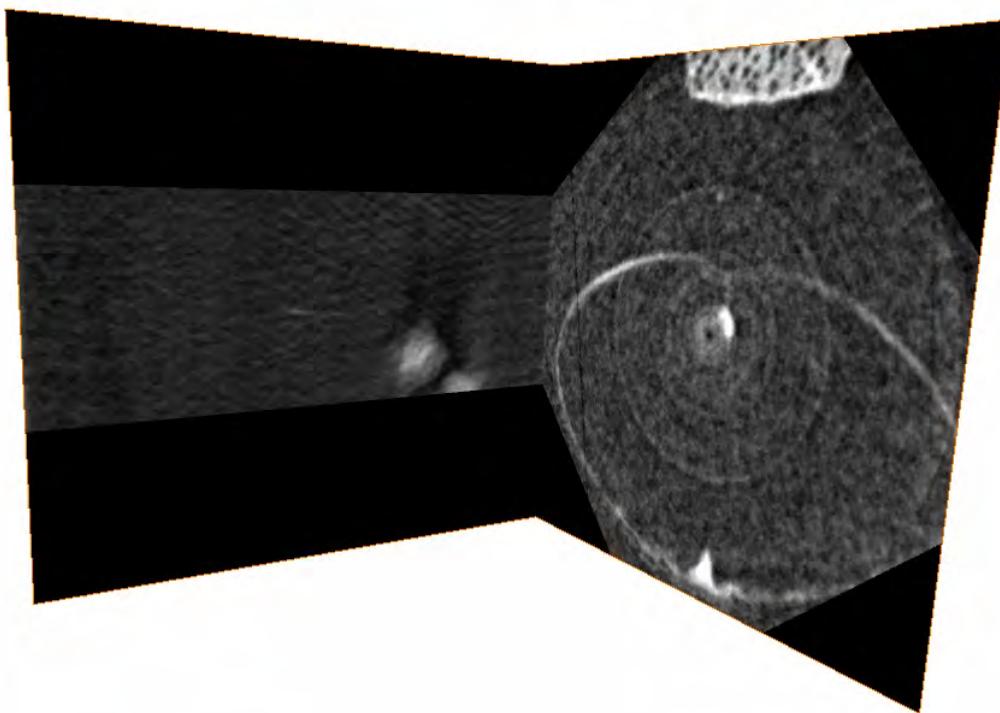


## In-situ visualization of operating fuel cell

J. Eller et al., Journal of the Electrochemical Society 158, B963 (2011)

# Imaging in 4D

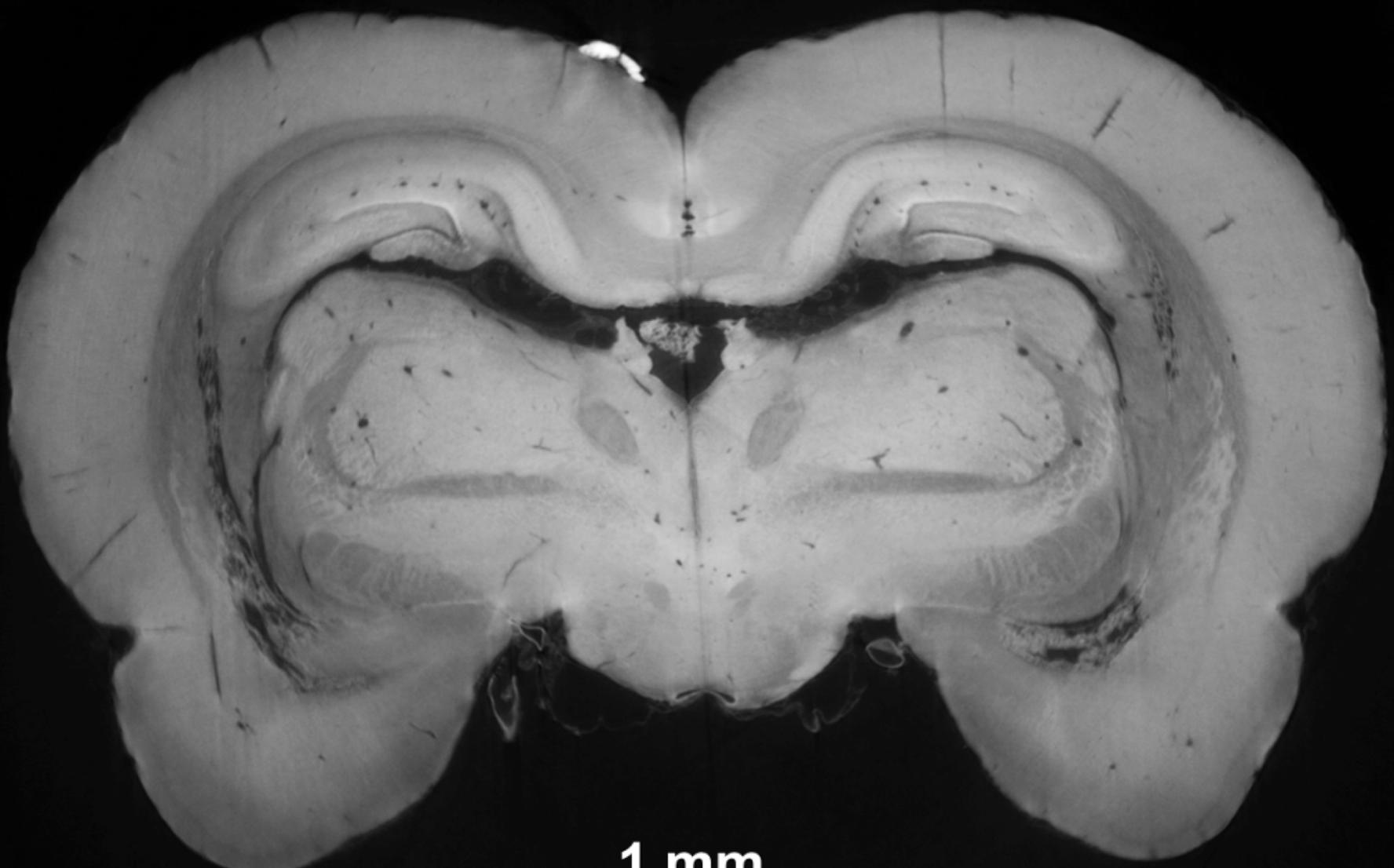
For instance: investigate the biomechanics underlying flight manoeuvres and gaze shifts



You will learn how to acquire such data and perform such investigations!

Movie courtesy of S. Walker *et al.*, IC, London

# Improve contrast from soft tissue

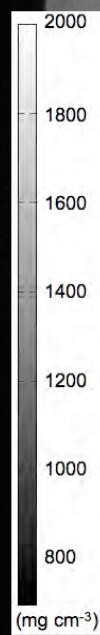


1 mm

# Improve contrast from soft tissue

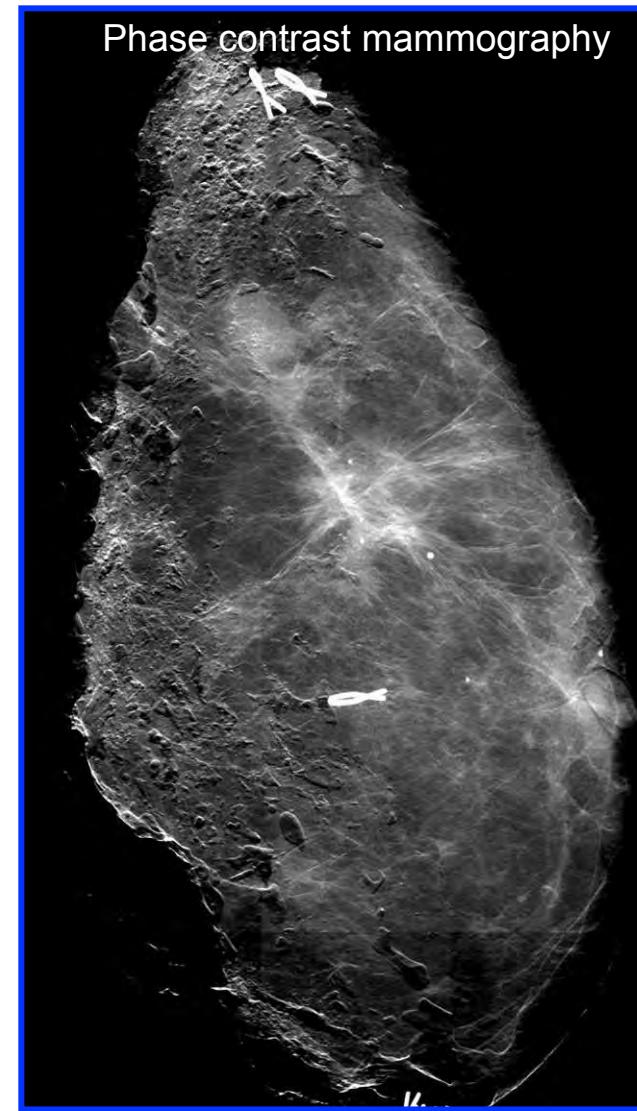
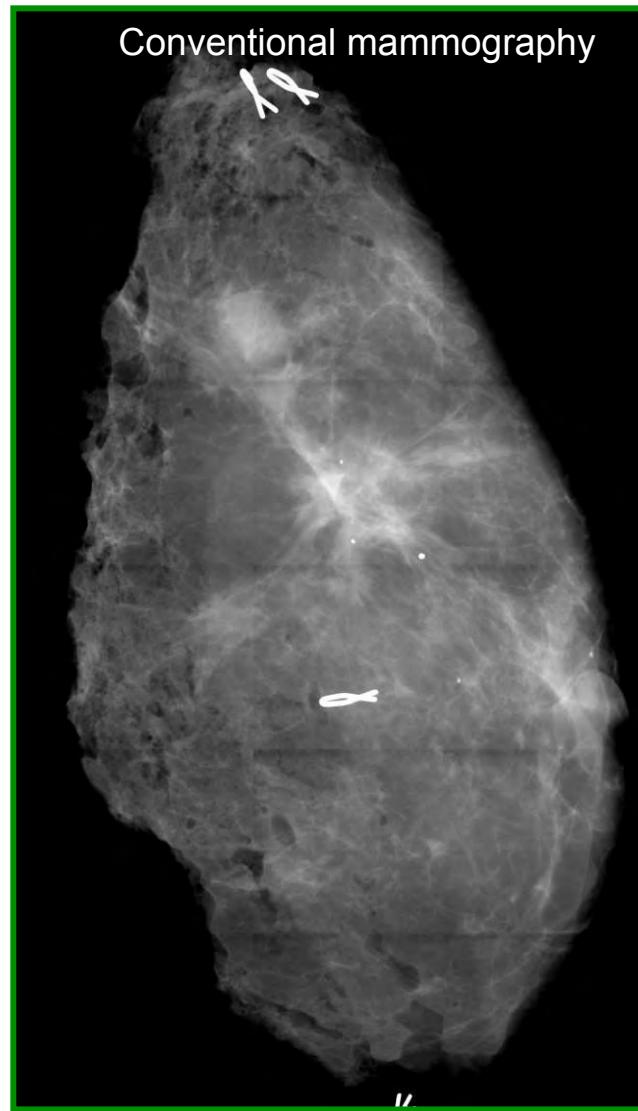
Resolution: 15 microns

Sensitivity: 1 mg/cm<sup>3</sup>



1 mm

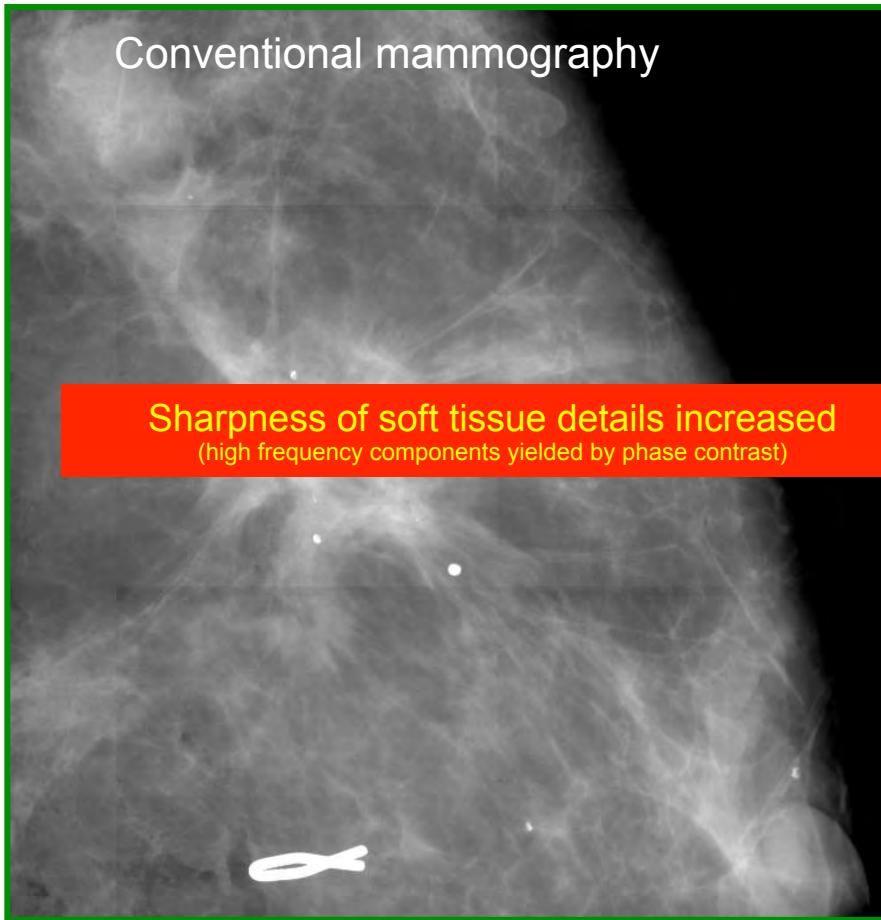
# Enhanced *spiculations* visibility



Z. Wang, XNPIG 2012

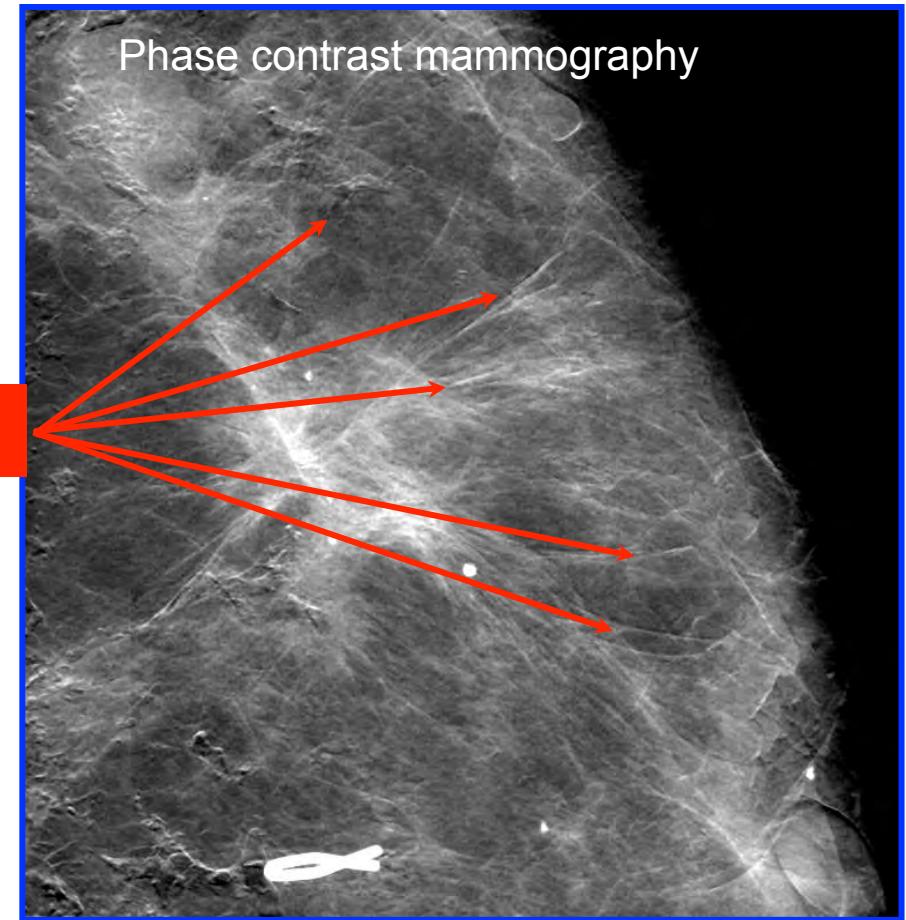
# Enhanced *spiculations* visibility

Conventional mammography



Sharpness of soft tissue details increased  
(high frequency components yielded by phase contrast)

Phase contrast mammography

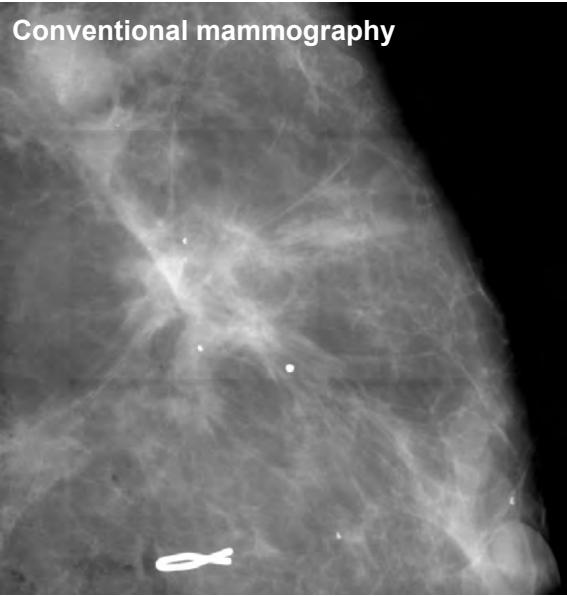


Same dose!

Z. Wang, XNPIG 2012

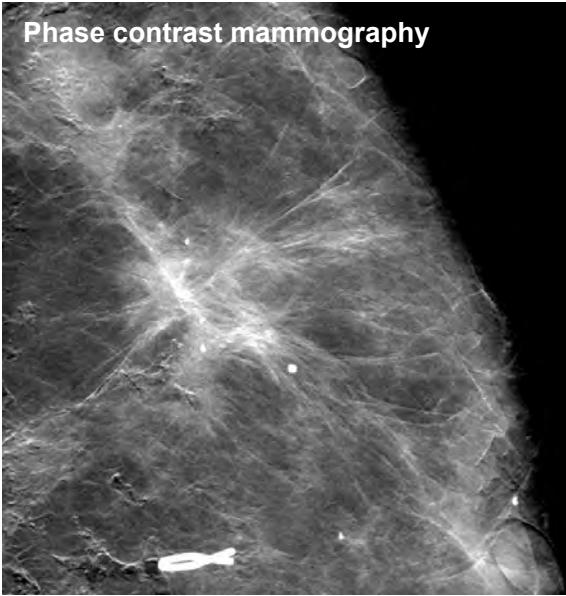
# New perspectives for medical imaging

Conventional mammography



M. Stampanoni et al., Investigative Radiology, 46:801 (2011)  
N. Hauser et al., Investigative Radiology 49:3 (2014)  
Z. Wang et al., Nat. Communications 5:3797 (2014)

Phase contrast mammography



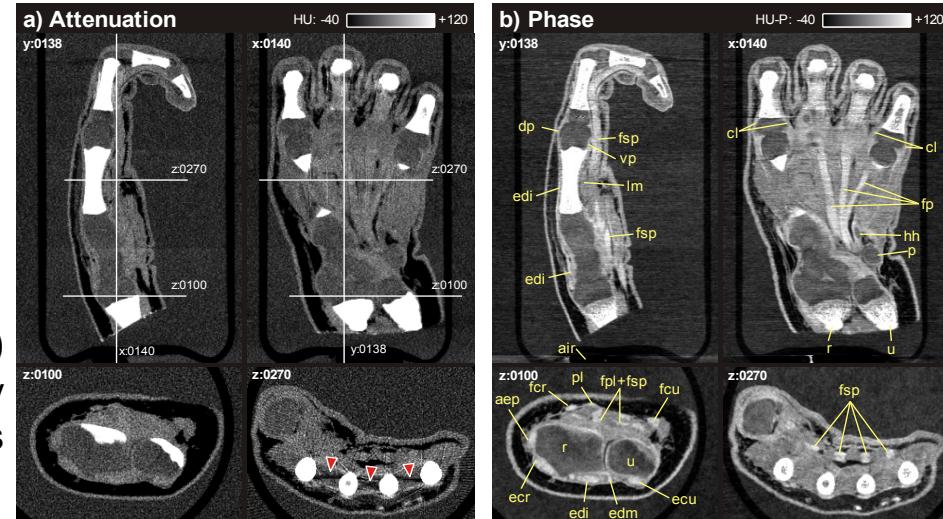
## EARLY BREAST CANCER DETECTION (2D)

- Sharper and better lesion delineation
- Sharper microcalcifications
- Non-invasive microcalcification classification
- Improved spiculations identifications
- Improved clinical relevance
- General better image quality

## ENHANCED HAND IMAGING (3D)

- Improved soft tissue visibility
  - Tendons and ligaments

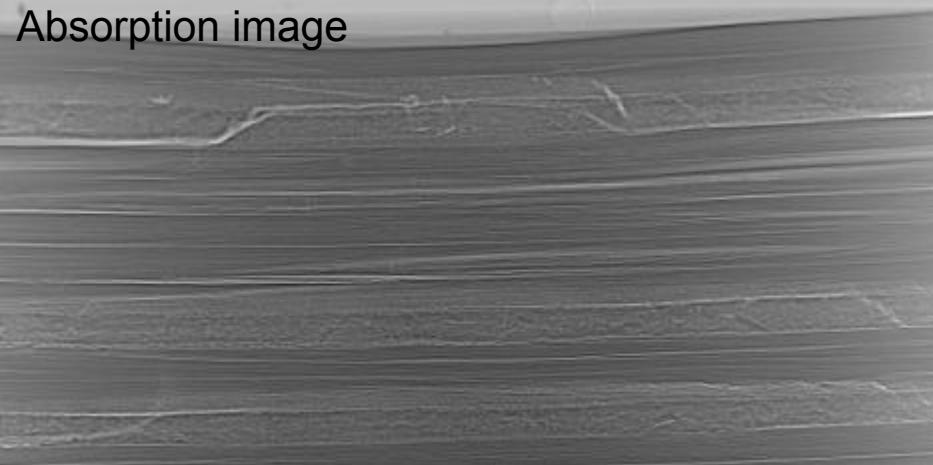
T. Donath et al., Investigative Radiology 45:7 (2010)  
T. Thüring et al., Skeletal Radiology 42 (2013)



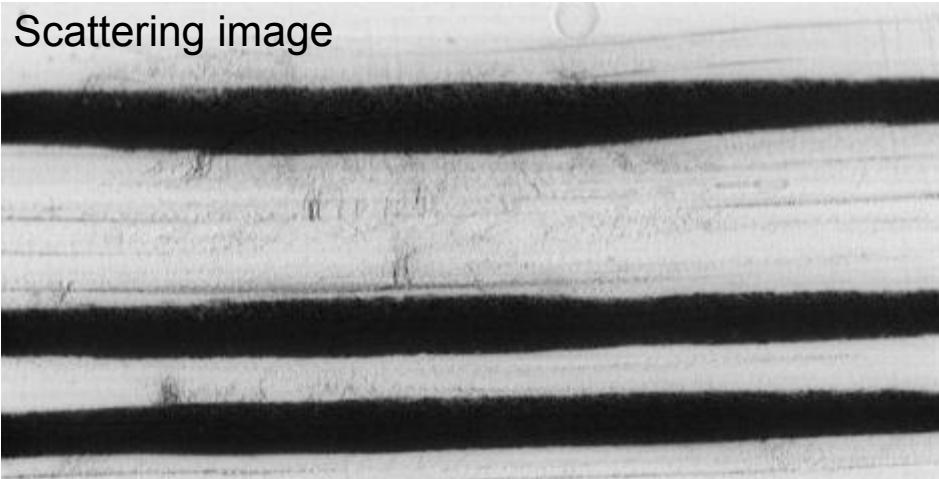
# New perspectives for material inspections

S. McDonald, M. Stampanoni et al., Journal of Synchrotron Radiation 16, 562-572, (2009)

Absorption image



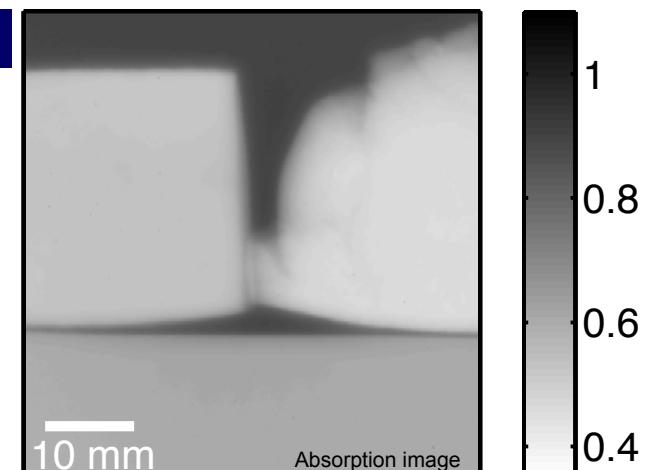
Scattering image



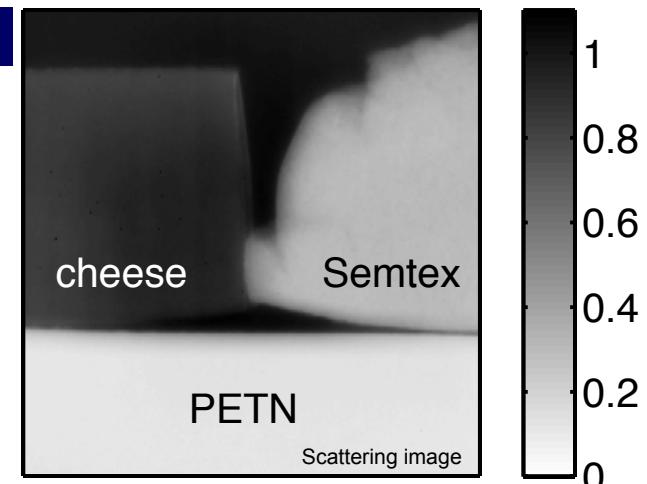
CFRP laminated structure consisting of alternate layers of plastic matrix and fiber reinforcement

F. Pfeiffer et al., Nature Methods, 7, 134 - 137 (2008)

a



b

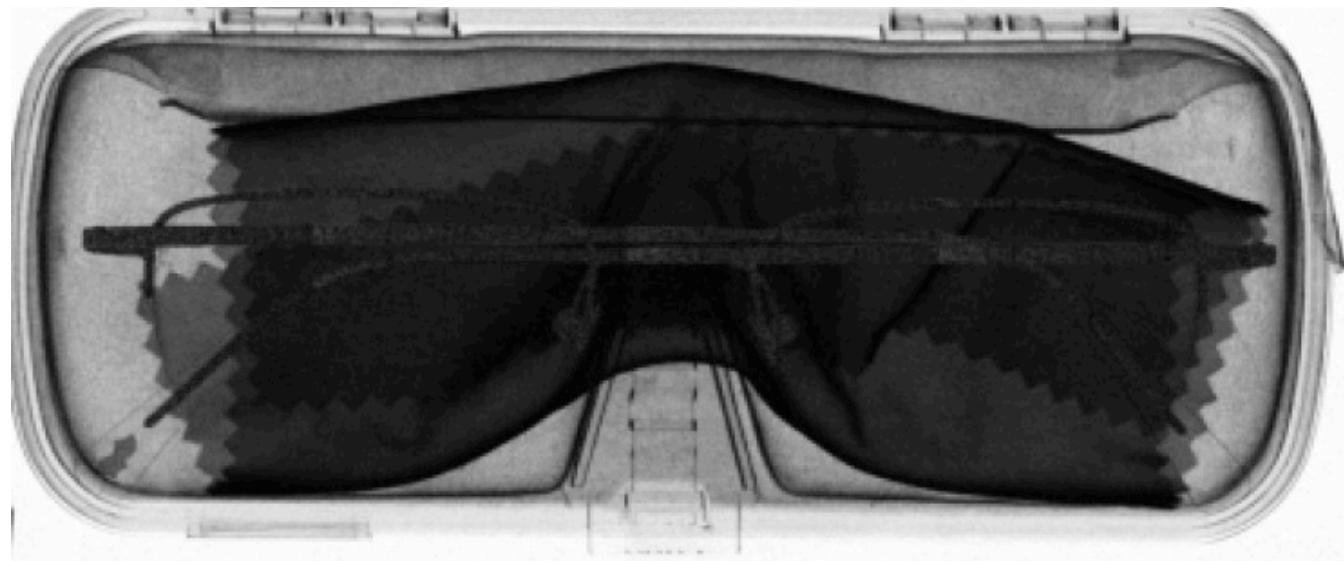


Different granular (strong-scattering) microstructure of explosives allows their discrimination from normal cheese

# Material discrimination...

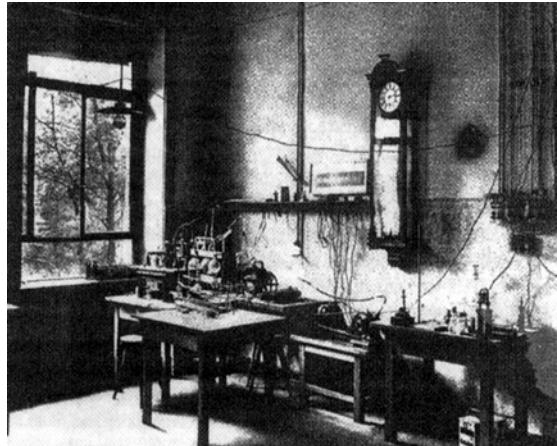


Absorption

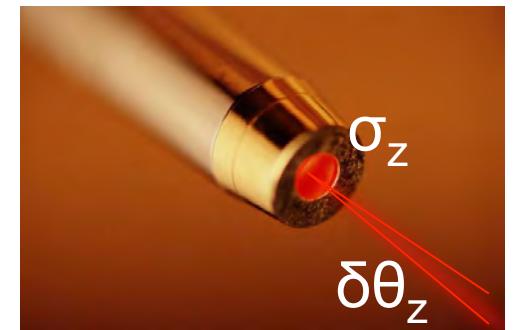


Scattering

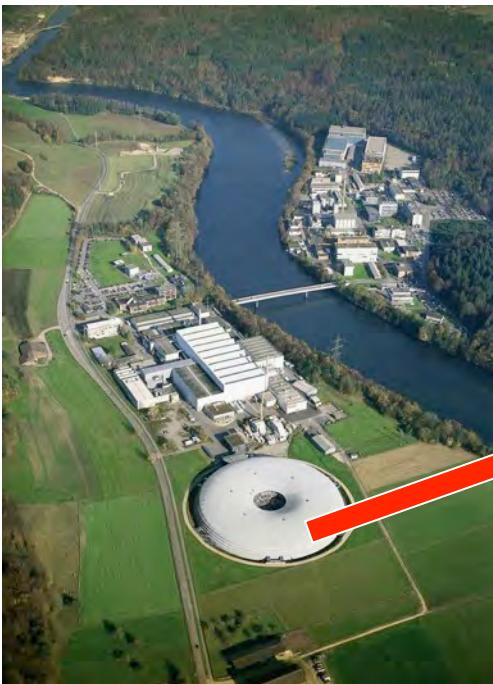
# X-ray sources of the 21<sup>st</sup> century



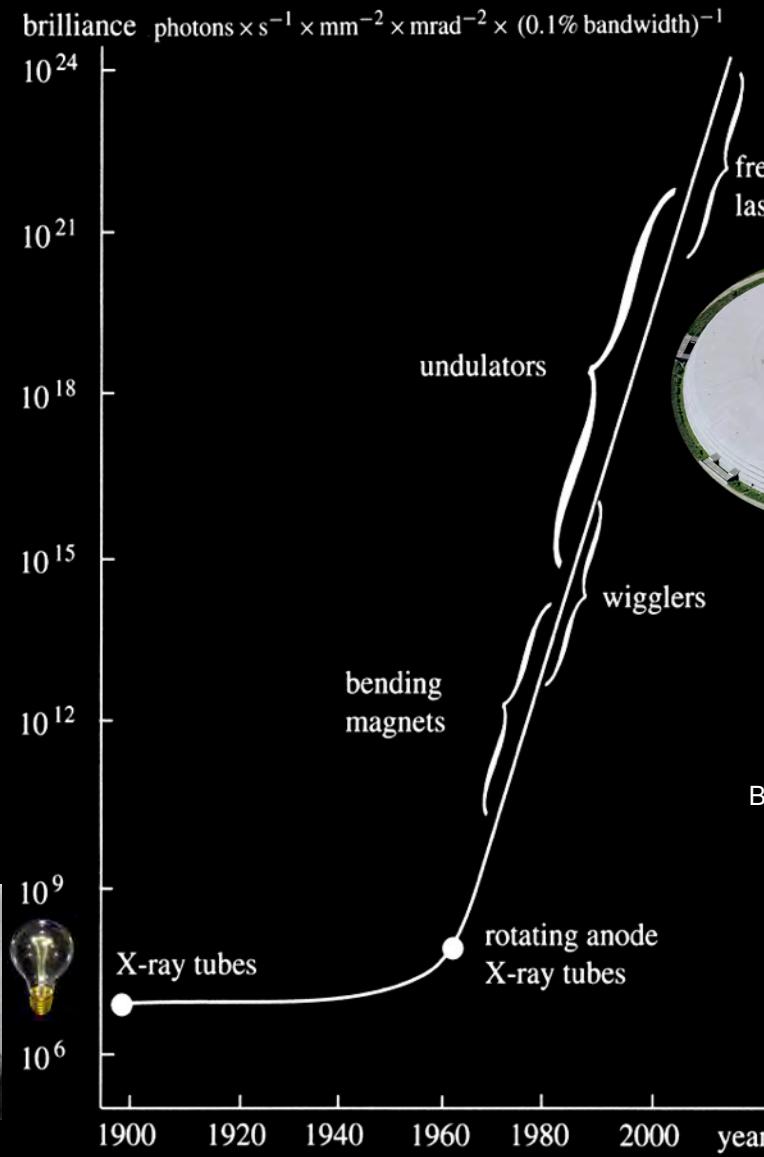
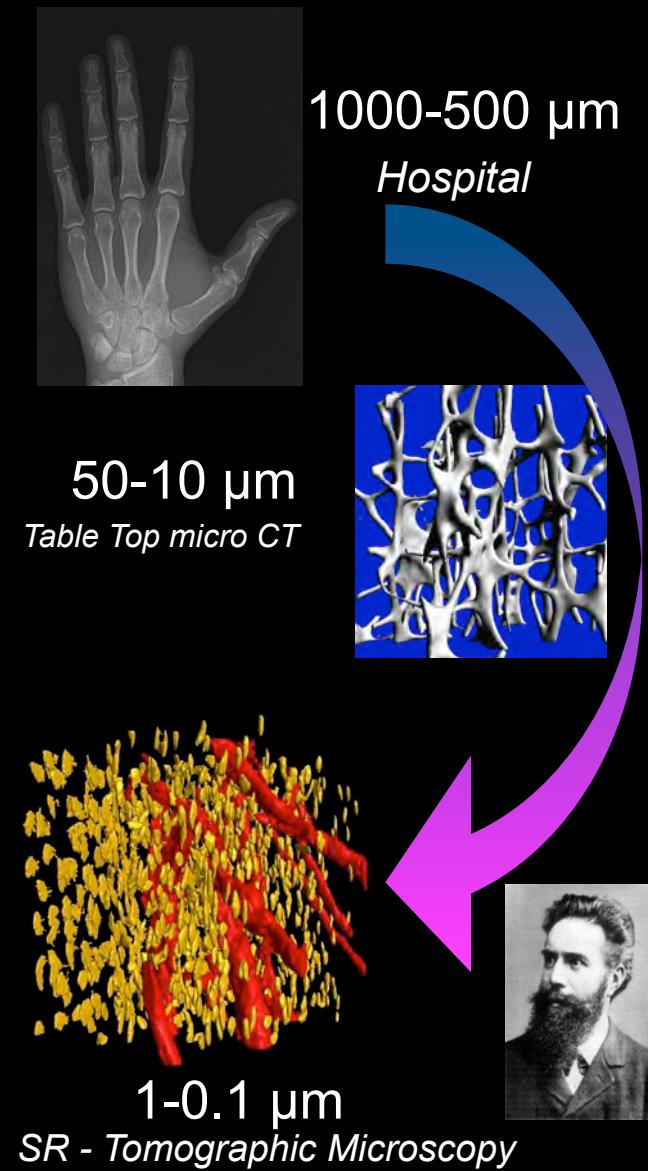
Röntgen's Lab, Late 19<sup>th</sup> century



Swiss Light Source, Today



# Why a synchrotron for imaging ?

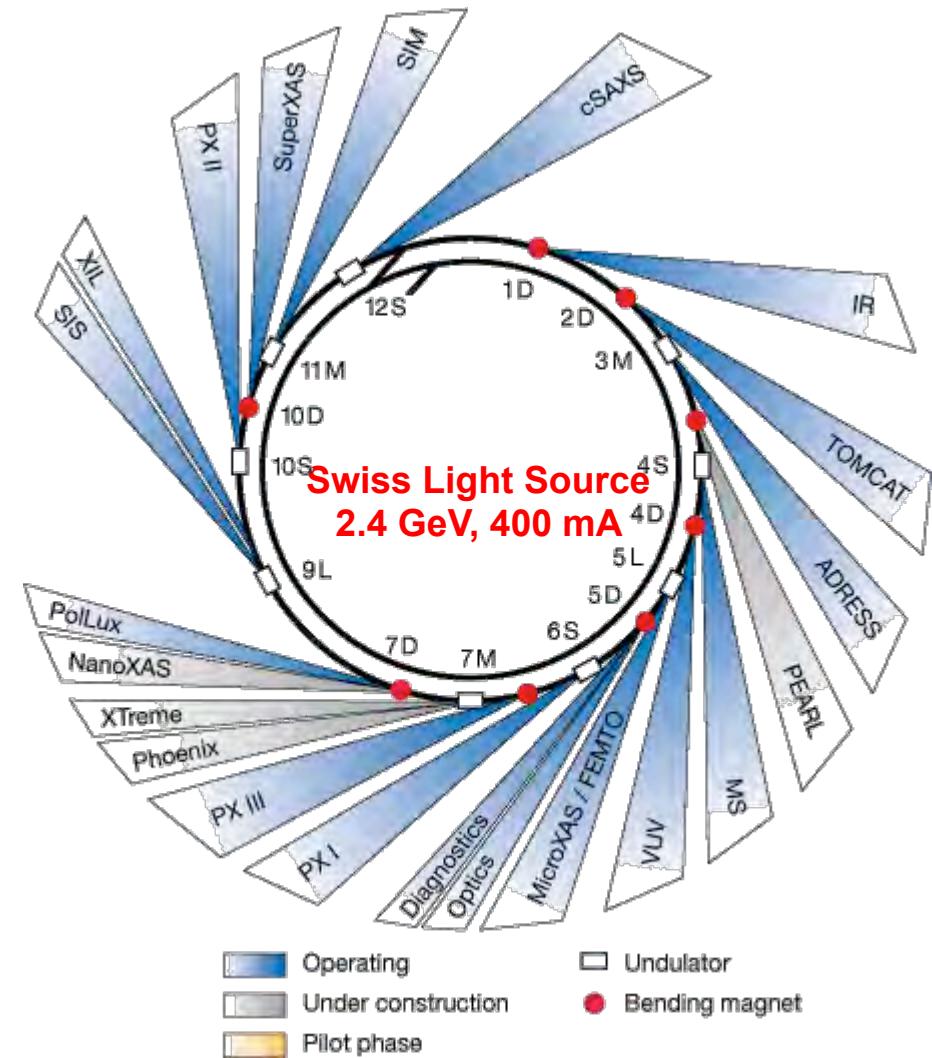


$$\Phi \propto \frac{\text{quality}^2}{\text{res}^4 \cdot \text{contr}^2}$$

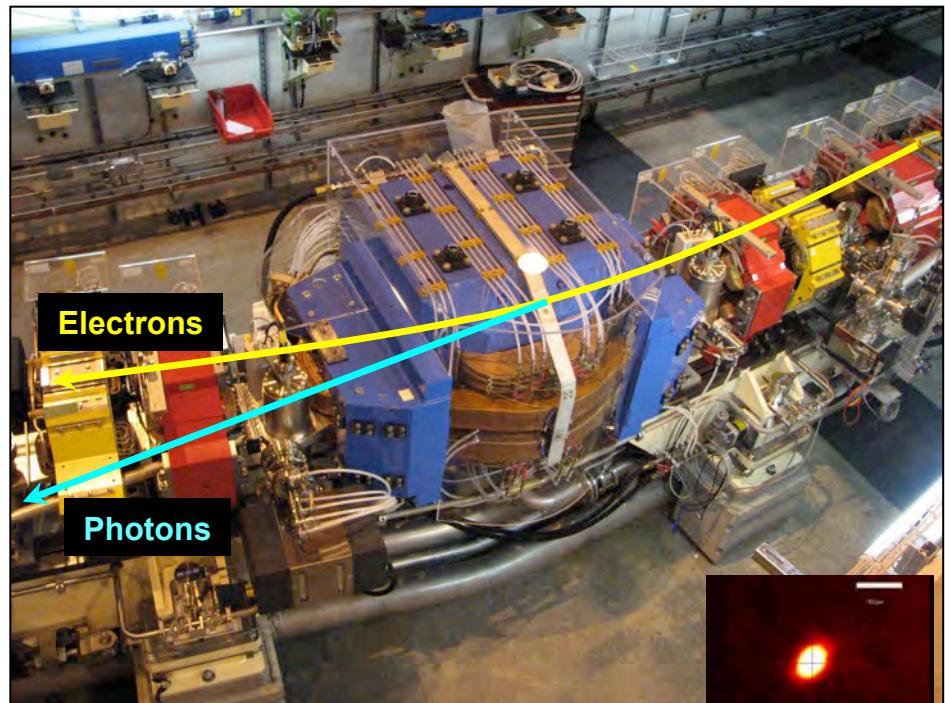
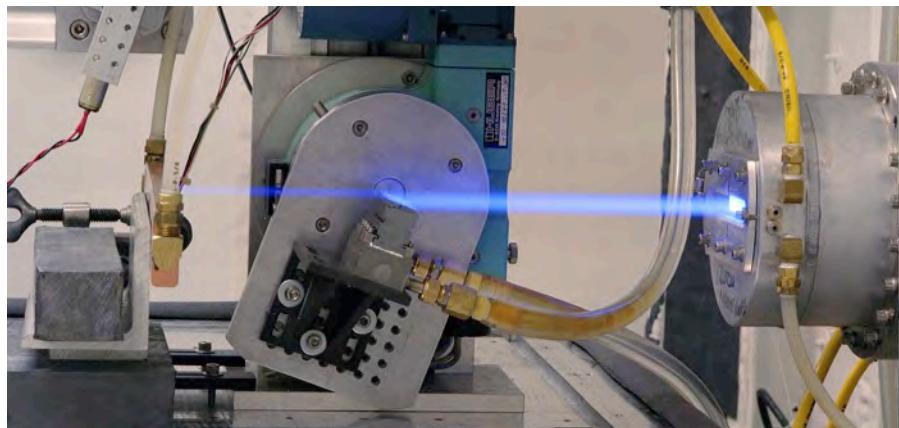
Bonse et al., Prog. Biophys. Molec. Biol., Vol. 65, No.1, pp. 133-169, 1996



# The Swiss Light Source at the Paul Scherrer Institute



# A very quick view into a synchrotron



Experiment

← →

30-200 m !!

Source  
(0.01-0.05 mm)

- Very intense flux
- Very small source size
- Strong collimated beam
- Large distance between source and experiment

→ We can observe interference phenomena with X-rays and exploit them for imaging!