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Chapter 5 – Phase retrieval and ptychography

Outline

- X-ray imaging

The phase problem (CDI)

Ptychography

Ultrafast X-ray imaging with free-electron lasers

X-ray imaging

Motivation and basics
Full-field vs. scanning



Why X-ray imaging? High penetration depth

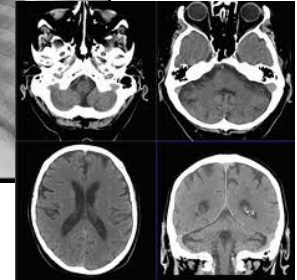
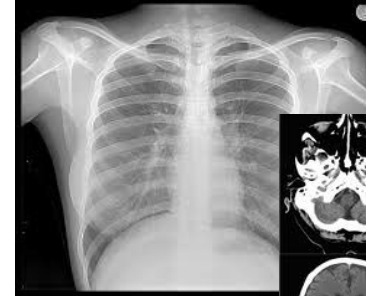
X-rays offer the opportunity to look through otherwise opaque objects without disturbing them (too much)



Hand mit Ringen first
"medical" X-ray 1895
Anna Bertha Ludwig's
hand



Wilhelm Röntgen
1901 First Physics
Nobel

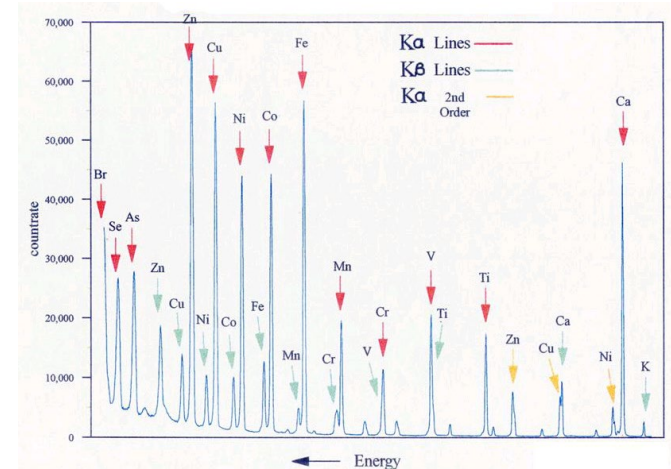
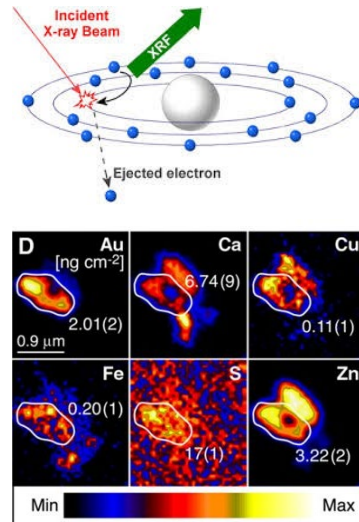


X-ray tomography

Why X-ray imaging? Element specificity

X-ray photons can remove electrons from inner atom orbitals

The resulting fluorescence upon relaxation leaves an element specific signature

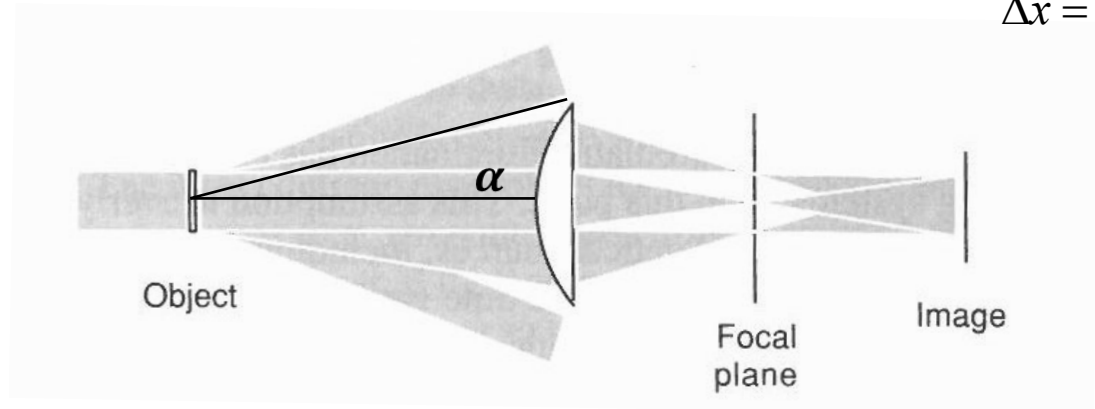
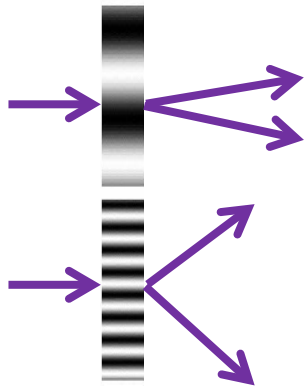


Why X-ray imaging? High resolution

Abbe theory of image formation:

Resolution depends on **wavelength** and **numerical aperture**. There is an upper limit for a given wavelength.

High-resolution = High diffraction angles



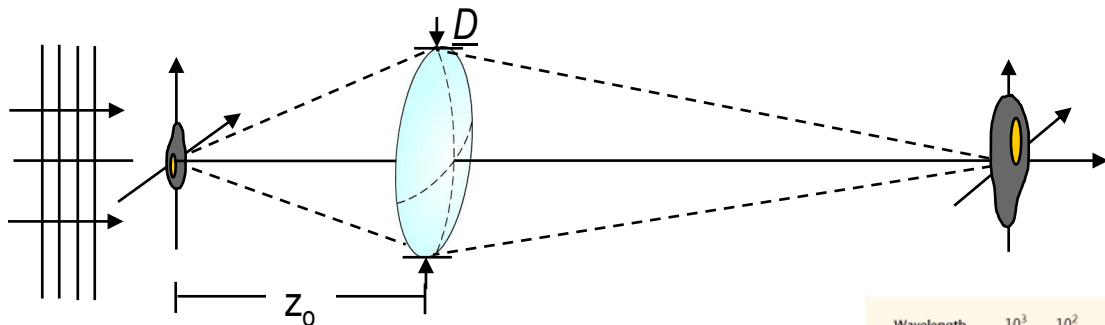
Rayleigh resolution

$$\Delta x = \frac{0.61\lambda}{n \sin \alpha}$$

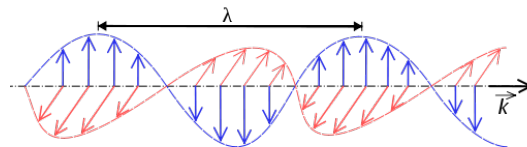
Electromagnetic waves – Resolution



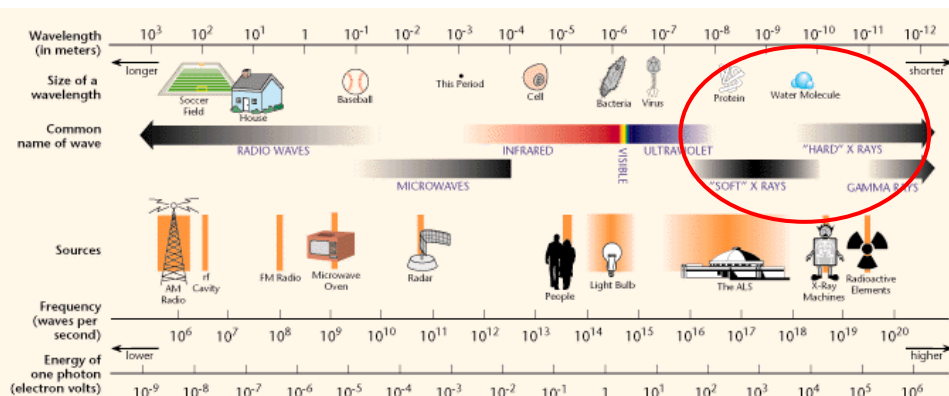
Image resolution depends on the numerical aperture of the lens, but there is a limit given by the wavelength.



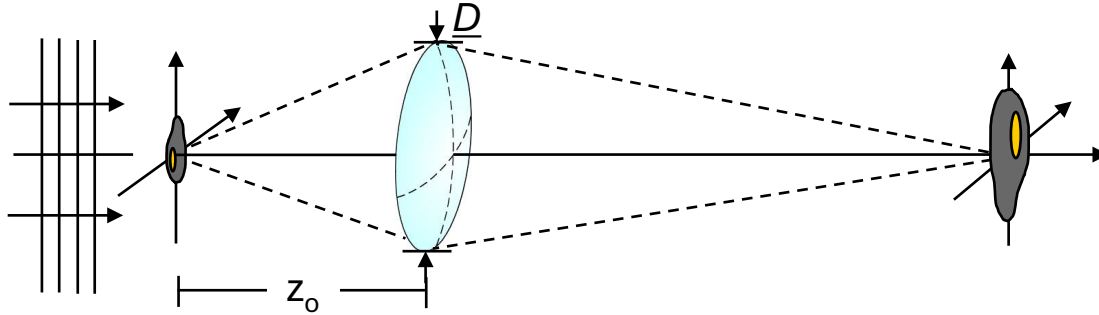
$$\Delta x \approx 0.61 \frac{\lambda}{NA} \approx 1.22 \lambda (f\#) \approx 1.22 \lambda \frac{z_0}{D}$$



X-ray wavelengths then have great potential for high-resolution



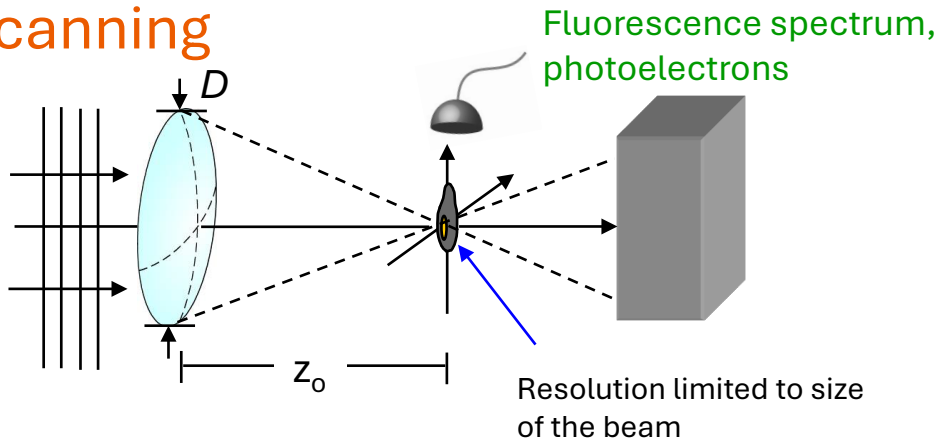
Full field imaging



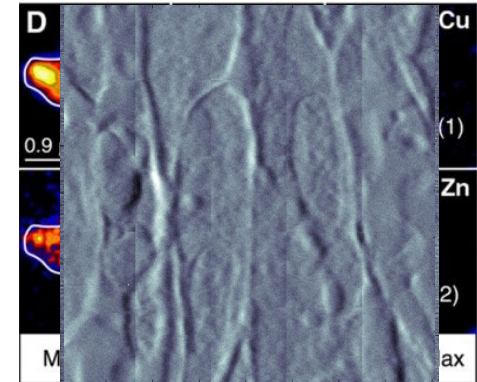
X-ray small wavelengths (0.01 – 10 nm)
can potentially deliver high resolution

$$\Delta x \approx 0.61 \frac{\lambda}{NA}$$

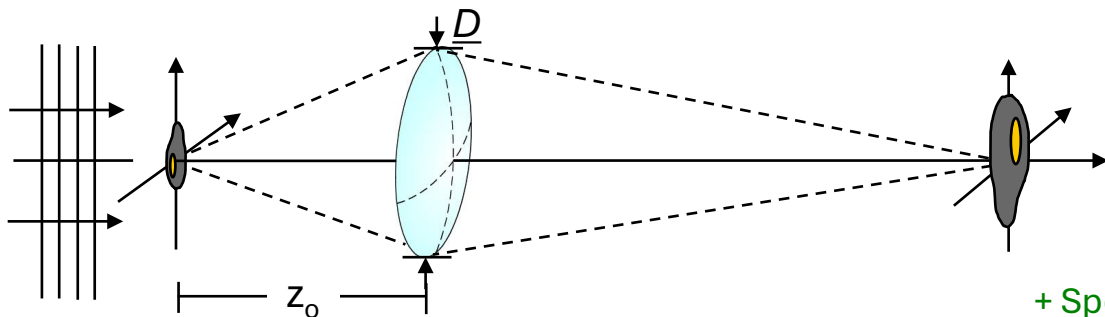
Scanning



measuring absorption.



Full field imaging

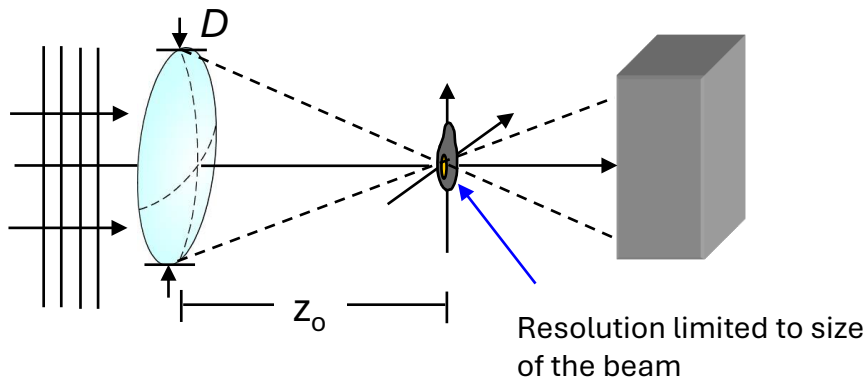


X-ray small wavelengths (0.01 – 10 nm)
can potentially deliver high resolution

$$\Delta x \approx 0.61 \frac{\lambda}{NA}$$

- + Speed: Whole image measured at once
- Photon efficiency
- Background from other diffraction orders

Scanning



- + Photon efficiency
- + Simultaneous imaging channels
- Speed: Point by point imaging
- More sensitive to drifts

Outline

X-ray imaging

● The phase problem (CDI)

Ptychography

Ultrafast X-ray imaging with free-electron lasers

The phase problem (CDI)

Computational imaging - lensless
3D nanoscale imaging with CDI

Imaging as an inverse problem

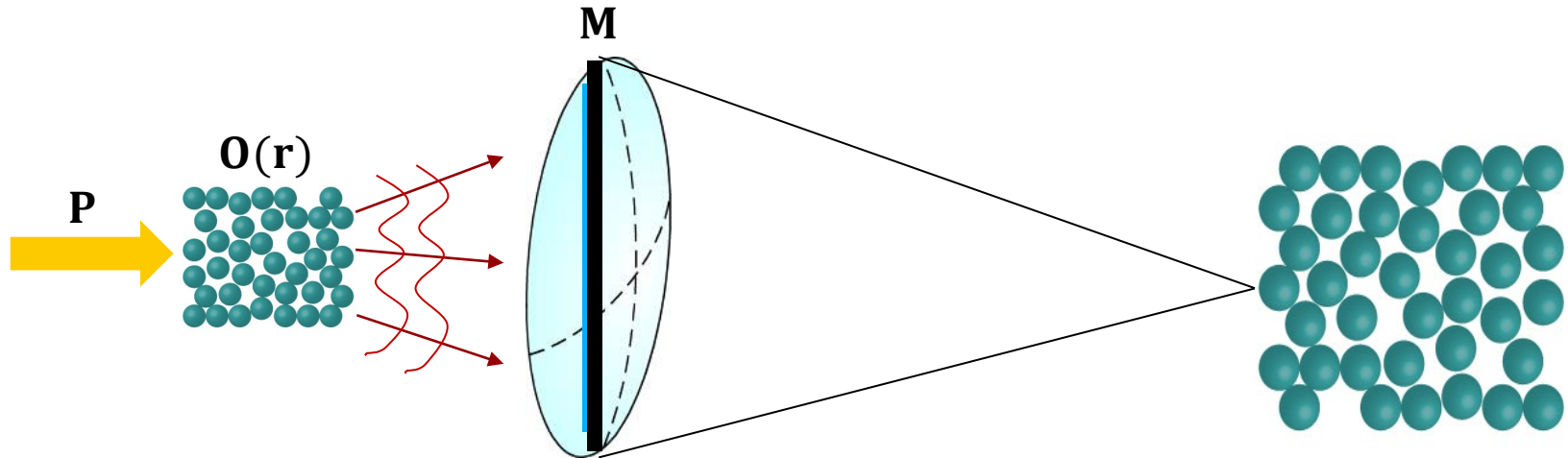
Physical model of interaction between incoming wave and object

Diversity - Can be used to encode more information, e.g. rotation, scanning, energy

r (dimensionality) can be 2D, 3D, time, spectra

O (contrast) matter-wave interaction can be a scalar, vector, tensor
Captures local anisotropy

M (modulation and measurement) images, diffraction, fluorescence, photo-electrons



Imaging as an inverse problem

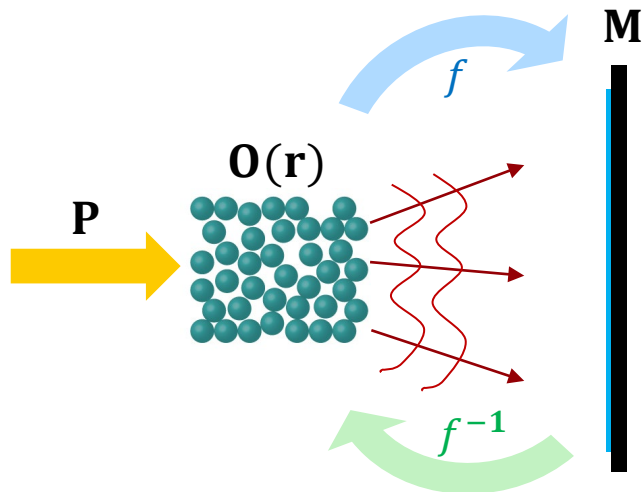
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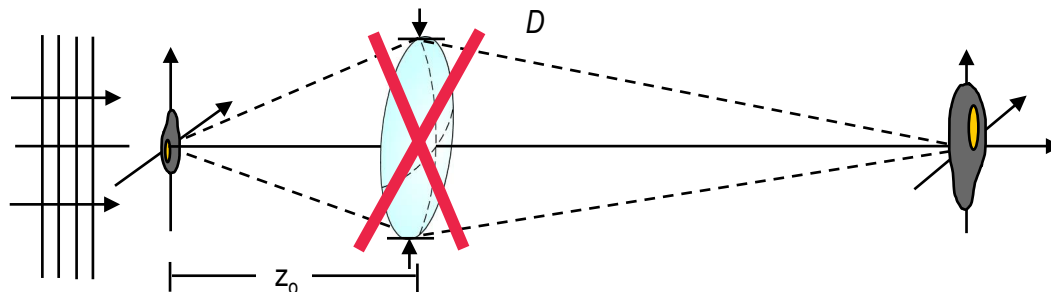
$$\mathbf{M} = f \{ \mathbf{P} \cdot \mathbf{O}(\mathbf{r}) \}$$

$$\mathbf{O}(\mathbf{r}) = f^{-1} \{ \mathbf{M}, \mathbf{P} \}$$

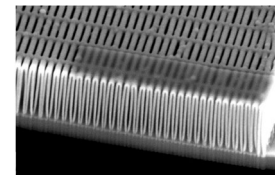
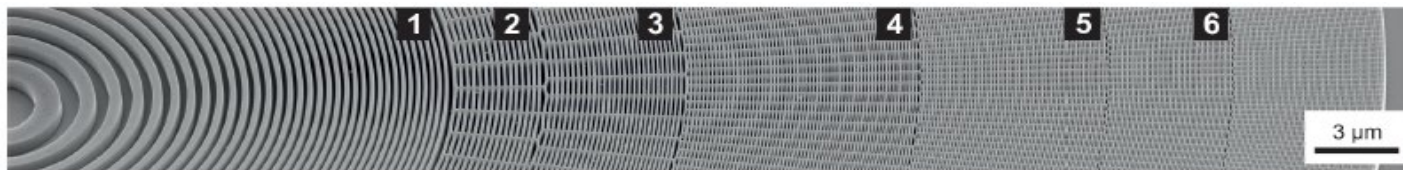
Diversity – measure in a way that makes the problem invertible and stable (small noise leads to small errors)

Find a reliable inversion strategy f^{-1}

X-ray coherent lensless imaging



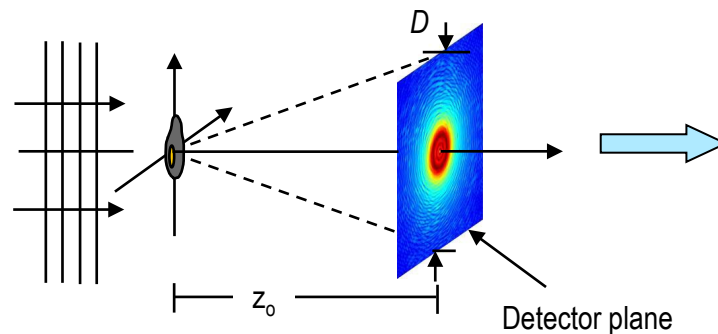
$$\Delta x \approx \frac{\lambda}{2NA} \approx \lambda(f\#) \approx \lambda \frac{z_0}{D}$$



Line doubled, ZW 20 nm, H 550 nm
<https://www.psi.ch/en/lxn/fresnel-zone-plate-for-x-ray-microscopy>

Imaging resolution limited by lens manufacturing

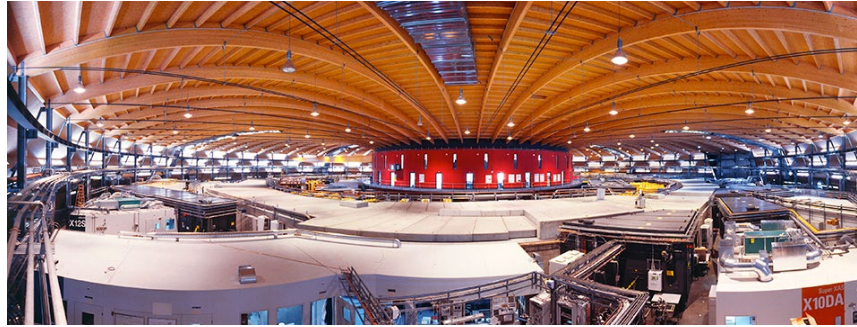
An alternative is
coherent lensless
imaging



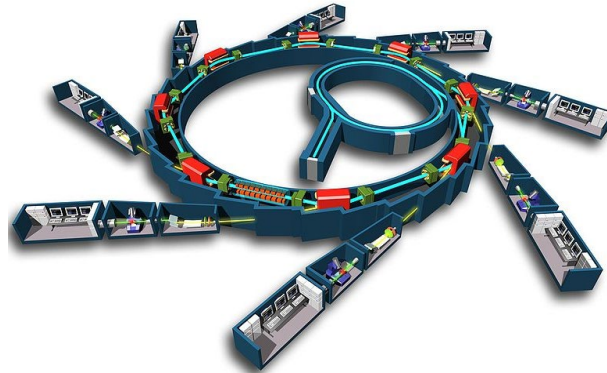
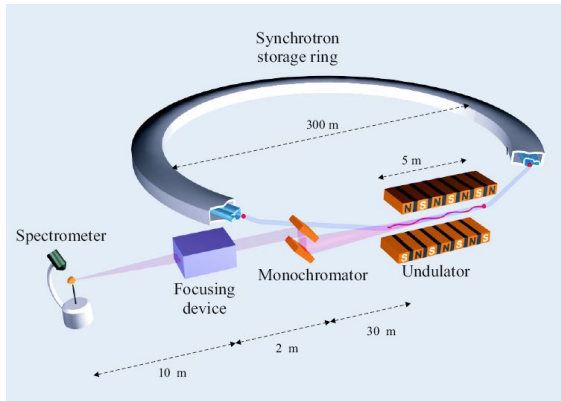
Complex-valued
reconstruction

$$\Delta x \approx \lambda \frac{z_0}{D}$$

Synchrotron X-ray sources



Swiss Light Source (SLS)



Synchrotrons have many beamlines with different experiments running simultaneously
Brightness $\sim 1e6-1e9$ higher than lab sources
Image: beamlines of Soleil (Wikipedia)

>75 years of synchrotrons



Scientists around the vacuum chamber of a 1947 General Electric synchrotron (photo courtesy of NSLS, Brookhaven).



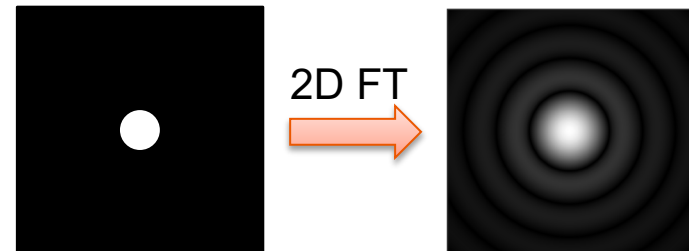
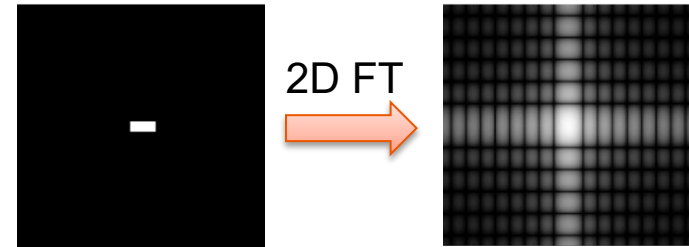
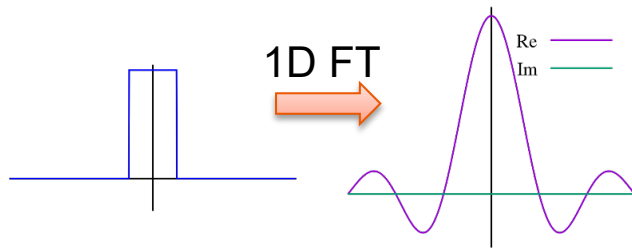
Sirius - Brazilian synchrotron

The 2D Fourier transform

The 2D FT is very important concept in **optics, imaging, and tomography**. It is a straightforward generalization of the 1D FT.

$$f(x) \xrightarrow{\text{1D FT}} F(u) = \int f(x) e^{-i2\pi(xu)} dx$$

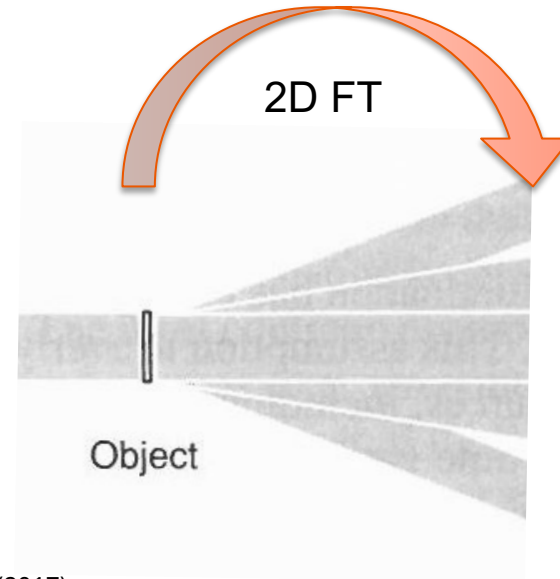
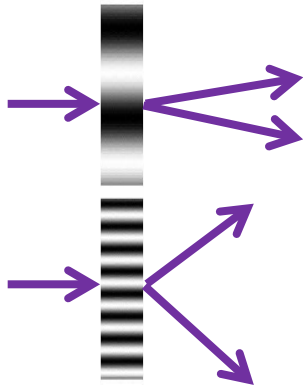
$$f(x, y) \xrightarrow{\text{2D FT}} F(u, v) = \iint f(x, y) e^{-i2\pi(xu+yv)} dx dy$$



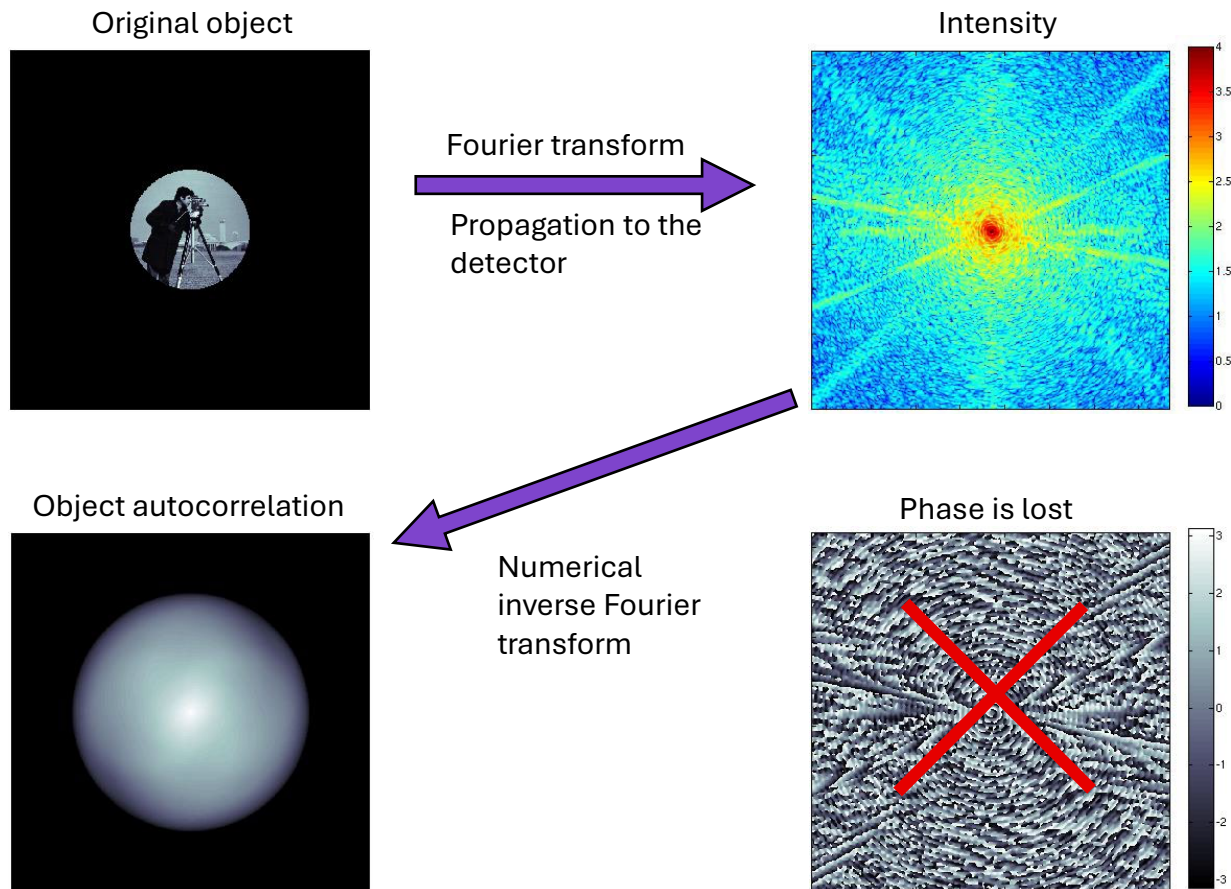
Far-field (Fraunhofer) propagation

Optical propagation (far field) is reduced to a 2D FT

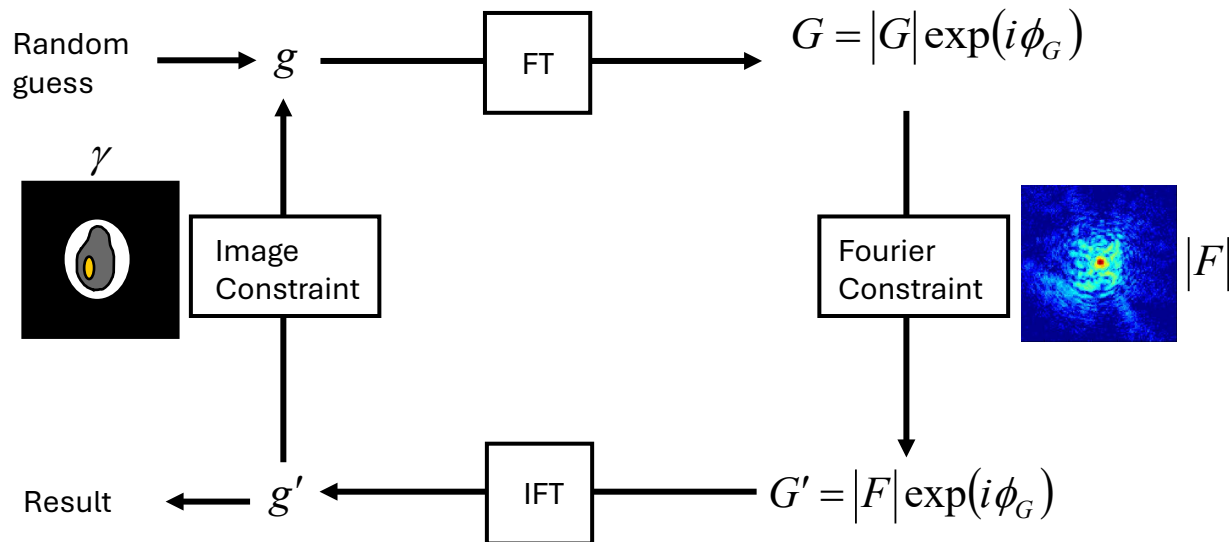
High resolution details propagate at higher angles



The phase problem



Phase retrieval with a support constraint (CDI)



Robust algorithms have been developed, e.g. hybrid input-output and difference-map

Using the measured **far-field intensity** and the **object support**

Note that additional constraints can be used

Hybrid Input-Output (HIO) Algorithm

Error reduction
(Gerchberg–
Saxton)

$$g_{k+1} = \begin{cases} g'_k & x \in \gamma \\ 0 & x \notin \gamma \end{cases}$$

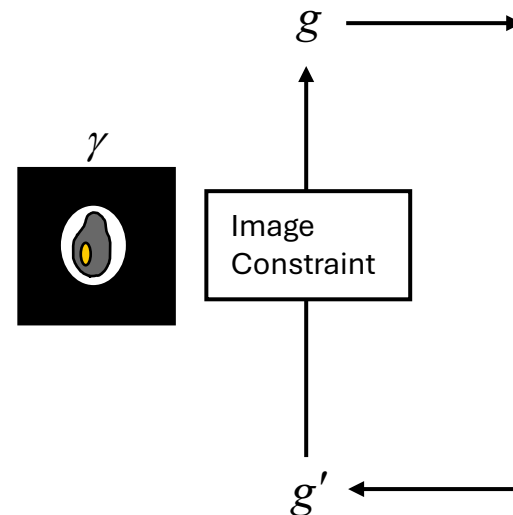
HIO

$$g_{k+1} = \begin{cases} g'_k & x \in \gamma \\ g_k - \beta g'_k & x \notin \gamma \end{cases}$$

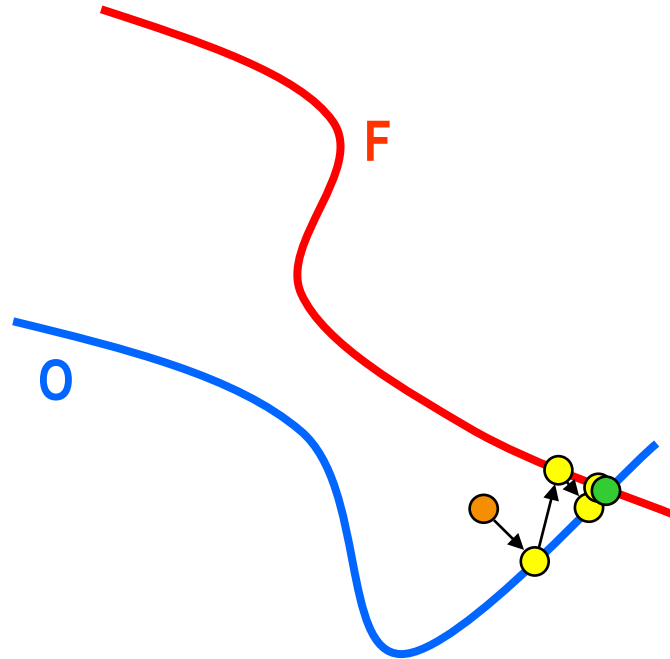
Instead of requiring the image to be zero outside the support, HIO uses the error as feedback.

Inspired in closed loop control theory.

Superior performance over the Error reduction (less prone to stagnation)

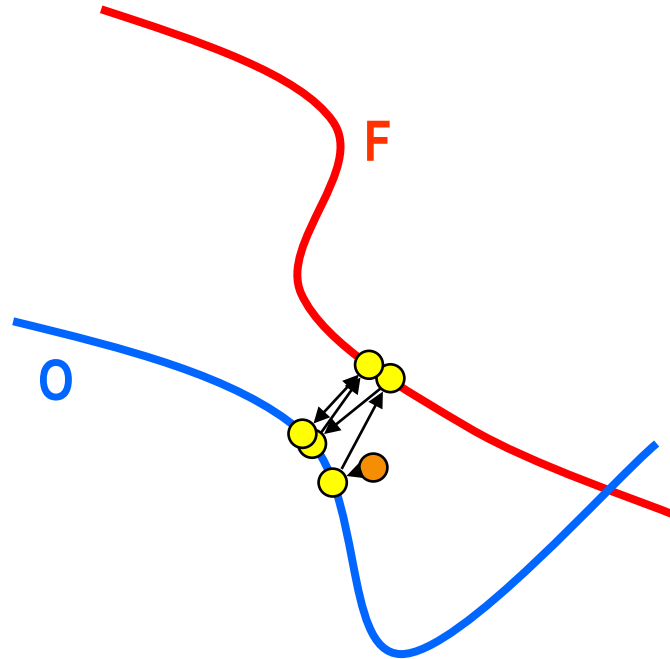


Iterative projection – Gerchberg Saxton



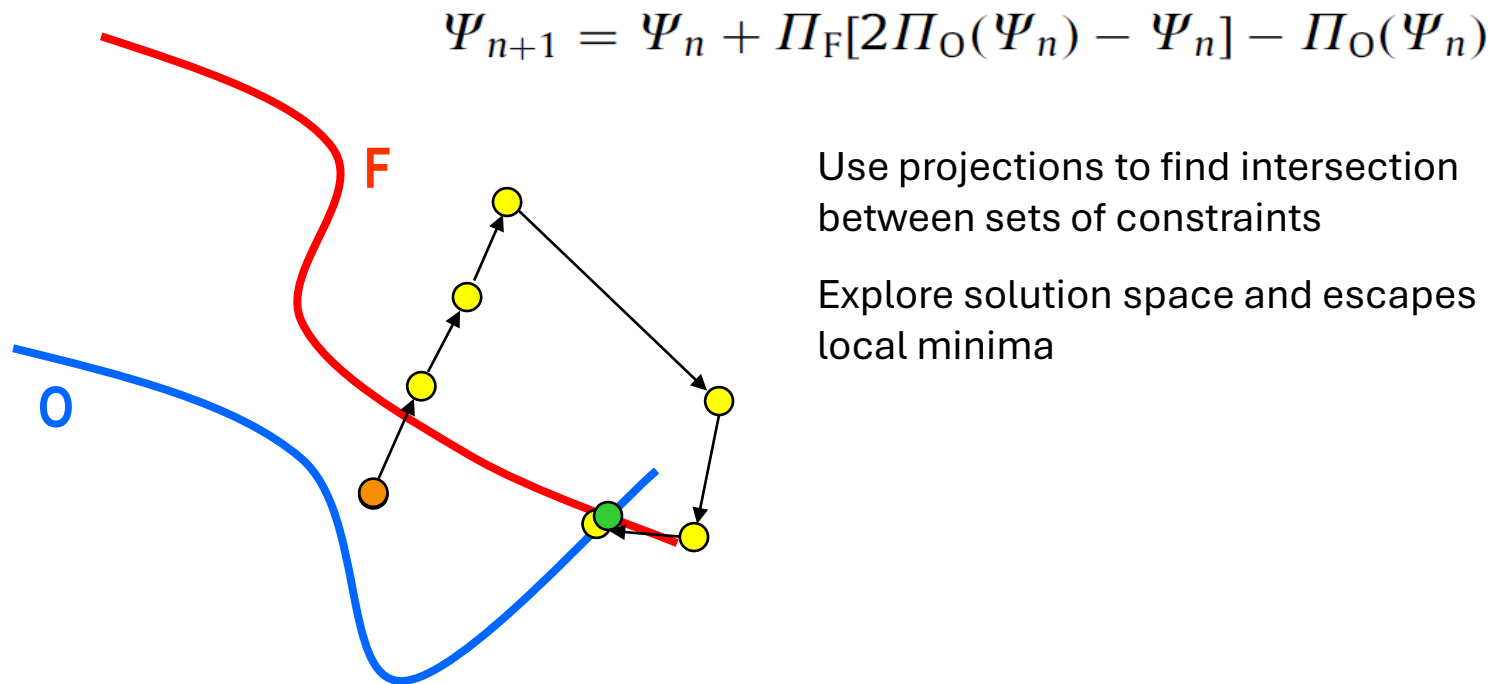
Project iteratively between
object and Fourier constraints

Iterative projection – Gerchberg Saxton

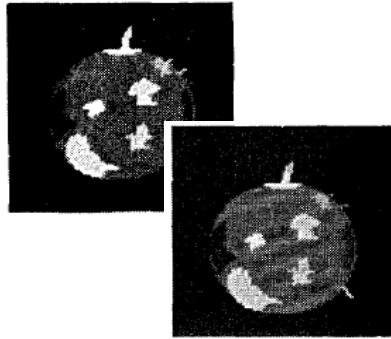


Project iteratively between
object and Fourier constraints

Difference map – HIO



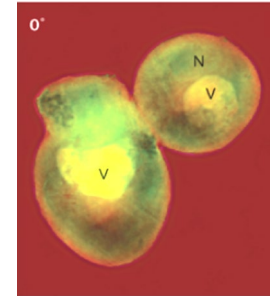
Phase retrieval with a support constraint (CDI)



J. R. Fienup, Opt. Lett. **3**, 27 (1978)



J. Miao et al., Nature **400**, 342 (1999)

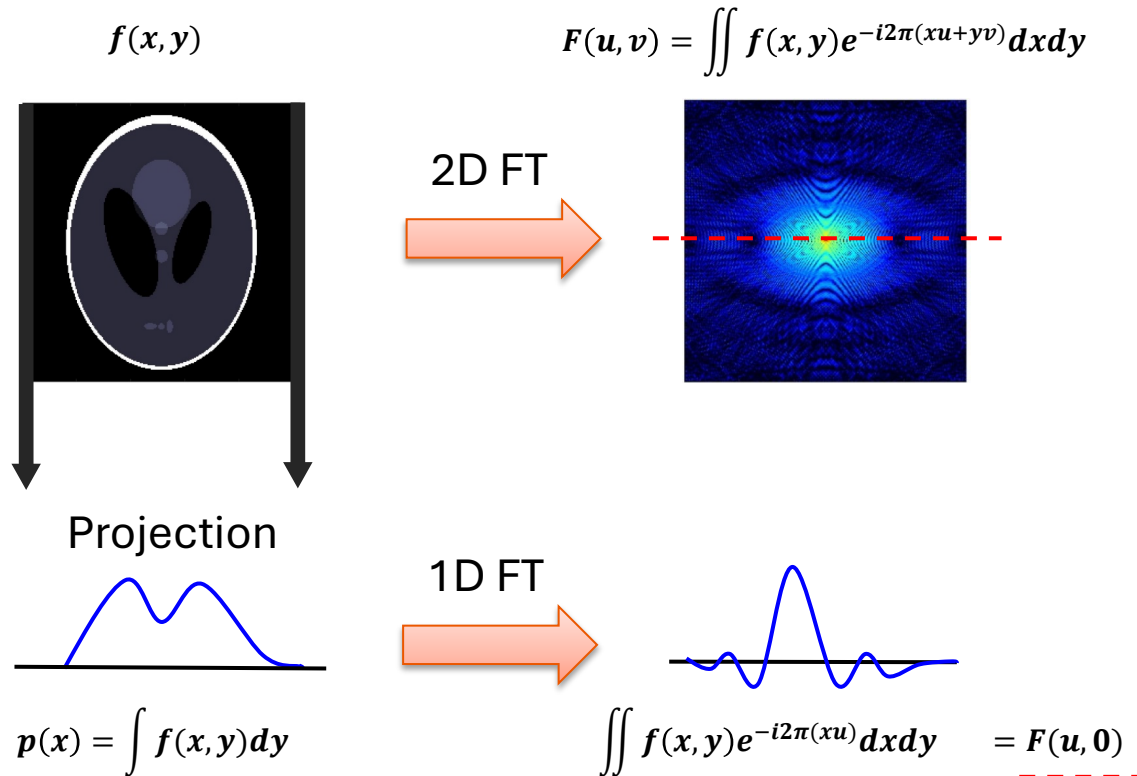


Specifically labeled freeze-dried yeast cell

J. Nelson et al., PNAS **107**, 7235 (2010)

Fourier projection-slice theorem

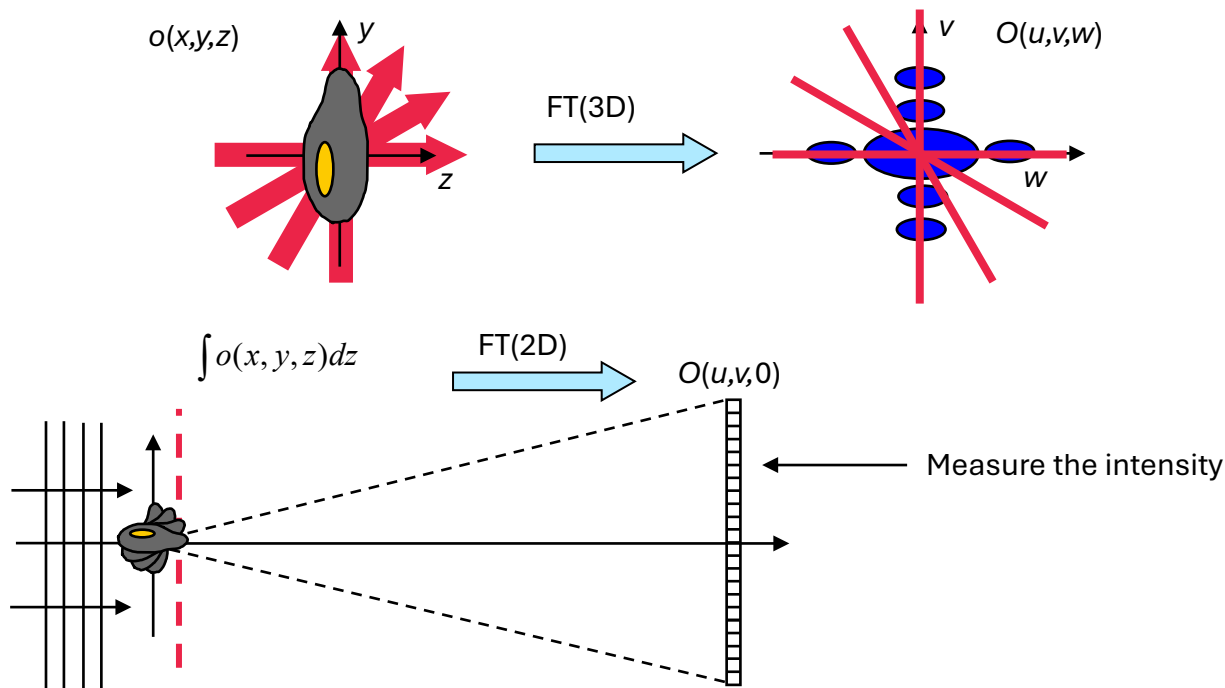
The Fourier transform of a parallel projection of an object $f(x,y)$ obtained at an angle θ equals a line of the 2D Fourier transform of $f(x,y)$ taken at the same angle.



3D measurement & reconstruction by phase retrieval

Attempt to reconstruct the scattering potential
of the object $o(x,y,z)$ by rotating the sample

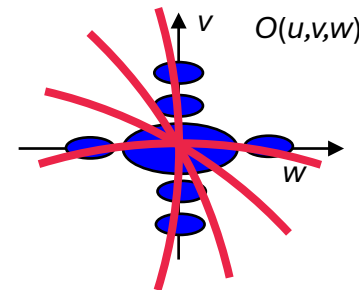
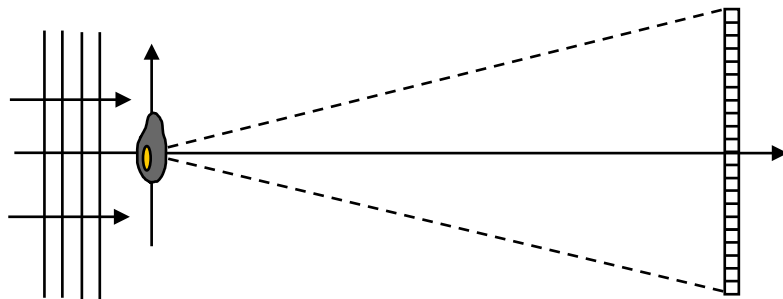
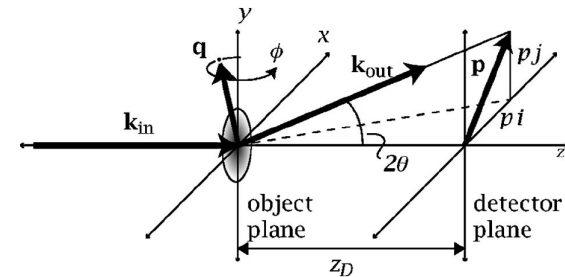
$$o(x, y, z) \approx \frac{2\pi}{\lambda^2} \Delta n(x, y, z)$$



Scattering from a 3D object

For elastic scattering each scattered angle is produced by a particular grating

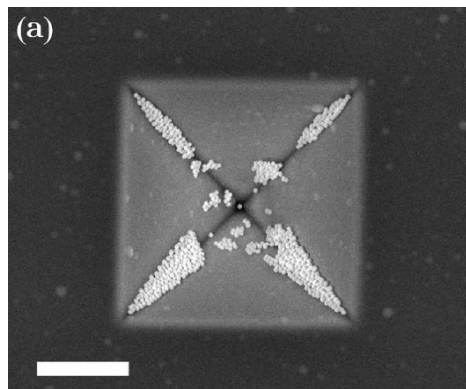
Bragg's law provides the mapping relation between the intensity in the detector plane and the 3D Fourier transform of the object



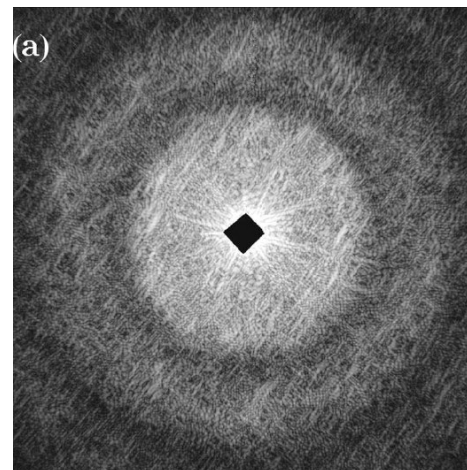
Each intensity measurement maps to a spherical shell on the 3D Fourier transform

The pyramid test object

50 nm diameter gold spheres on a pyramidal indentation on silicon nitride membrane



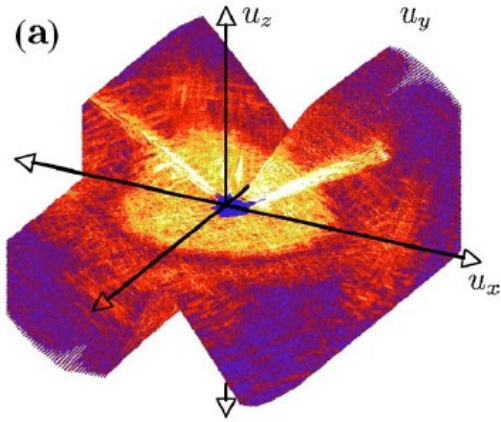
SEM image, surface sensitive only



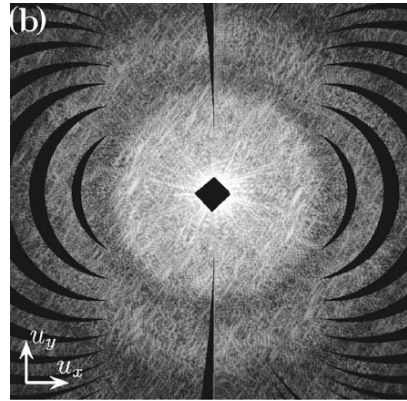
Measured diffraction pattern

10+ exposures to accommodate large dynamic range

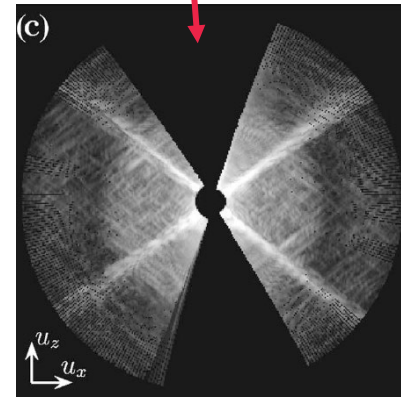
Cuts through 3D Fourier intensity



Data voids from beam stop
and large rotation
increments



Missing wedge from
limited range of
rotations

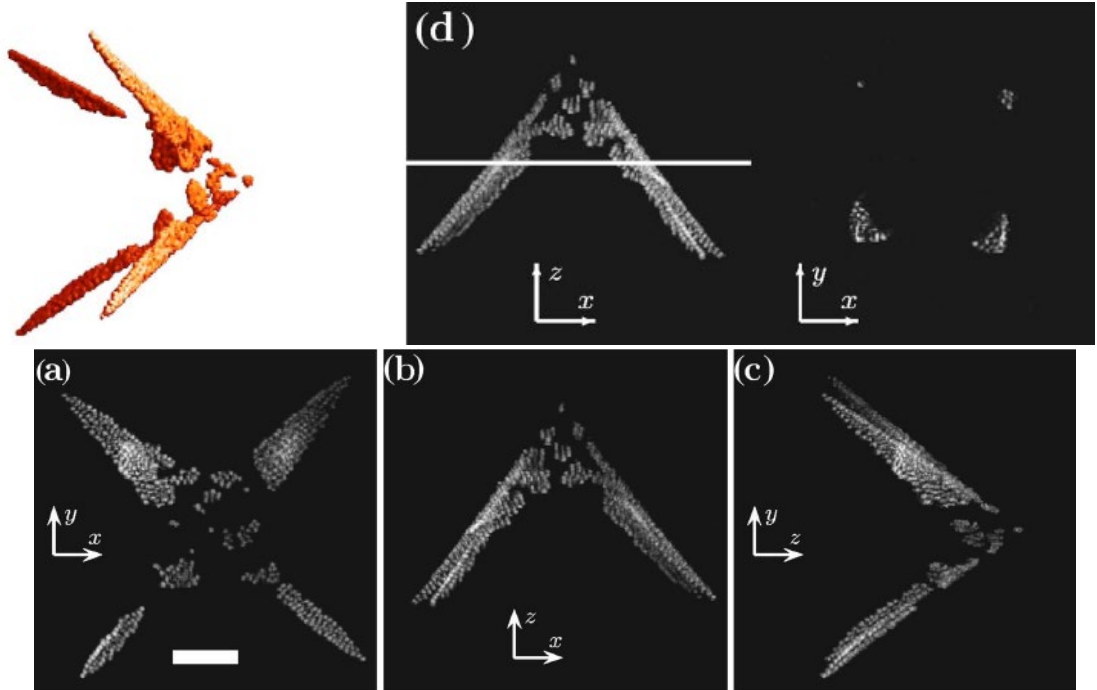


Total integrated exposure ~ 3.2 hours

3D reconstruction

Phase retrieval algorithm
was used to iteratively
interpolate gaps in the data

Final resolution $\sim 10 \times 10 \times 50$
nm (missing wedge)

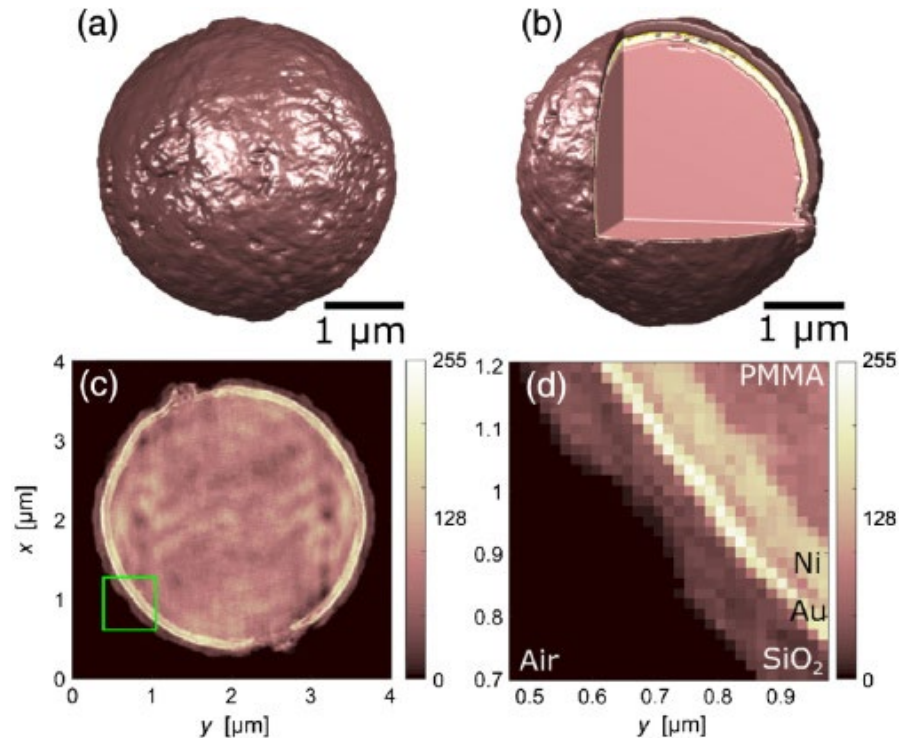


3D CDI in routine use at ID10 of ESRF

Metal-coated monodisperse
polymer spheres

Resolution better than 20 nm

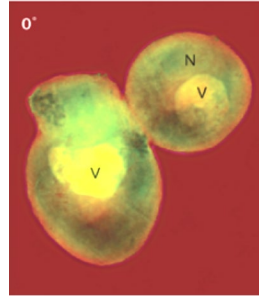
Micro-composite of PMMA, Ni, Au,
and SiO₂



Phase retrieval with a support constraint (CDI)

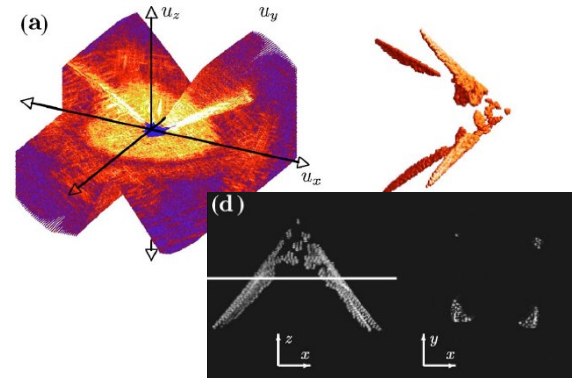


J. Miao et al., Nature
400, 342 (1999)



*Specifically
labeled freeze-
dried yeast cell*

J. Nelson et al.,
PNAS **107**, 7235
(2010)



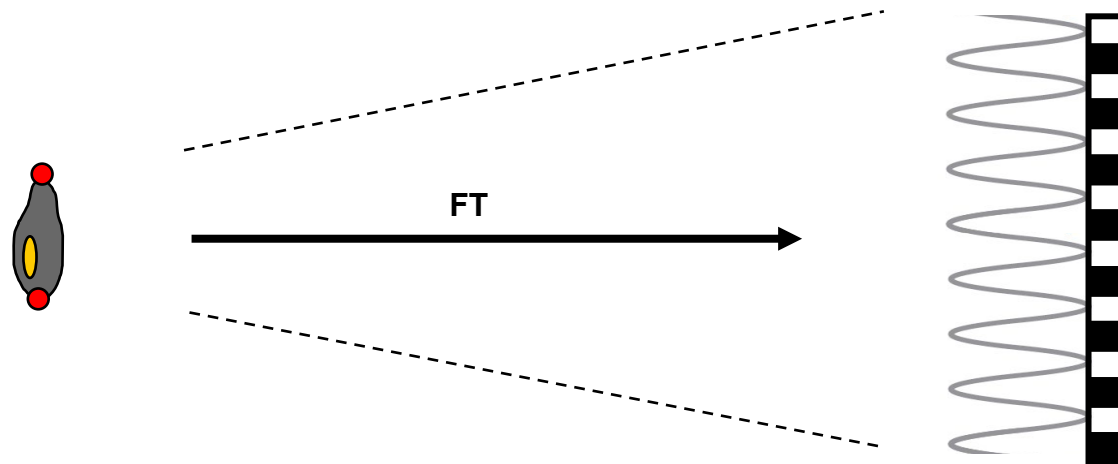
H. N. Chapman et al., J. Opt. Soc. Am. A **23**,
1179 (2006)

Some limitations include

- Occasional stagnation
- Field of view limited by detector pixel
(e.g. cSAXS@6.2 keV ~ 4 microns)
- Isolated sample (missing wedge)

$$fov = \frac{\lambda z}{2\Delta}$$

Phase retrieval with a support constraint (CDI)

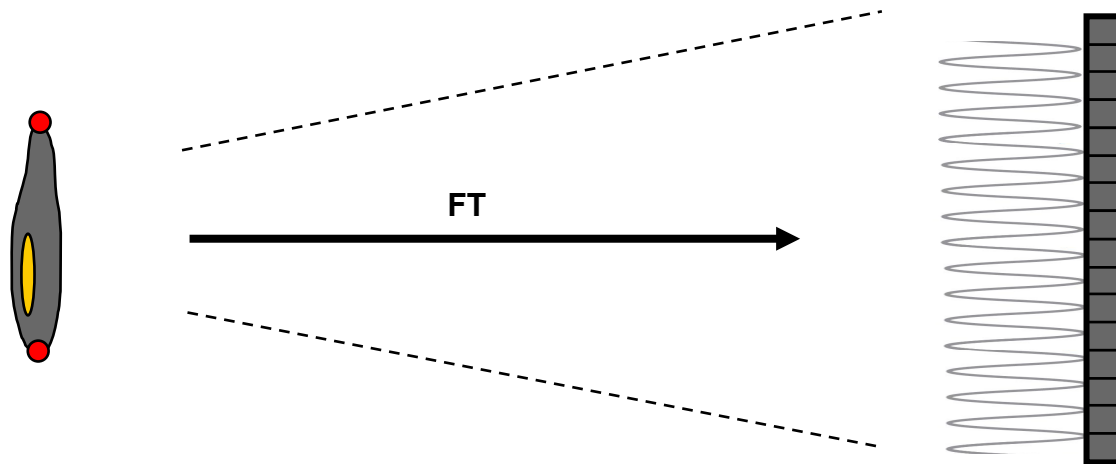


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Phase retrieval with a support constraint (CDI)



Some limitations include

- Occasional stagnation
- Field of view limited by detector pixel
(e.g. cSAXS@6.2 keV ~ 4 microns)
- Isolated sample (missing wedge)

$$fov = \frac{\lambda z}{2\Delta}$$

Ambiguities in CDI

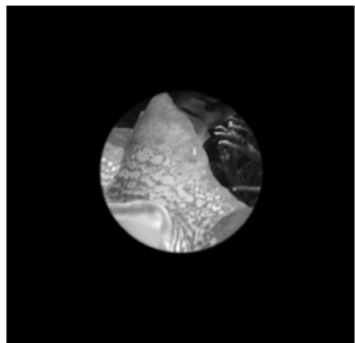
Inherent ambiguities exist in CDI reconstructions. These are functions that can take arbitrary values → They are not constrained by the data

$$\begin{aligned} f(x, y) &\rightarrow F(u, v) \\ f(x, y) \exp(ia) &\rightarrow F(u, v) \exp(ia) \\ f(x - b, y) &\rightarrow F(u, v) \exp(-i2\pi bu) \\ f^*(-x, -y) &\rightarrow F^*(u, v) \\ &\text{if support is symmetric} \\ &\text{either one could appear} \\ f(x, y) \exp(i2\pi cx) &\rightarrow F(u - c, v) \end{aligned} \quad \left. \vphantom{\begin{aligned} f(x, y) &\rightarrow F(u, v) \\ f(x, y) \exp(ia) &\rightarrow F(u, v) \exp(ia) \\ f(x - b, y) &\rightarrow F(u, v) \exp(-i2\pi bu) \\ f^*(-x, -y) &\rightarrow F^*(u, v) \\ &\text{if support is symmetric} \\ &\text{either one could appear} \\ f(x, y) \exp(i2\pi cx) &\rightarrow F(u - c, v) \end{aligned}} \right\} \text{Measure } |F(u, v)|^2$$

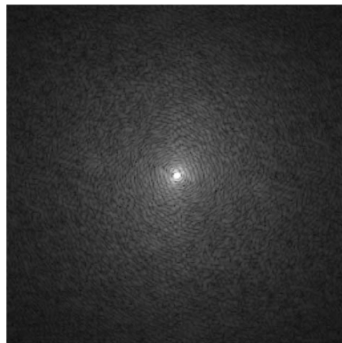
They are all successful reconstructions, but should be aware of them for interpretation of the reconstructions

Twin-image problem – Numerical simulation

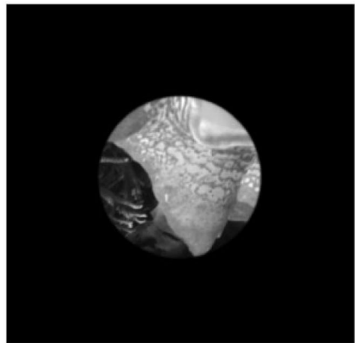
True image



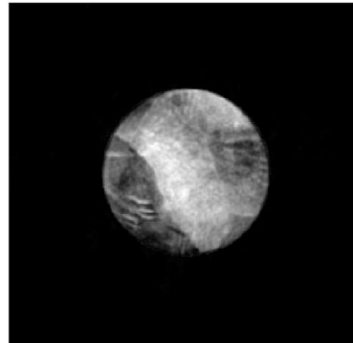
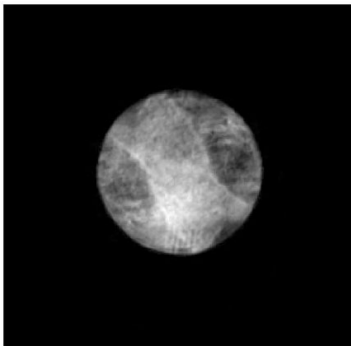
Fourier transform magnitude



Twin image



Twin image stagnation



Outline

X-ray imaging

The phase problem (CDI)

● Ptychography

Ultrafast X-ray imaging with free-electron lasers

Ptychography

Resolving ambiguities of CDI
3D ptychography



Ptychography (transverse translation diversity)

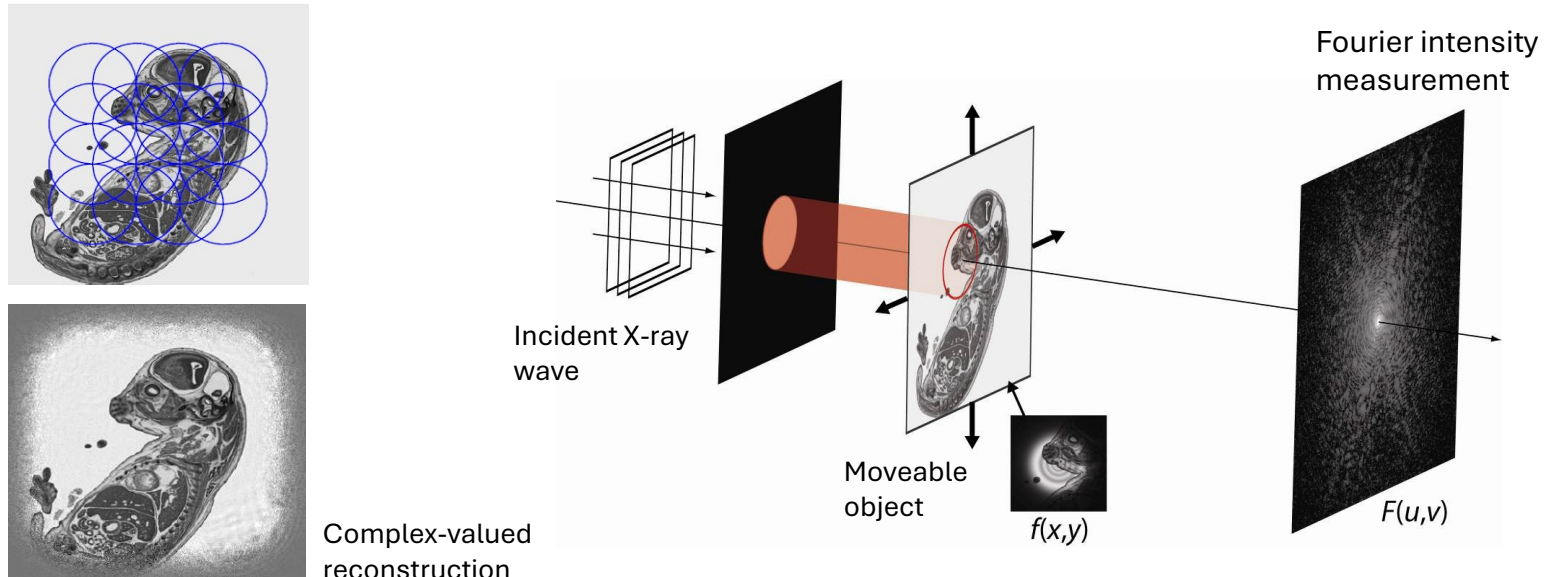


EPFL

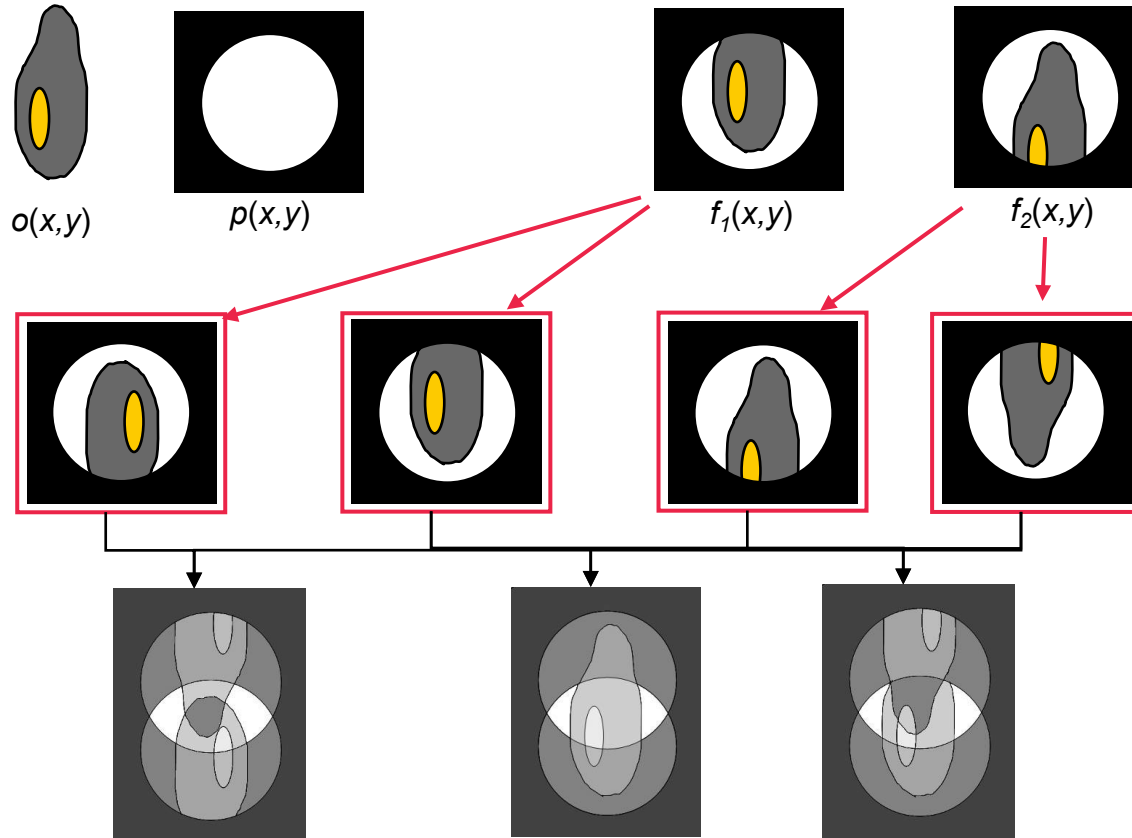
Moving the sample with respect to a known illumination pattern can provide suitably diverse measurements

Makes phase retrieval more robust to stagnation, noise and ambiguities

Allows for extended samples, resolution is finer than the illumination size and scanning step



Overlap in the fields breaks the twin-image ambiguity



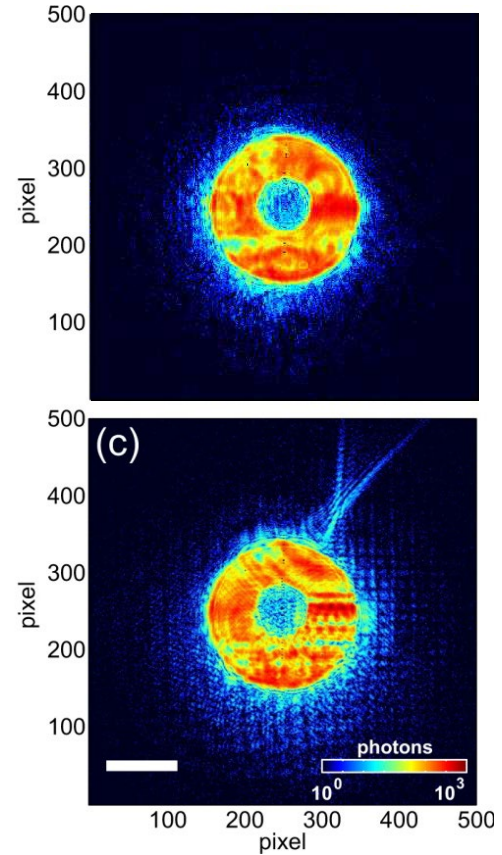
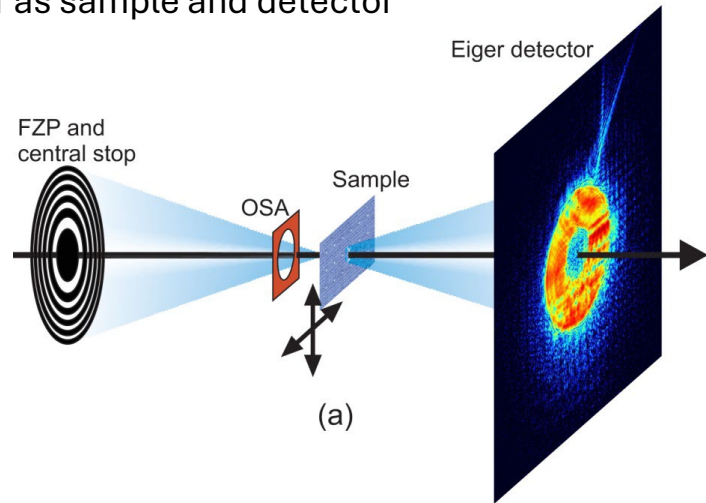
Imaging throughput – The Eiger self portrait

Sample 5 mm downstream of focus

Beam at sample ~ 10 microns

Scanning average step 3.5 microns

Eiger as sample and detector



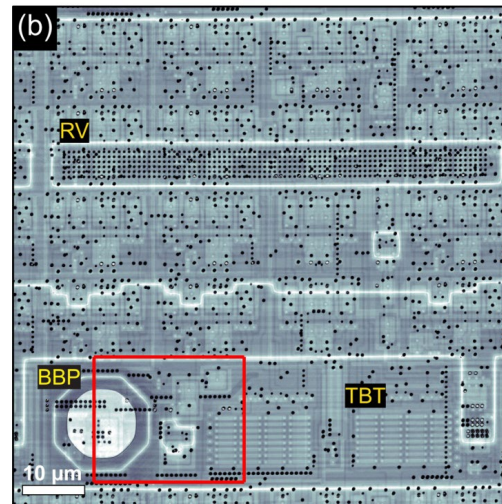
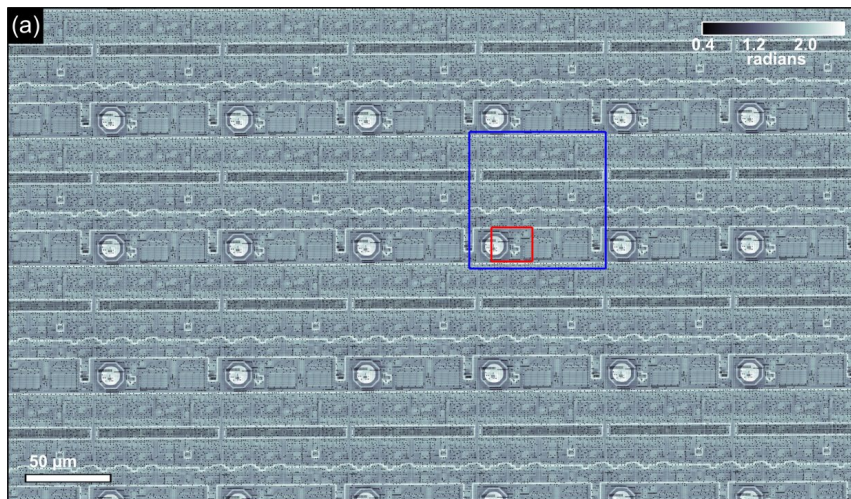
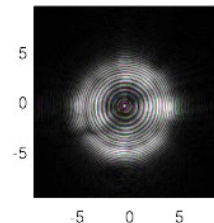
Imaging throughput – The Eiger self portrait

98.4 Mpixel (13,028 x 7,556)

Resolution 41 nm, 38.4 nm pixel

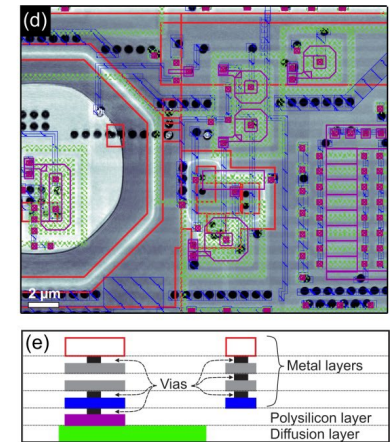
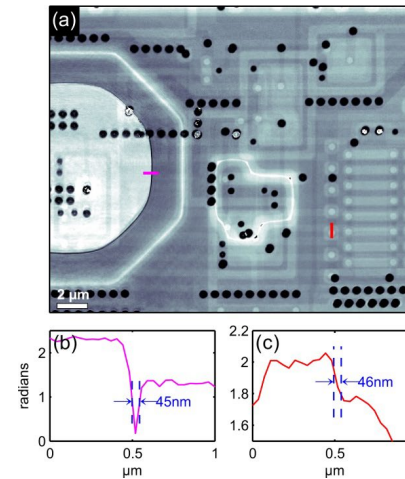
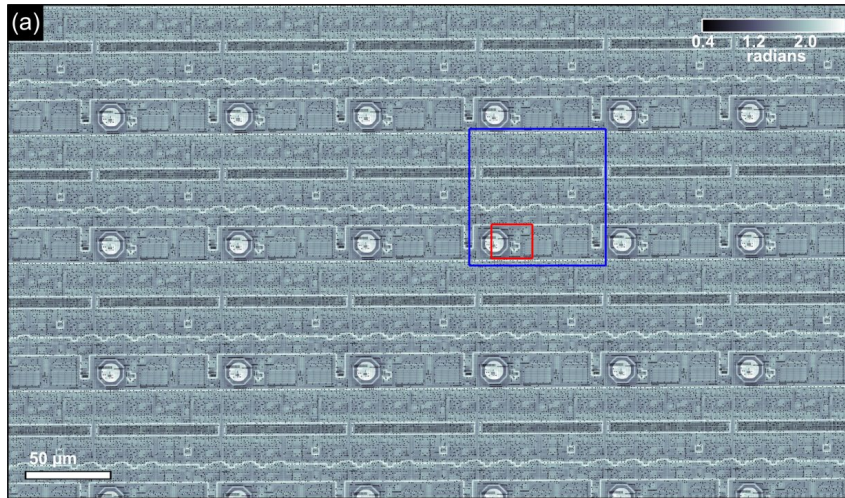
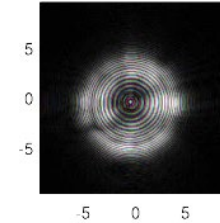
> 25,000 resolution elements / second

40 microsecond per resolution element



Imaging throughput – The Eiger self portrait

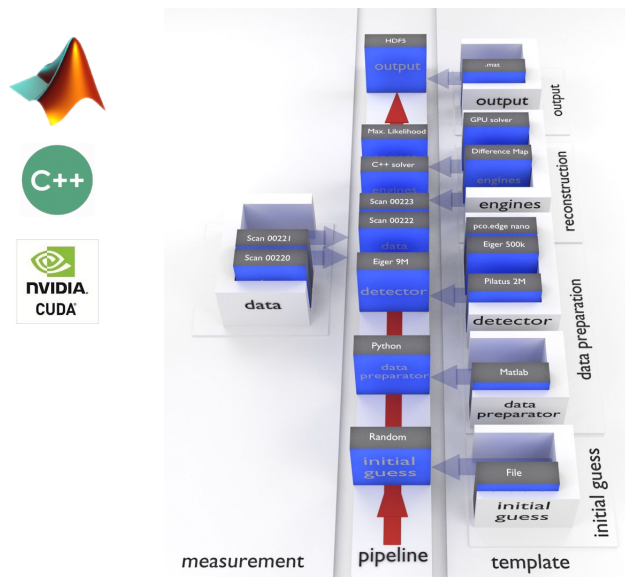
98.4 Mpixel (13,028 x 7,556)
Resolution 41 nm, 38.4 nm pixel
> 25,000 resolution elements / second
40 microsecond per resolution element



PtychoShelves



A versatile high-level framework for high-performance analysis of ptychographic data



Modular framework: Matlab, C++, GPU Cuda

Distributed: MPI, multiple GPU cards, minimal memory synchronization

High-performance reconstruction engines (Scientific computing)

Batch processing and online reconstructions

SLS (cSAXS, SIM), APS, SOLEIL, Cornell Univ. (electron ptychography)

Multiple reconstruction algorithms can be concatenated

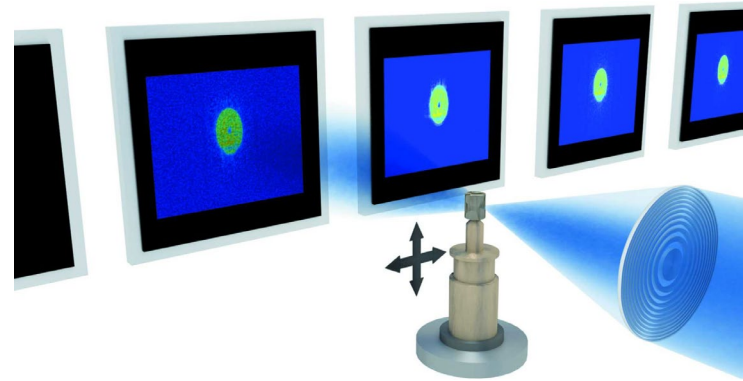
Multislice, mixed coherent modes, modal probe relaxation, sharing reconstructions between scans, position refinement, global position geometry refinement

Ptychographic X-ray computed tomography (PXCT)

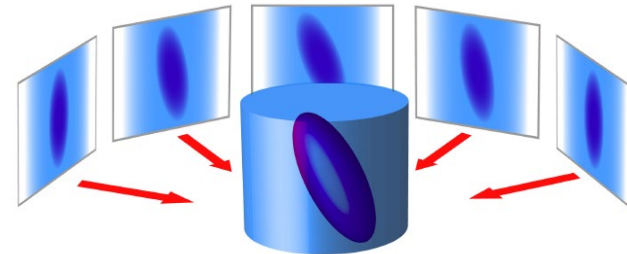
Phase of reconstruction corresponds to the integrated x-ray phase-shift

Combined with sample rotation and computed tomography algorithms the real part of the 3D index of refraction can be reconstructed

$$t(x, y, \theta) = \exp \left\{ \frac{i2\pi}{\lambda} \int [n(\mathbf{r}') - 1] dz \right\}$$
$$n(\mathbf{r}) = 1 - \delta(\mathbf{r}) + i\beta(\mathbf{r})$$

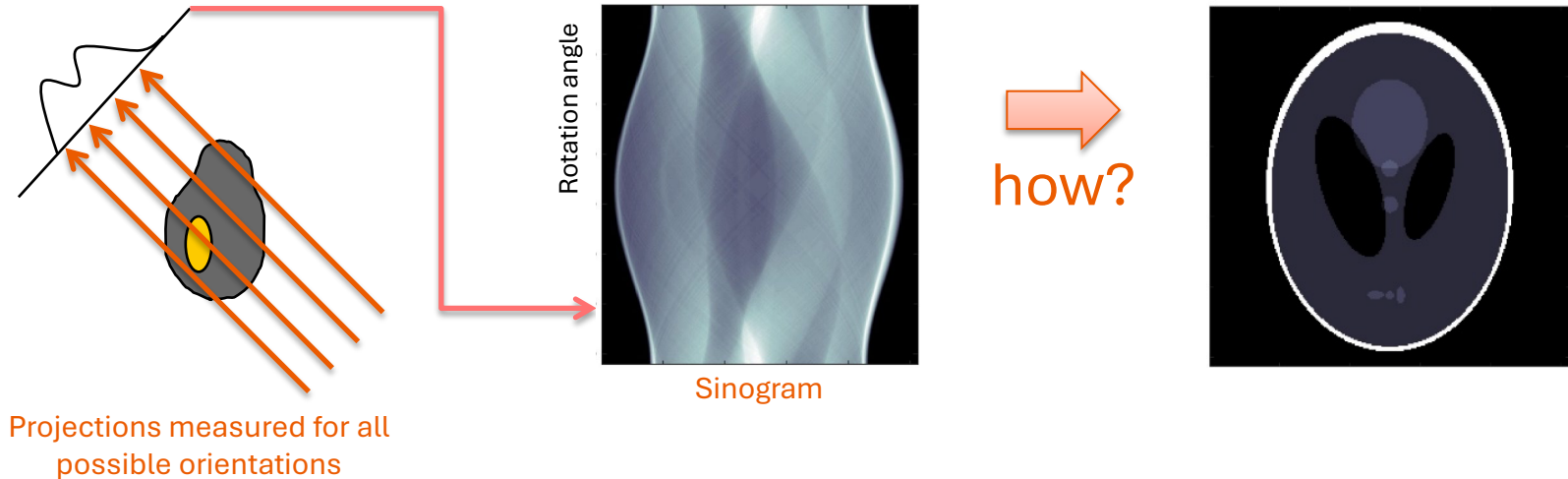


K. Wakonig,* H.-C. Stadler, M. Odstrčil, E. H. R. Tsai, A. Diaz, M. Holler, I. Usov, J. Raabe, A. Menzel, and M. Guizar-Sicairos*, J. Appl. Cryst. **53**, 574 (2020)

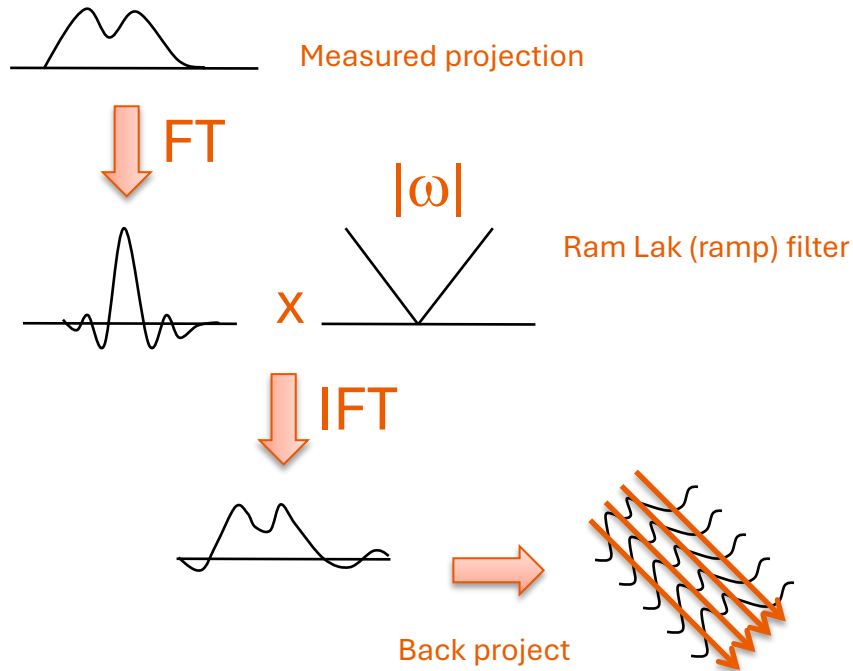


Basics of computed tomography

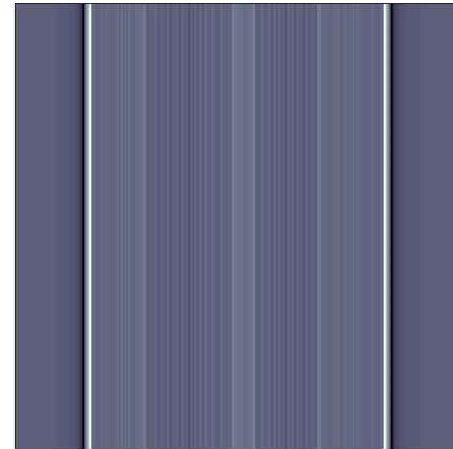
Imaging sections of the interior without physical sectioning
Starting from projections, line integrals from different orientations,
how to reconstruct the object?



Filtered back-projection



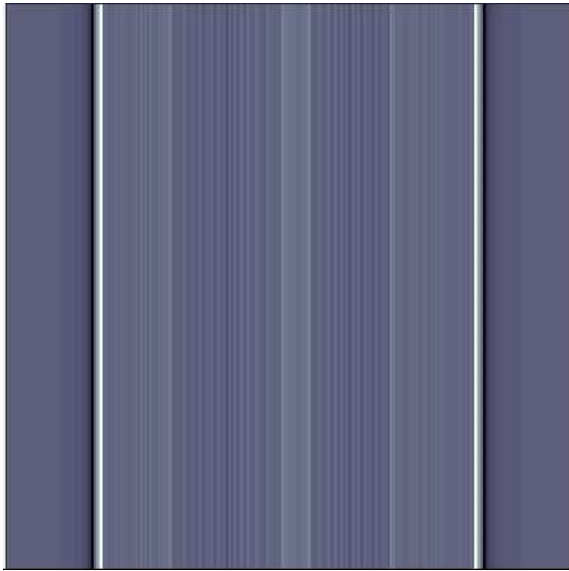
$$\mu(x, y) = \int_0^{\pi} d\theta \int_{-\infty}^{\infty} \tilde{P}(\omega, \theta) |\omega| e^{j2\pi\omega t} d\omega$$



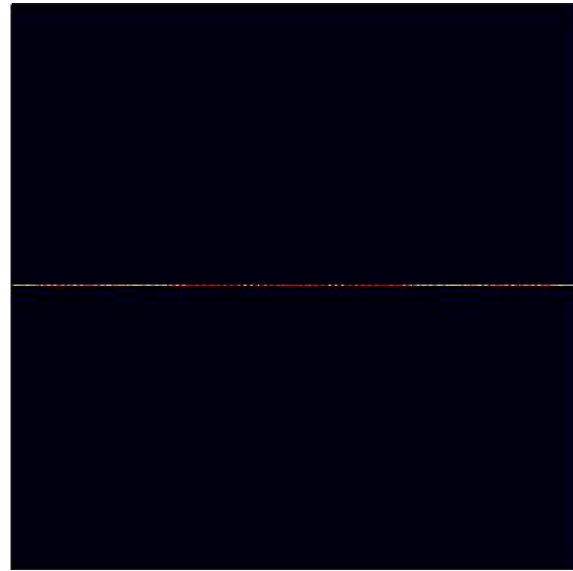
Filtered back-projection



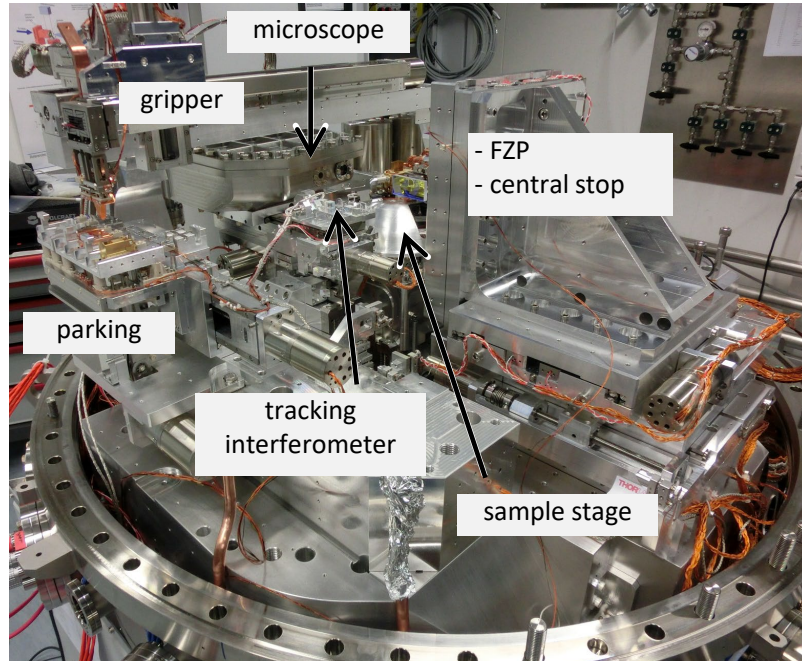
$$\mu(x, y) = \int_0^{\pi} d\theta \int_{-\infty}^{\infty} \tilde{P}(\omega, \theta) |\omega| e^{j2\pi\omega t} d\omega$$



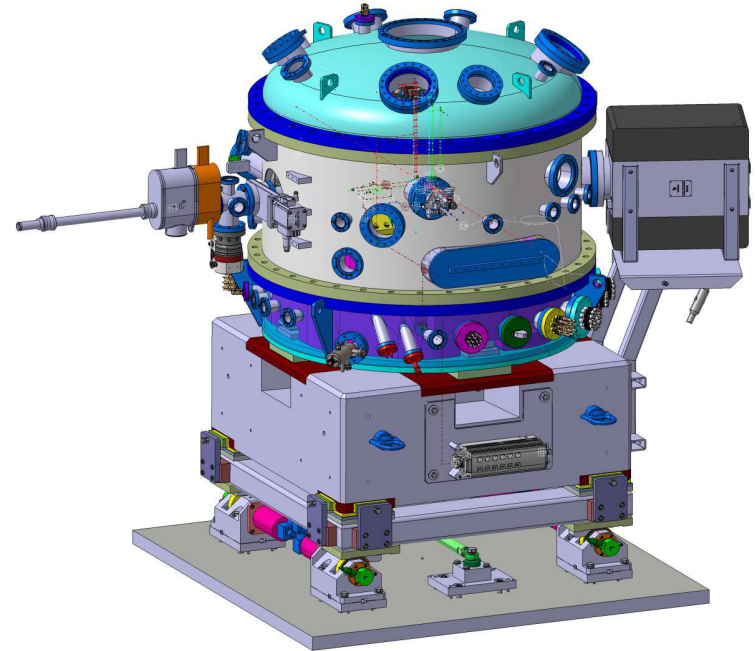
FT
→



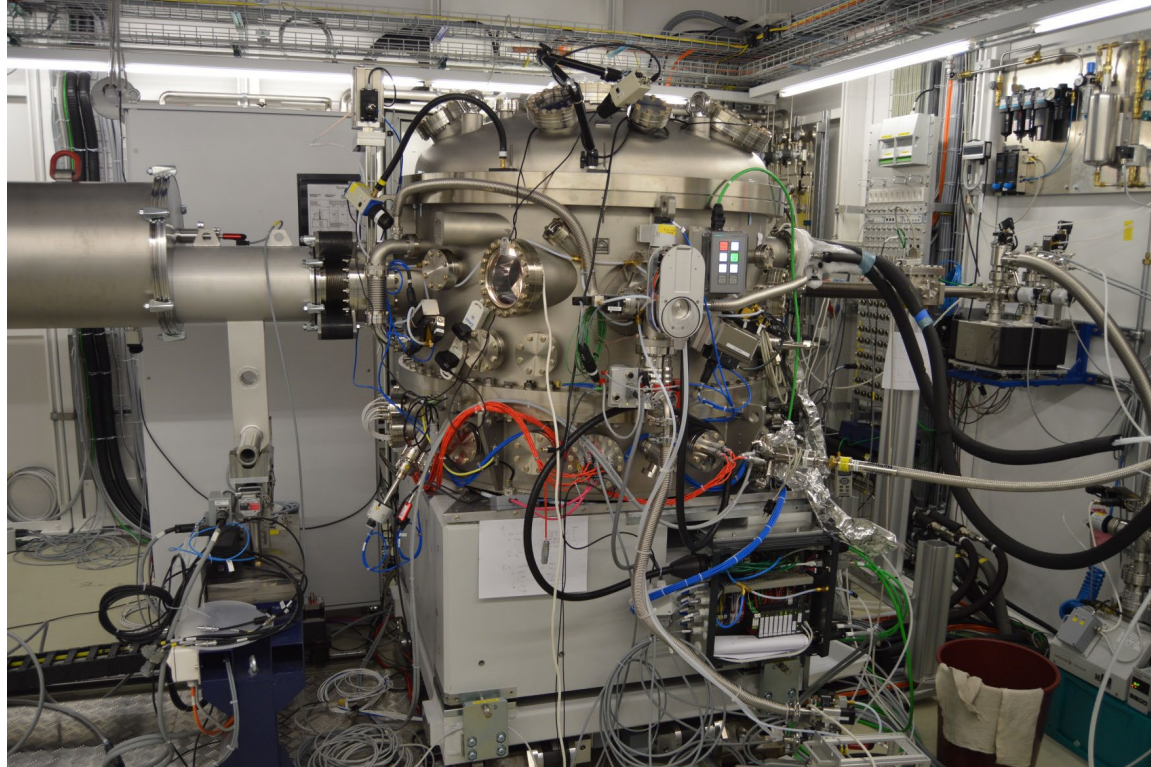
OMNY: The cryo-stage instrument



M. Holler, J. Raabe, and engineer team at PSI



OMNY: The cryo-stage instrument

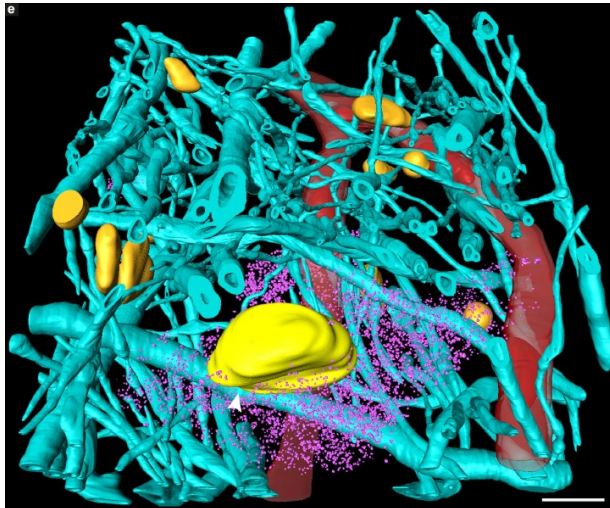


First visit at the beamline June 3-15, 2015 for commissioning and measurements

Unstained human brain tissue

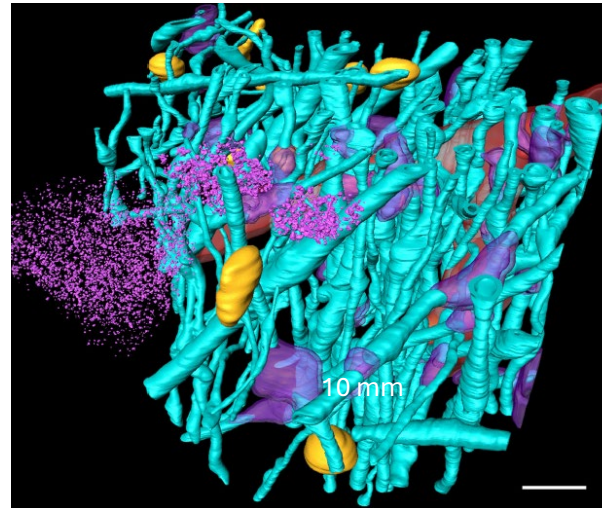
Brain region: substantia nigra pars compacta
Chemically fixed, hydrated, unstained

healthy



5 specimens imaged from a healthy individual as control

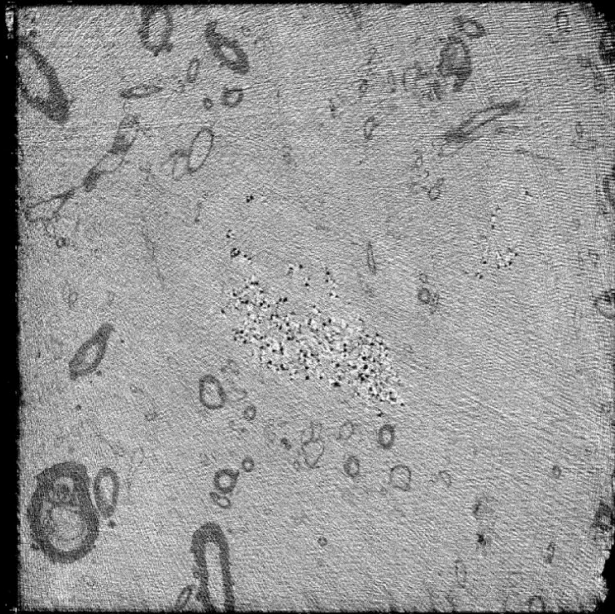
Parkinson-affected



4 specimens imaged from a Parkinson-affected individual

Myelinated axons
Swellings along axons
Cell nuclei
Neuromelanin-containing organelles
Blood vessels
Blood cells

Unstained human brain tissue



Tran, H. T. et al.
Front. Neurosci. 14:570019.

Myelinated axons
Swellings along axons
Cell nuclei
Neuromelanin-containing
organelles
Blood vessels
Blood cells

25 μm

Nanoscale 3D imaging

Combine ptychography with sample rotation

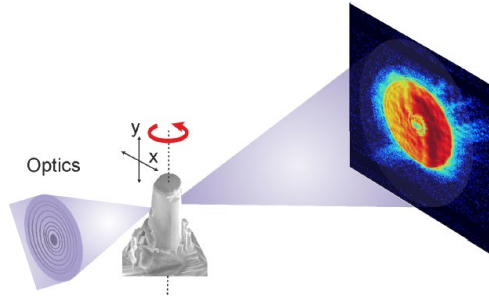
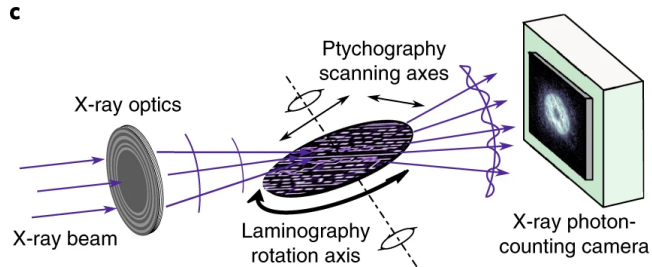


Image modified from Donnelly *et al.* Nature 547, 328 (2017)

Ptychographic X-ray computed tomography (PXCT)

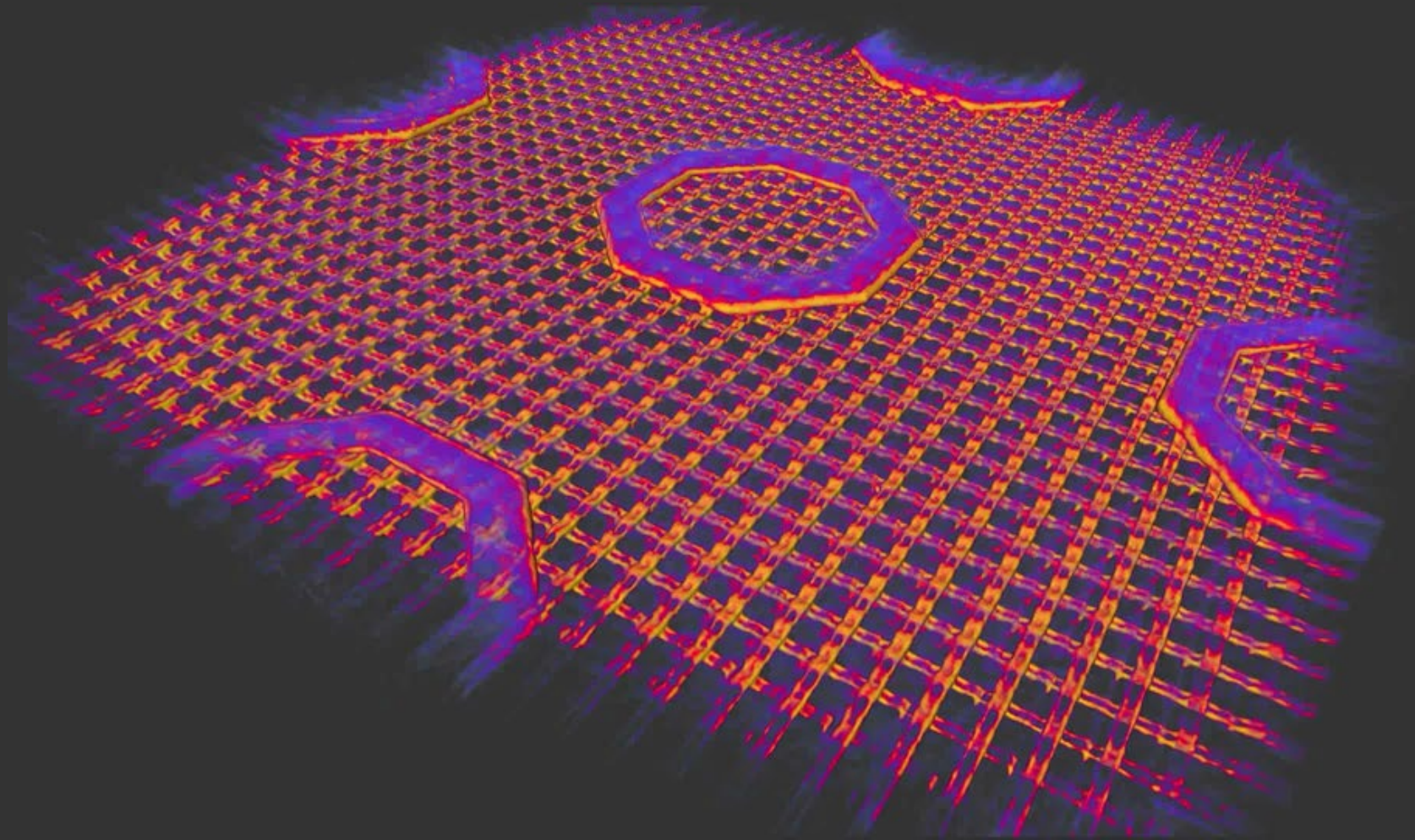
Dierolf *et al.* "Ptychographic X-ray computed tomography at the nanoscale," Nature, **467** 436 (2010)



Ptychographic X-ray laminography (PyXL)

Holler *et al.*, "Three-dimensional imaging of integrated circuits with macro- to nanoscale zoom," Nat. Electron. **2**, 464 (2019)

Integrated circuit (16 nm CMOS FinFET) at 20 nm resolution. Measurement in SLS, cSAXS.



Laminography Nano Imaging (LamNI)

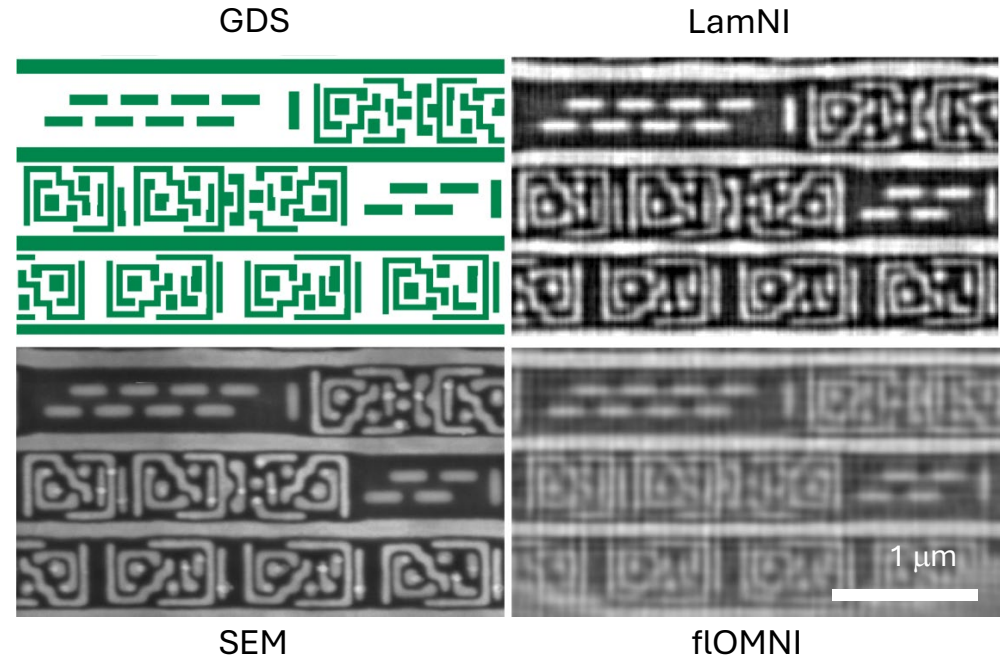
Integrated circuit

FOV 40x40 microns

20 nm resolution

Smallest gaps and metal connects
~30 nm

Laminography configuration also
reduces streak artifacts



Further reading

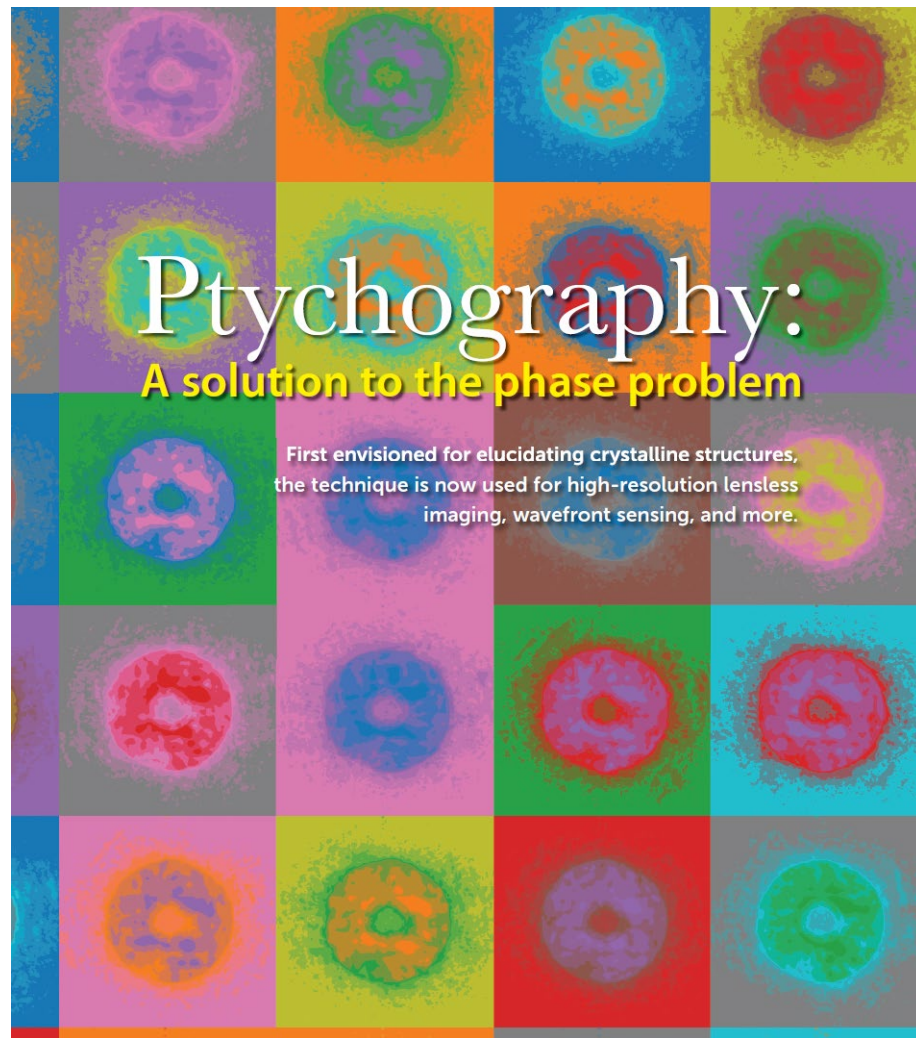
M. Guizar-Sicairos and P. Thibault, Physics Today **74**,
42 (2021). September 2021

History

Links to other techniques

Different ptychography flavours

Applications



Resolution record in electron microscopy

Resolution record in electron microscopy

1948 – Holography invented (Dennis Gabor, Physics Nobel 1971)

1958 – Laser invented, Townes (Physics Nobel 1964) and Schawlow
(Physics Nobel 1981) are mostly credited, but it's a complicated story

1969 – Ptychography is proposed for electron microscopy by Walter Hoppe

Instrumentation and coherence was not really ready for electron microscopy,
and optical wavelengths already had good imaging techniques

Electron ptychography achieves atomic-resolution limits set by lattice vibrations

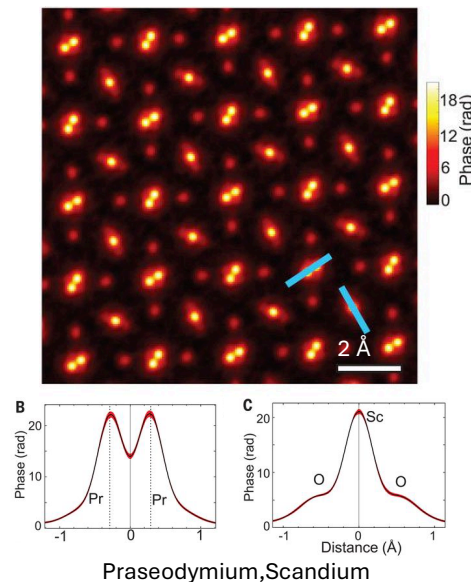
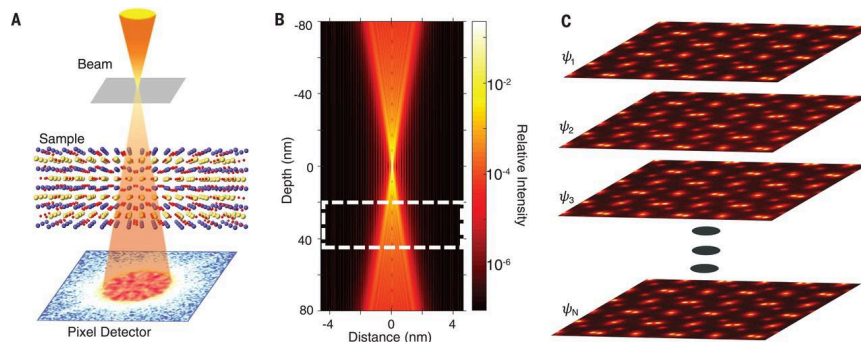
Back full circle – Ptychography was first conceived in 1969 by W. Hoppe for electron microscopy

Resolution **15 pm**

PrScO₃ sample with a thickness of **21 nm**

Column width of reconstruction limited by finite size of atoms (thermal fluctuations)

Ptycho overcomes lens aberrations and multiple scattering



Electron ptychography achieves atomic-resolution limits set by lattice vibrations

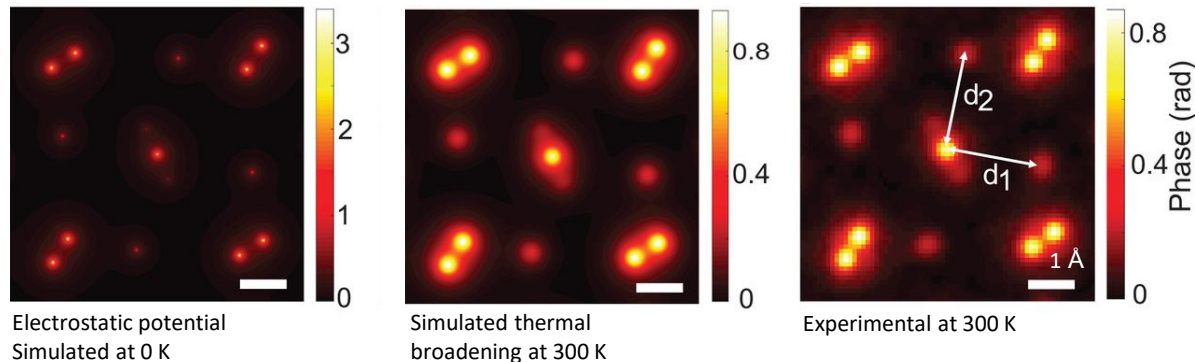
Back full circle – Ptychography was first conceived in 1969 by W. Hoppe for electron microscopy

Resolution **15 pm**

PrScO₃ sample with a thickness of **21 nm**

Column width of reconstruction limited by finite size of atoms
(thermal fluctuations)

Ptycho overcomes lens aberrations and multiple scattering



Resolution record in X-ray tomography

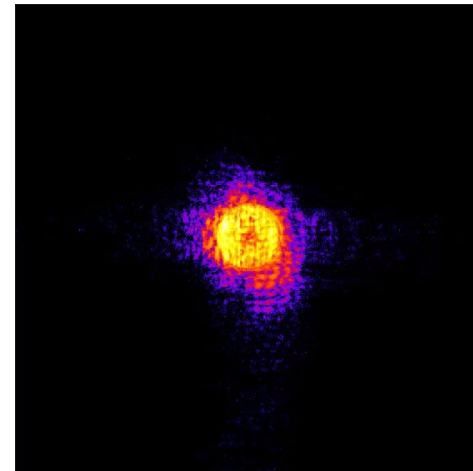
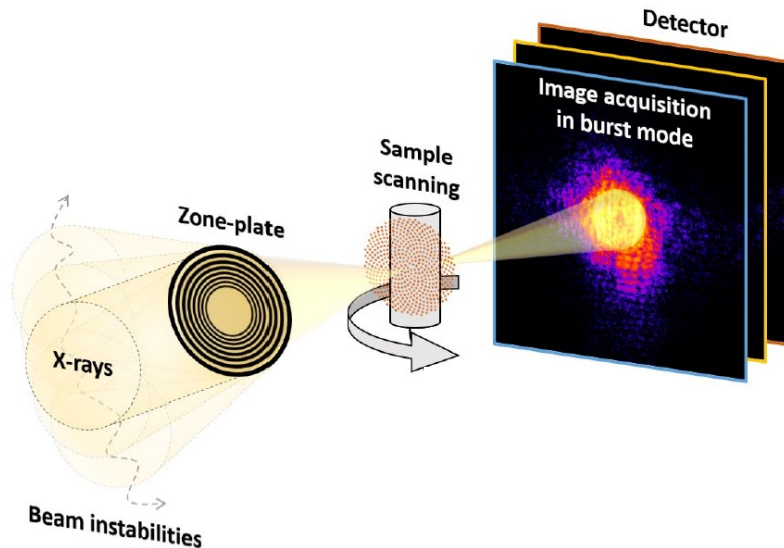
Pushing the limits of X-ray imaging resolution

A plateau/bottleneck in resolution was observed → increased statistics did not improve resolution

Fast short exposures at a fixed position revealed instabilities of the X-ray illumination



Tomas
Aidukas



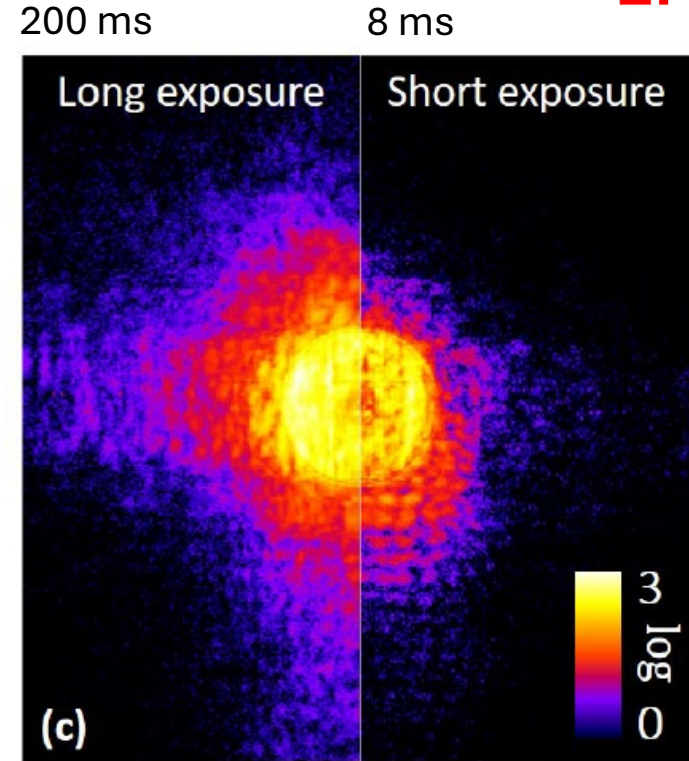
8 ms exposure time

Pushing the limits of X-ray imaging resolution

Higher photon statistics

Blurred diffraction patterns → lower SNR

Breaches assumption of constant illumination



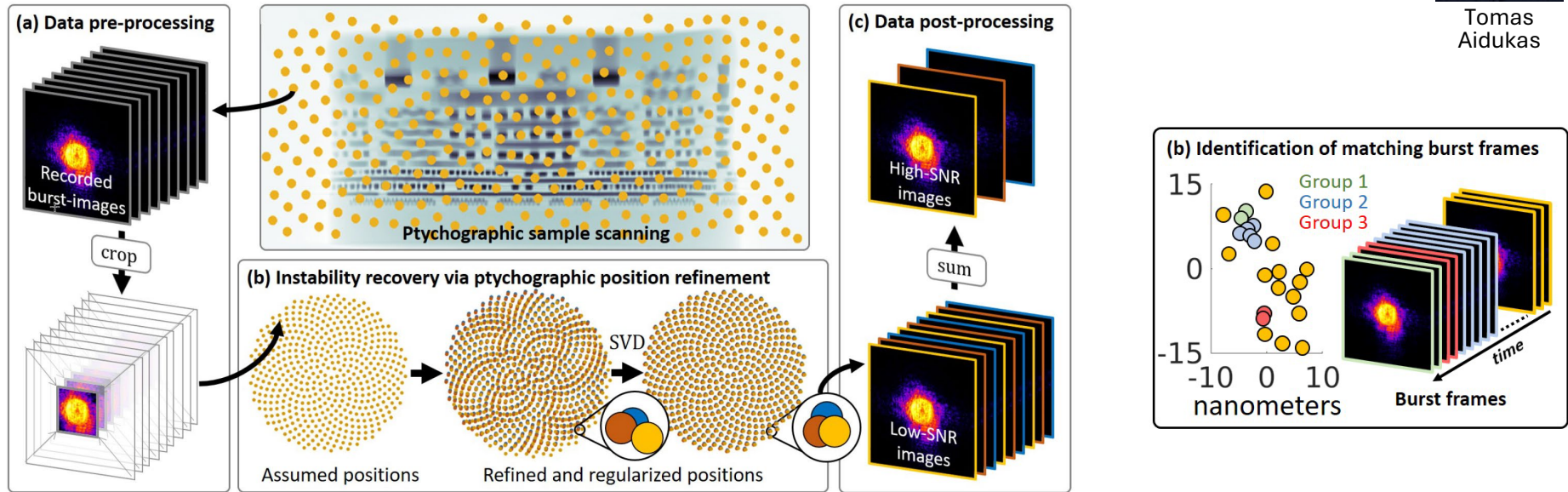
Burst ptychography

Many fast acquisitions per scanning point

Use ptychography position refinement to identify and average frames with similar positions → All data is used

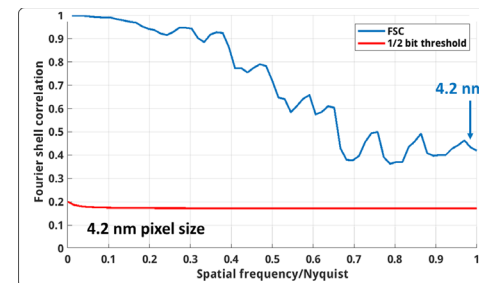
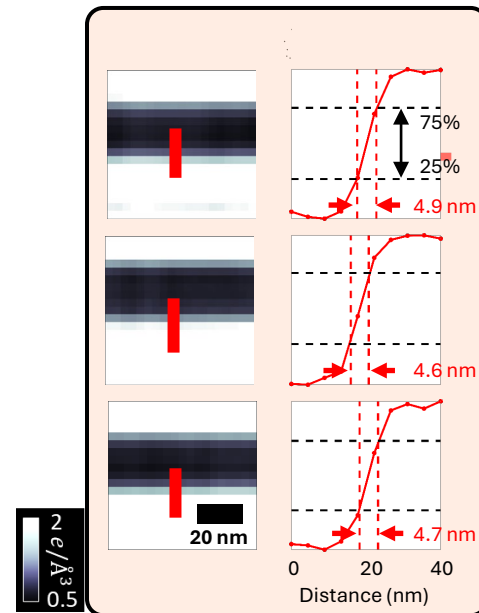
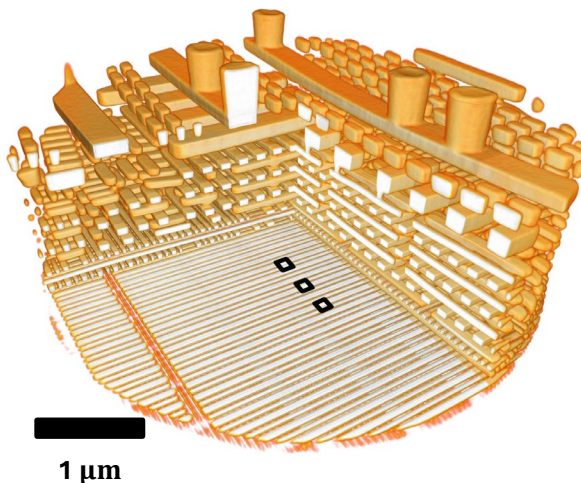
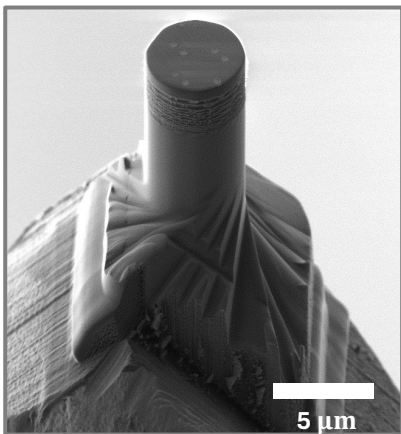


Tomas
Aidukas



AMD Ryzen 5 5600G GPU IC

TSMC 7 nm node technology (measure of transistor density)
38 hour measurement @cSAXS beamline



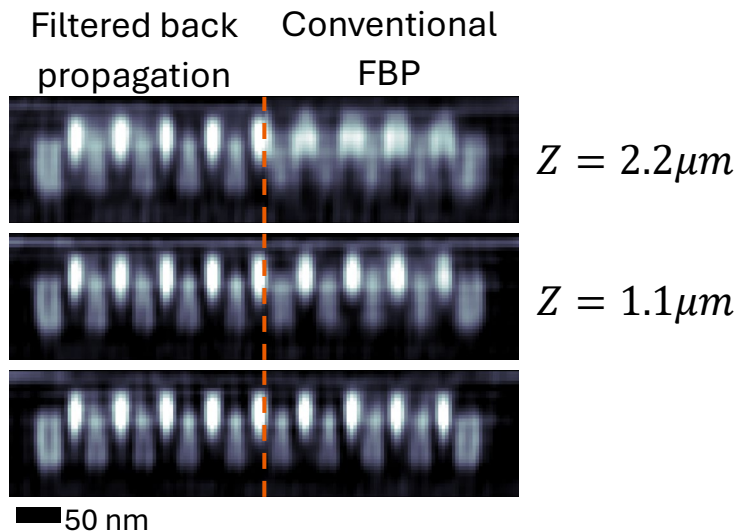
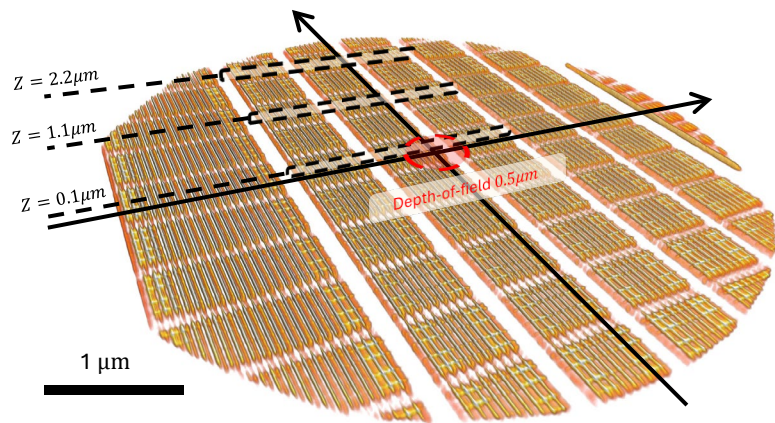
T. Aidukas, N. W. Phillips, A. Diaz, E. Poghosyan, E. Müller, A. F. J. Levi, G. Aepli, M. Guizar-Sicairos, and M. Holler,
“High-performance 4-nm-resolution X-ray tomography using burst ptychography,” Nature **632**, 81 (2024)

Extended depth of field

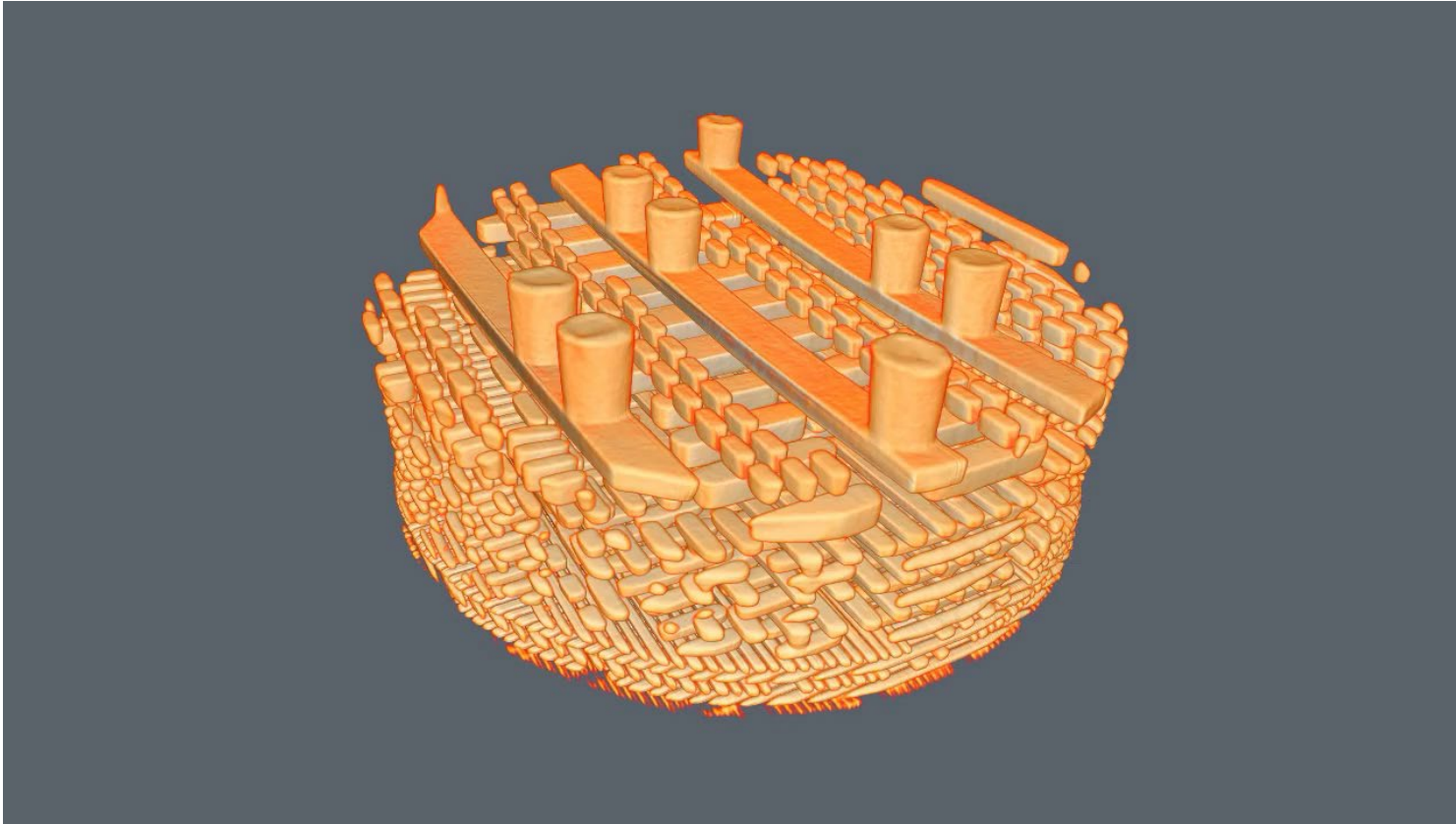
We have not obtained good results with multi-slice ptychography in X-rays

→ Proper modeling of beam propagation through the sample

We get a complex-valued transmissivity → here we use filtered back-propagation instead of filtered back projection in the tomographic step



The metal connectome – 4 nm resolution



T. Aidukas, N. W. Phillips, A. Diaz, E. Poghosyan, E. Müller, A. F. J. Levi, G. Aeppli, M. Guizar-Sicairos, and M. Holler, “High-performance 4-nm-resolution X-ray tomography using burst ptychography,” *Nature* **632**, 81 (2024)

Outline

X-ray imaging

The phase problem (CDI)

Ptychography

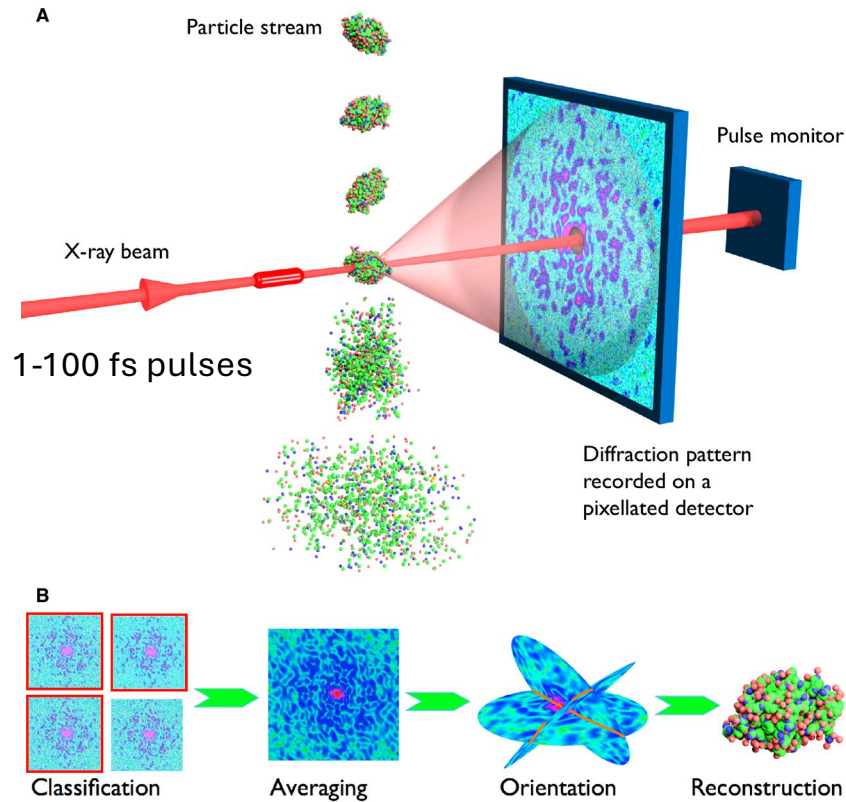
- Ultrafast X-ray imaging with free-electron lasers

Ultrafast X-ray imaging with free-electron lasers

Catching molecules in action

X-ray free electron lasers (X-FELs)

Diffract-before-destroy



Swiss FEL – Swiss Free Electron Laser @ PSI



Innovations on the electron source enabled a compact and cost-effective design

Eduard Prat, et al. “A compact and cost-effective hard X-ray free-electron laser driven by a high-brightness and low-energy electron beam,” *Nature Photonics* **14**, 748 (2020)

The SwissFEL movie

<https://www.youtube.com/watch?v=sMWnA-vUlw0&list=PL0b-ynhMVTd4Y2wU-1B39Kpnxwg0-YmU&index=2>

Ultrafast serial crystallography

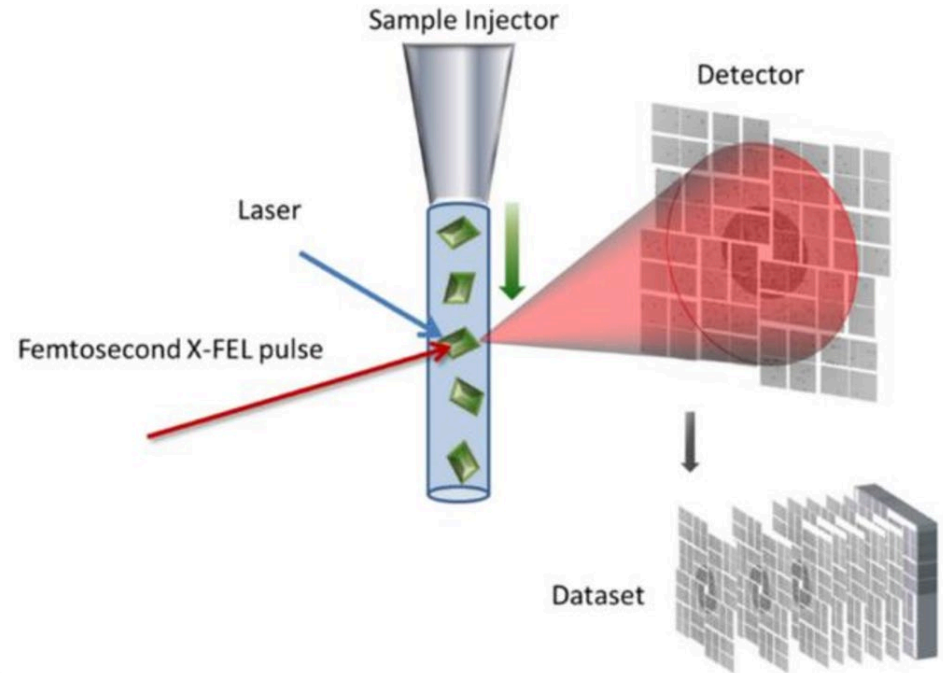
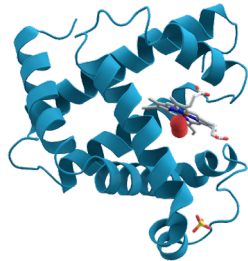
Catching molecules in action

Crystals instead of single molecules

➤ Boost signal

Delay between laser and X-ray pulse

➤ Time resolution



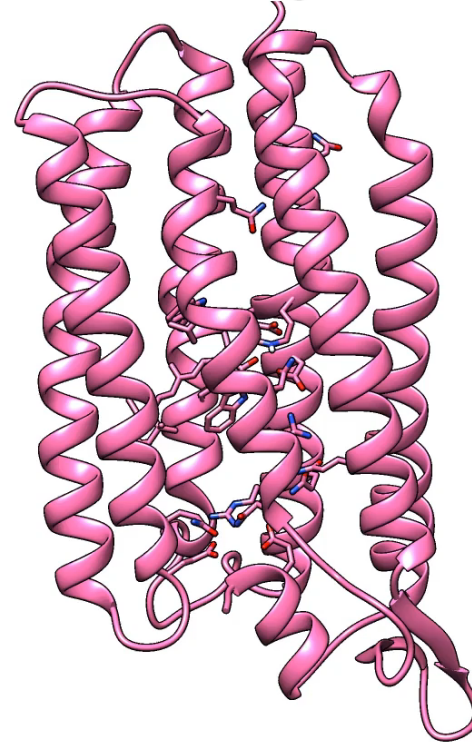
Ultrafast serial crystallography

Catching molecules in action – Light activated sodium pumps

Sodium differences (transport) plays a very important role in in the way nerve cells conduct stimuli, neurons have powerful sodium pumps in their membranes. Also important for light sensing and energy harvesting.

Static structure is known, but how do pumps change to allow the sodium ions, and only sodium ions, to be transported?

KR2 resting state



Questions?

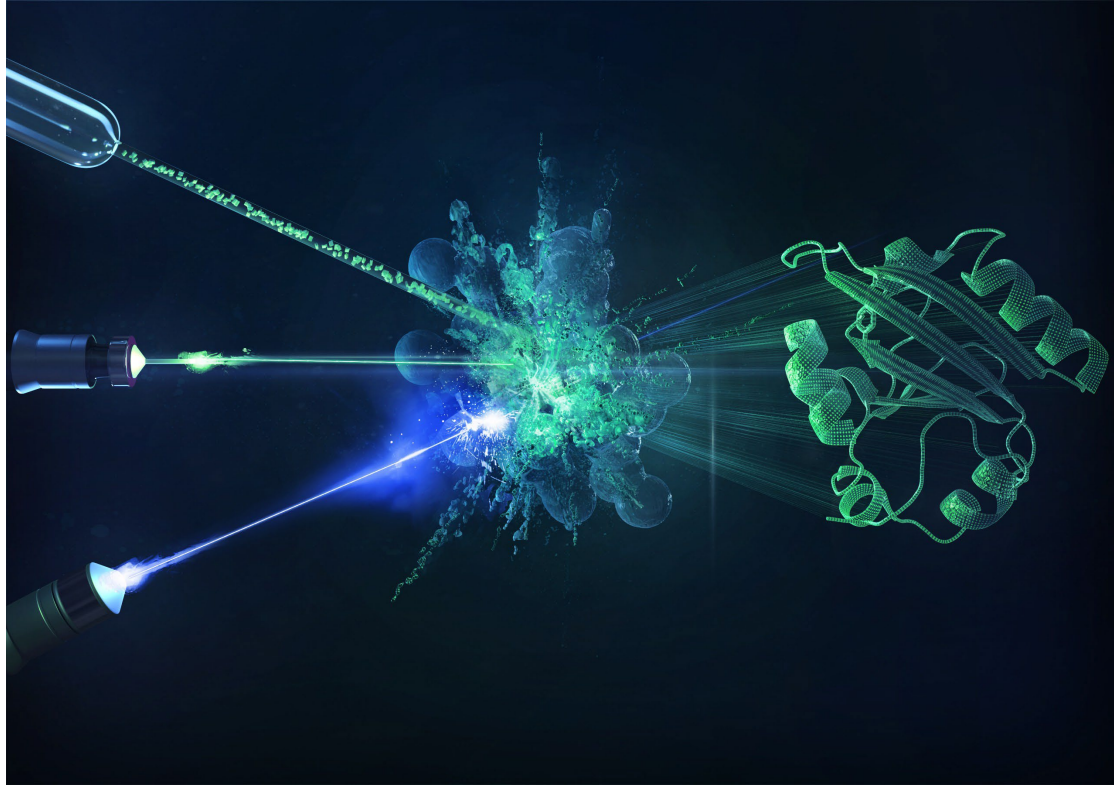


image copyright: European XFEL/Blue Clay Studios