# Science opportunities with coherent x-rays: a focus on cells

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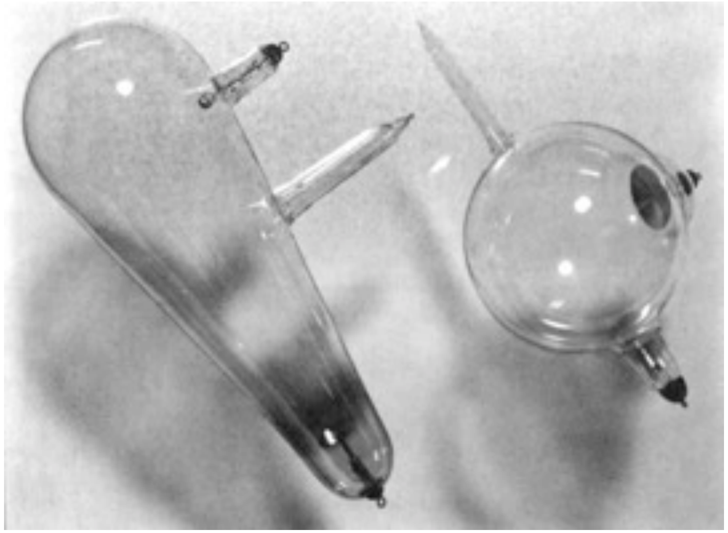
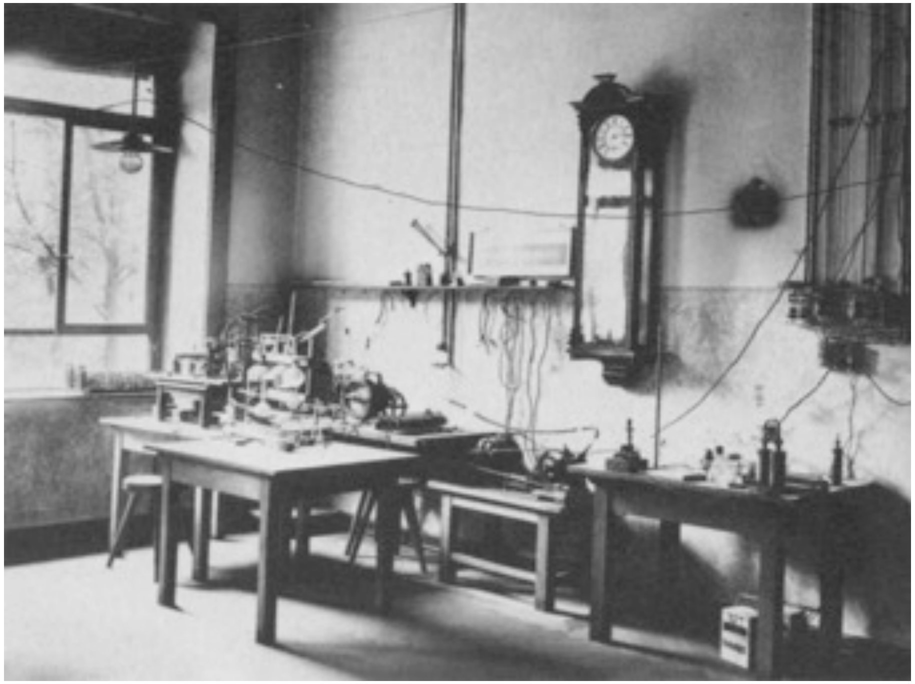
NORTHWESTERN UNIVERSITY

U.S. DEPARTMENT OF ENERGY

# Wilhelm Conrad Röntgen: late Friday afternoon, Nov. 8, 1895





# Things happened slowly before the internet, right?

132 Sitzungsberichte der physikal.-medicin. Gesellschaft. Jahrg. 1895.

früheren Mitglieder der Gesellschaft lediglich deshalb nicht mehr im Personalverzeichnisse geführt wurden, weil sie bei ihrem Weggange aus Würzburg vergessen hatten, den entsprechenden Antrag zu stellen.

Herr von Kölliker stellt deshalb einen Antrag auf diesbezügliche Aenderung der Statuten. — Ueber denselben soll in der ersten Sitzung des nächsten Geschäftsjahres berathen werden.

Am 28. Dezember wurde als Beitrag eingereicht:

**W. C. Röntgen: Ueber eine neue Art von Strahlen.**

(Vorläufige Mittheilung.)

1. Lässt man durch eine *Hittorf*'sche Vacuumröhre, oder einen genügend evacuirten *Lenard*'schen, *Crookes*'schen oder ähnlichen Apparat die Entladungen eines grösseren *Ruhmkorff*'s gehen und bedeckt die Röhre mit einem ziemlich eng anliegenden Mantel aus dünnem, schwarzem Carton, so sieht man in dem vollständig verdunkelten Zimmer einen in die Nähe des Apparates gebrachten, mit Bariumplatincyanür angestrichenen Papierschirm bei jeder Entladung hell aufleuchten, fluoresciren, gleichgültig ob die angestrichene oder die andere Seite des Schirmes dem Entladungsapparat zugewendet ist. Die Fluorescenz ist noch in 2 m Entfernung vom Apparat bemerkbar.

Man überzeugt sich leicht, dass die Ursache der Fluorescenz vom Entladungsapparat und von keiner anderen Stelle der Leitung ausgeht.

2. Das an dieser Erscheinung zunächst Auffallende ist, dass durch die schwarze Cartonhülse, welche keine sichtbaren oder ultravioletten Strahlen des Sonnen- oder des elektrischen Bogenlichtes durchlässt, ein Agens hindurchgeht, das im Stande ist, lebhafte Fluorescenz zu erzeugen, und man wird deshalb wohl zuerst untersuchen, ob auch andere Körper diese Eigenschaft besitzen.

Man findet bald, dass alle Körper für dasselbe durchlässig sind, aber in sehr verschiedenem Grade. Einige Beispiele führe ich an. Papier ist sehr durchlässig:[1] hinter einem eingebun-

[1] Mit „Durchlässigkeit" eines Körpers bezeichne ich das Verhältniss der Helligkeit eines dicht hinter dem Körper gehaltenen Fluorescenzschirmes zu derjenigen Helligkeit des Schirmes, welcher dieser unter denselben Verhältnissen aber ohne Zwischenschaltung des Körpers zeigt.

- Submitted Saturday, Dec. 28, 1895
- Printed Wednesday, Jan. 1, 1896
- Front page news in Vienna, Sunday, Jan. 5, 1896
- *New York Electrical Engineer*: Jan. 8
- *Nature*: Jan. 16

Die Presse.

Nr. 5. Wien, Sonntag den 5. Jänner 1896. 49. Jahrgang.

Eine sensationelle Entdeckung.



Thursday, July 9, 15

**Wilhelm Röntgen**
**Universität Würzburg**
**Dec. 1895**

**Michael Pupin**
**Columbia University/New York**
**Feb. 1896**

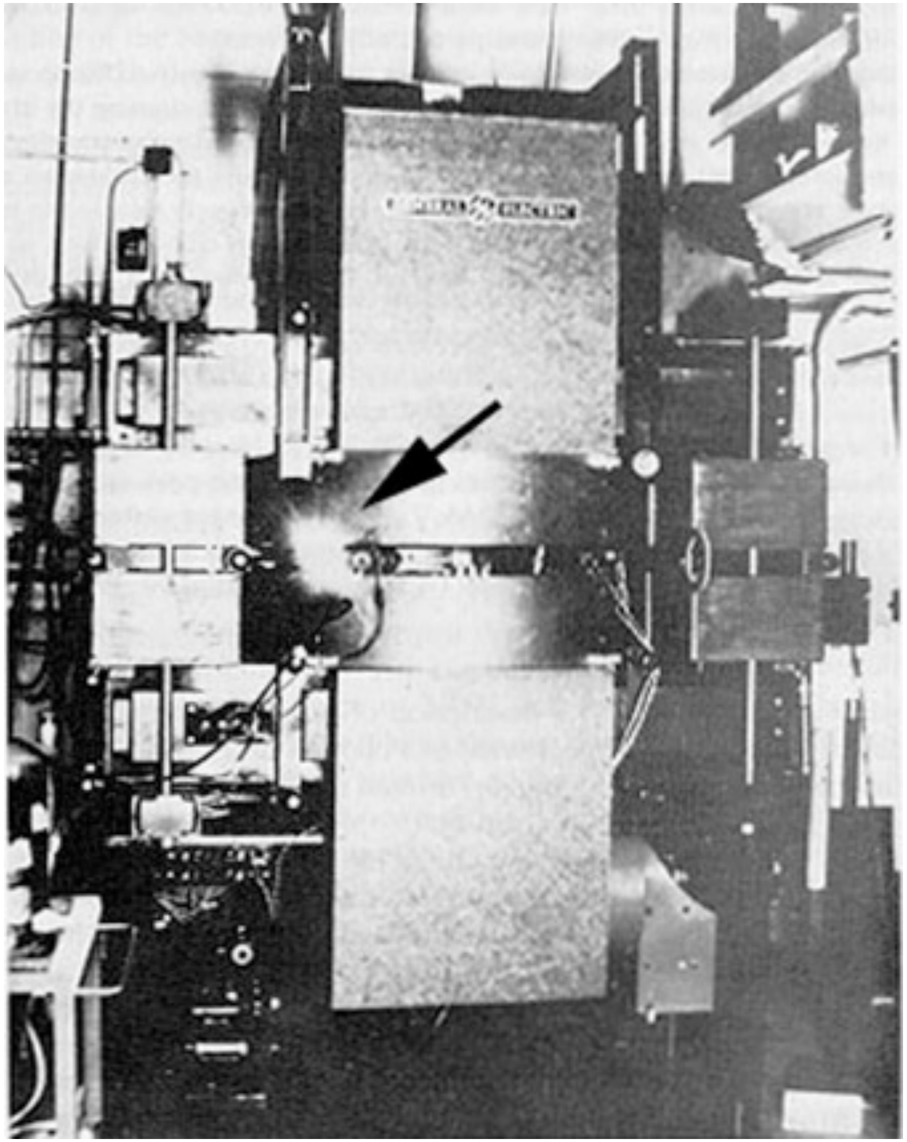
“This is of the hand of a gentleman resident in New York, who, while on a hunting trip in England a few months ago, was so unfortunate as to discharge his gun into his right hand, no less than forty shot lodging in the palm and fingers. The hand has since healed completely; but the shot remain in it, the doctors being unable to remove them, because unable to determine their exact location. The result is that the hand is almost useless, and often painful.” - Cleveland Moffett, McClure’s Magazine, April 1896

# Laboratory x-ray sources

- Limited in brightness (photons per area per angle) due to melting of the target.
- Emit into 2π, and continuum spectrum plus fluorescence lines

# Synchrotron radiation

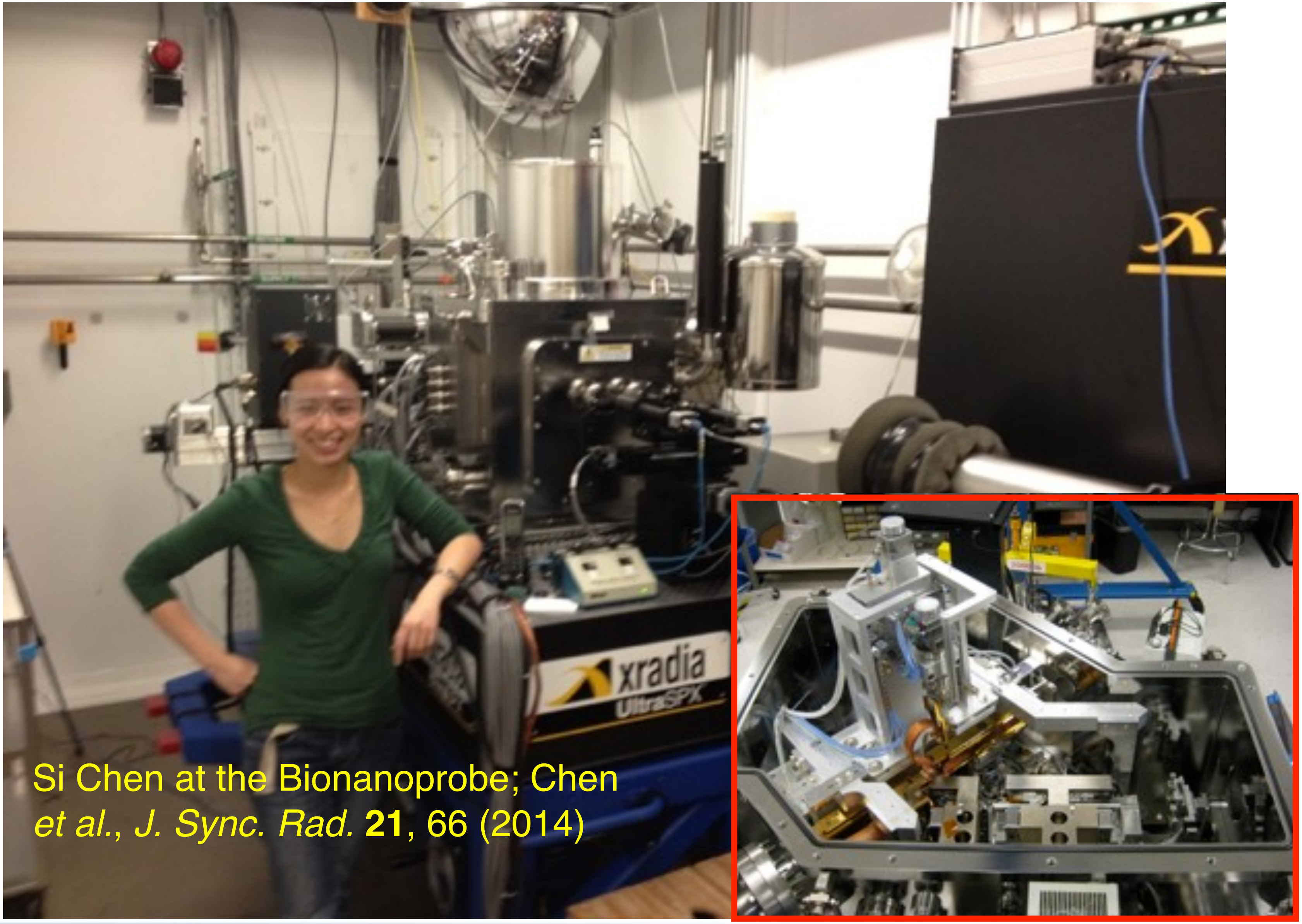
- General Electric, Schenectady, New York; April 24, 1947
- Herb Pollock: "On April 24, Robert Langmuir and I were running the machine and as usual were trying to push the electron gun and its associated pulse transformer to the limit. Some intermittent sparking had occurred and we asked the technician to observe with a mirror around the protective concrete wall. He immediately signaled to turn off the synchrotron as `he saw an arc in the tube.' The vacuum was still excellent, so Langmuir and I came to the end of the wall and observed."



Advanced Photon Source at Argonne Lab: 7 GeV, ~$10^{12}$ photons/sec ($10^8$ coherent) at 10 keV, ~65 simultaneous experiments, built ~1995

Borland talk tomorrow: upgrade project to increase the brightness by a factor of >100!

# The “light bulb” is big; the experiments are small

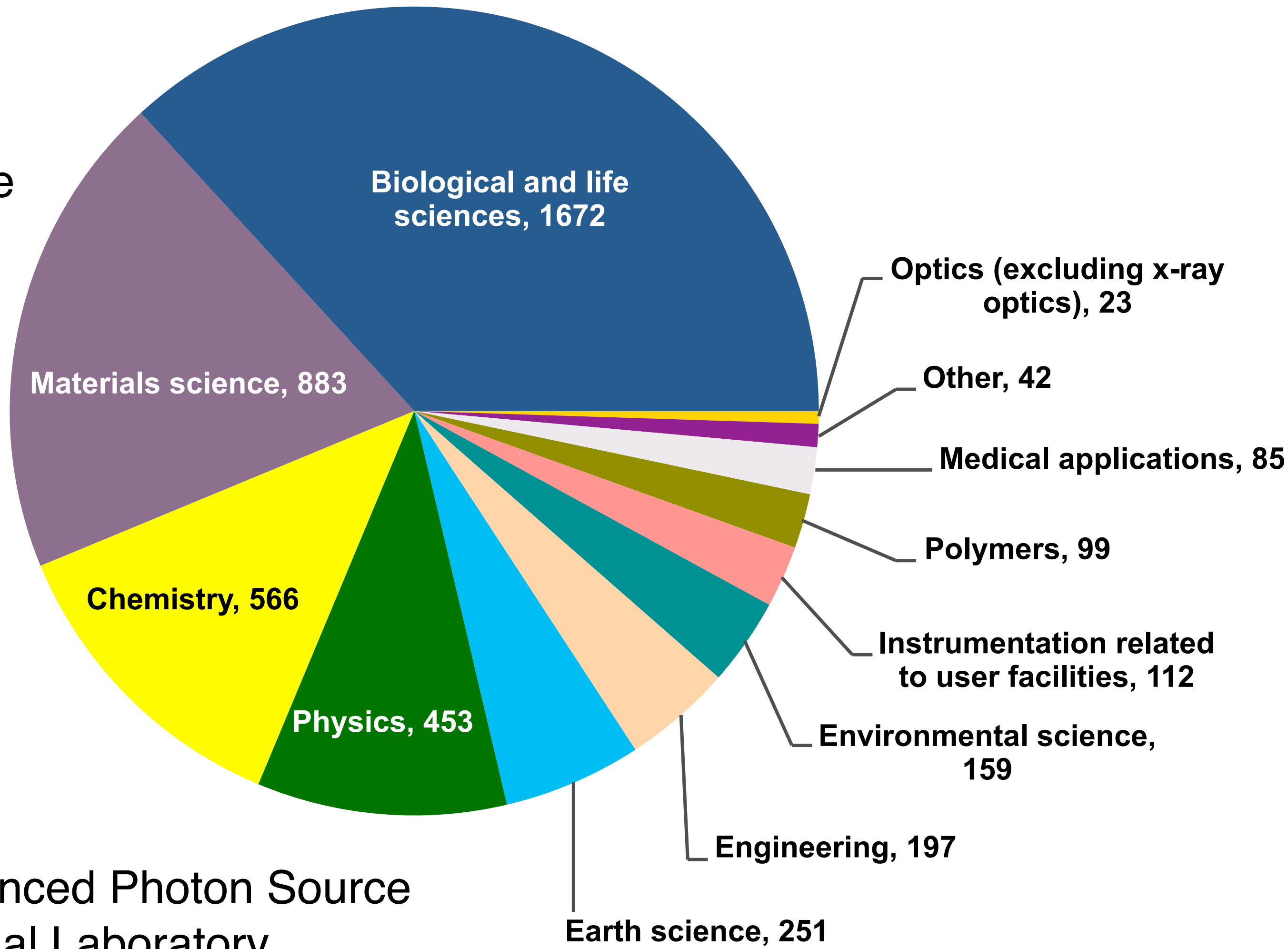



Si Chen at the Bionanoprobe; Chen *et al.*, *J. Sync. Rad.* **21**, 66 (2014)

# Synchrotron light sources: serving a wide and varied set of scientific communities

Per year, over 65 beamlines:
- About 2000 unique experiments
- About 4500 scientists

Many experiments are scheduled for 1-3 visits per year, 3-6 days per visit



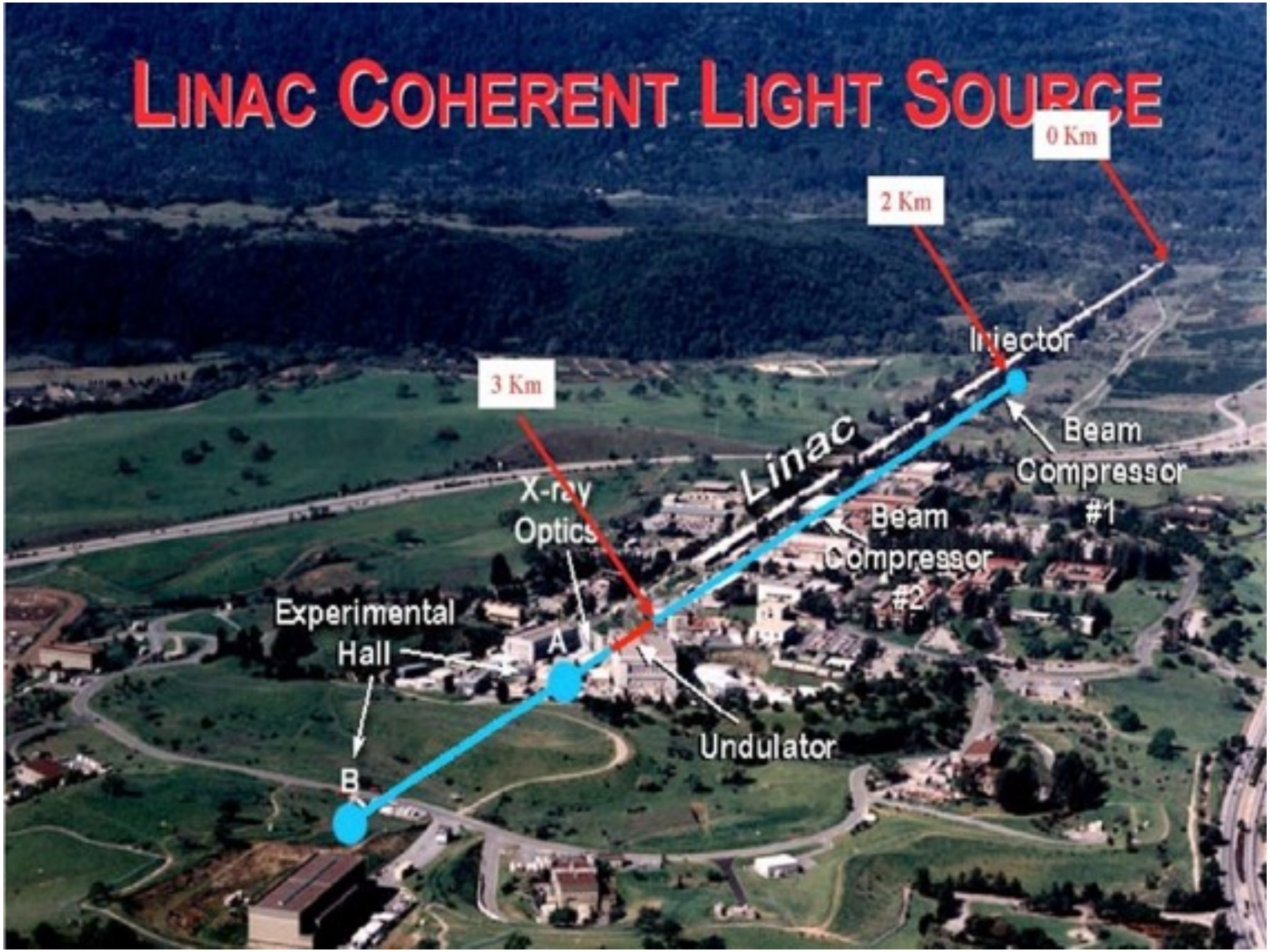

Users of the Advanced Photon Source at Argonne National Laboratory, 10/2012-09/2013

# Synchrotron light sources



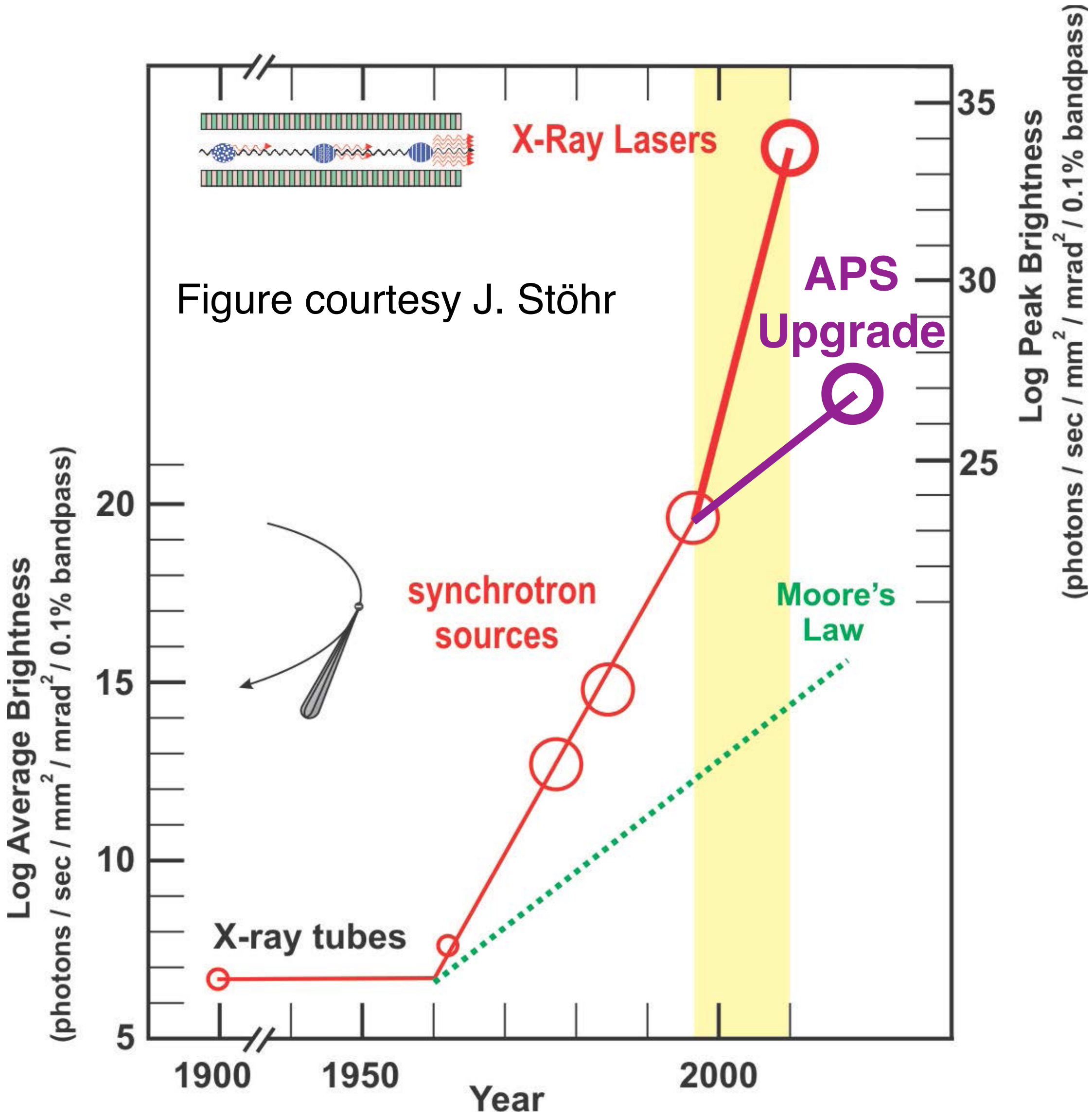

Thursday, July 9, 15

# LCLS at Stanford: first hard x-ray free electron laser



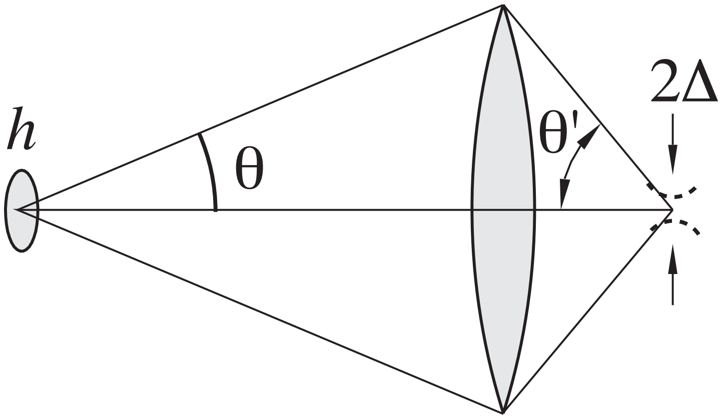
# X-ray brightness: beyond Moore's law in computing

- Synchrotron light sources deliver high time-averaged brightness, for many experiments simultaneously.
- X-ray free electron lasers (XFELS) deliver high instantaneous brightness in <100 fsec (sample-destroying) pulses, for one or a few experiments simultaneously.



# Brightness and coherence

- Brightness measures the photon flux per source area per solid angle within a given bandwidth.
  - Typical units: photons/sec/mm$^2$/mrad$^2$/0.1%
- Nanofocusing from lenses requires coherence across the optic
  - Rayleigh resolution (radius of focal spot) is $\Delta=0.61\lambda/\theta'$
  - So focus spot diameter $2\Delta$ times full angle $2\theta'$ accepted is $2.44\lambda$

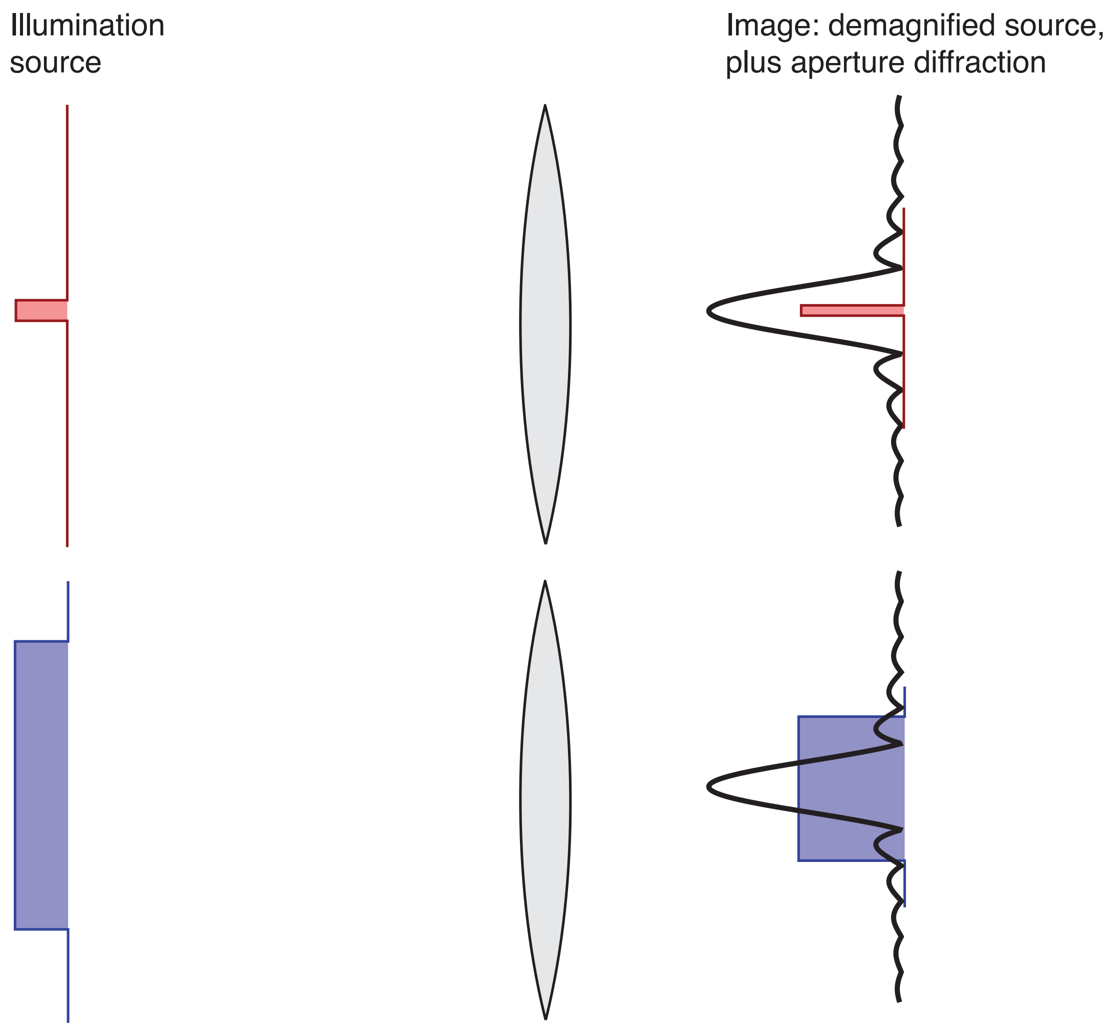



$$\left[2 \cdot 0.61 \frac{\lambda}{\theta'}\right] \cdot [2\theta'] = 2.44\lambda$$

- This must be done in $\boldsymbol{x}$ and in $\boldsymbol{y}$, so coherent flux involves phase space of $\lambda^2$.
  - See Green, BNL-50522 (1976); Kondratenko and Skrinsky, *Optics and Spectroscopy* **42**, 189 (1977).

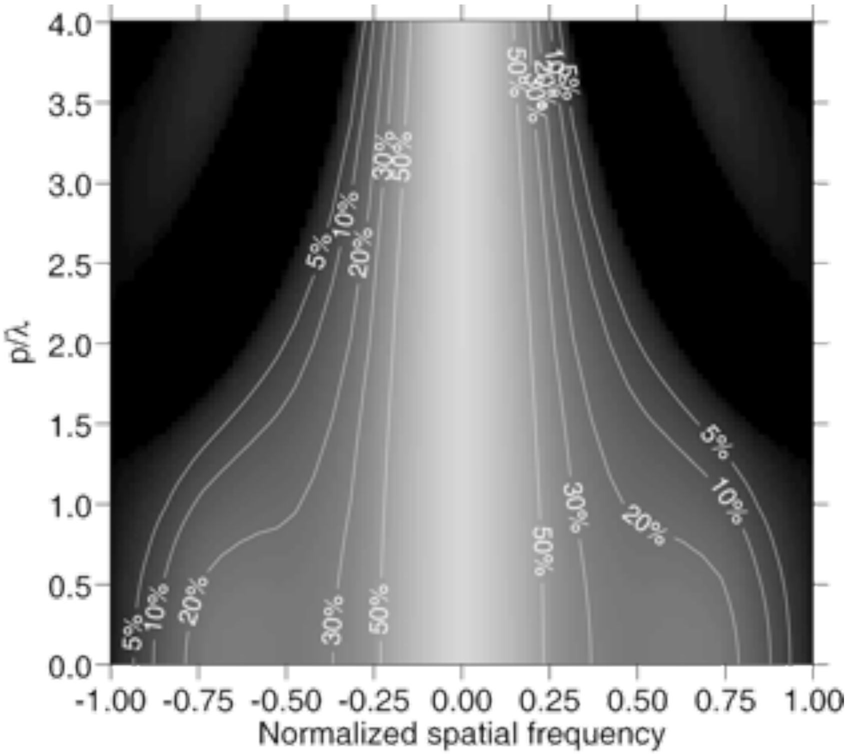
# Nanofocusing requires coherent illumination

- Full-width, full-angle phase space of a diffraction limited lens with numerical aperture θ: (2θ)·(2·0.61λ/θ)=2.44λ
- Thus need to limit source phase space to ~λ both in $x$ and $y$

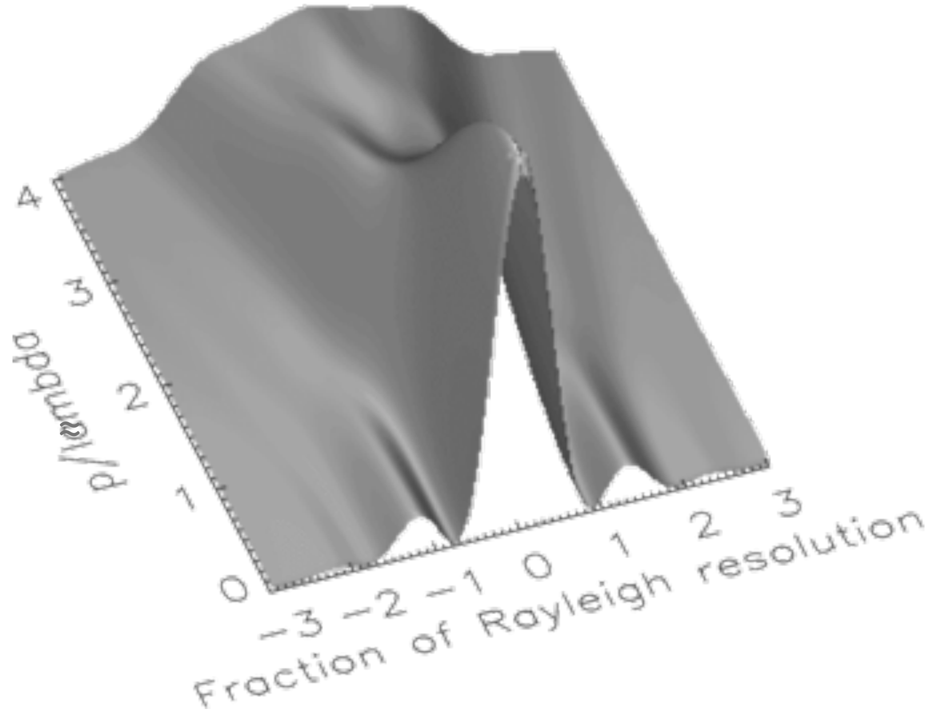


# Phase space area and probe focus

How close must p=(source diameter)•(optic's full subtended angle) be to λ? p≈1•λ works pretty well!




Effect on modulation transfer function MTF (50% central stop)

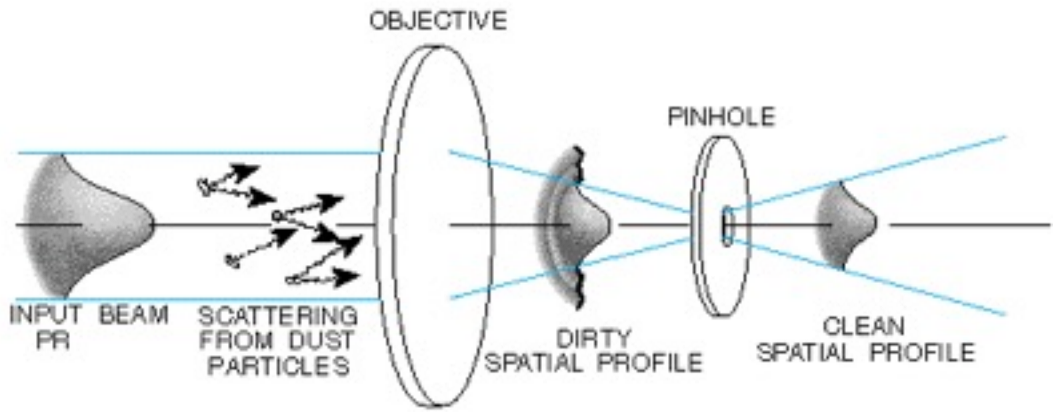



Effect on point spread function PSF (50% central stop)

Jacobsen *et al.*, *Ultramicroscopy* **47**, 55 (1992); Winn *et al.*, *J. Synch. Rad.* **7**, 395 (2000).

# Controlling spatial coherence

- Spatial filter: pinhole at the focus of a lens.  Passes only the spatially coherent fraction of an incident beam.
- X-ray beamlines: image the source to a secondary position with an aperture, for a flux-versus-coherence tradeoff.




Diagram, photo from Newport catalog

# Holography predates the laser

NATURE Vol. 161 777 May 15, 1948

## A NEW MICROSCOPIC PRINCIPLE

By Dr. D. GABOR
Research Laboratory, British Thomson-Houston Co., Ltd., Rugby

- Single spectral line from high pressure mercury lamp light source, with 3 µm pinhole for spatial coherence.

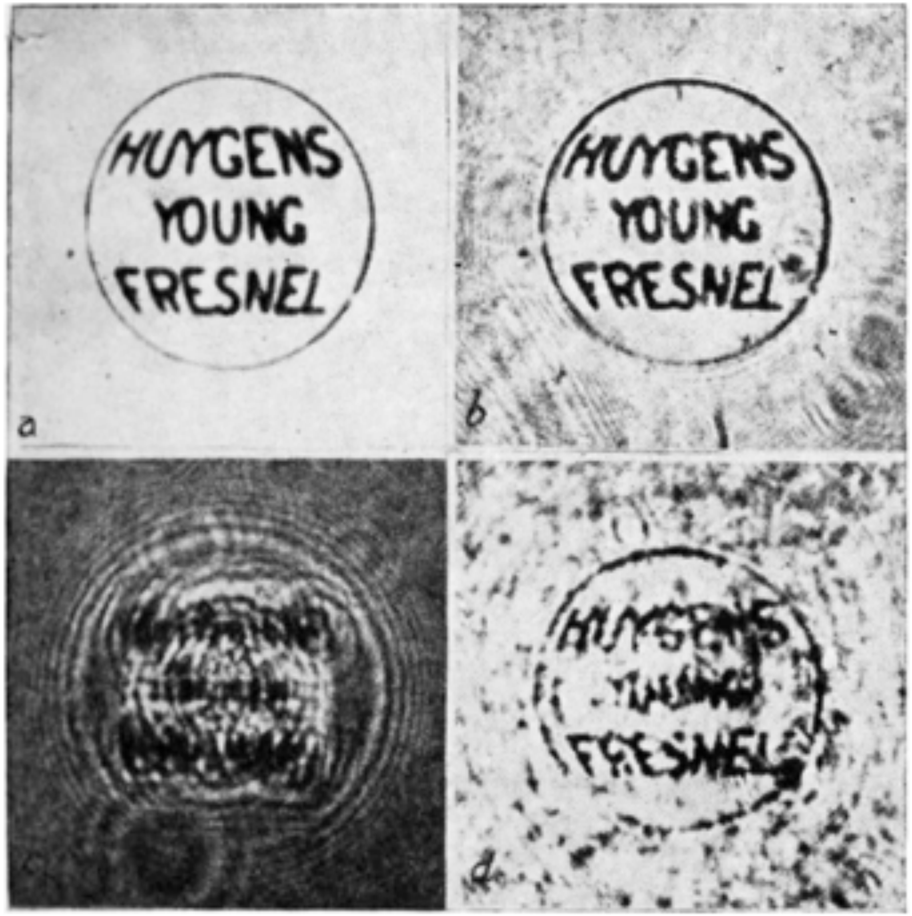
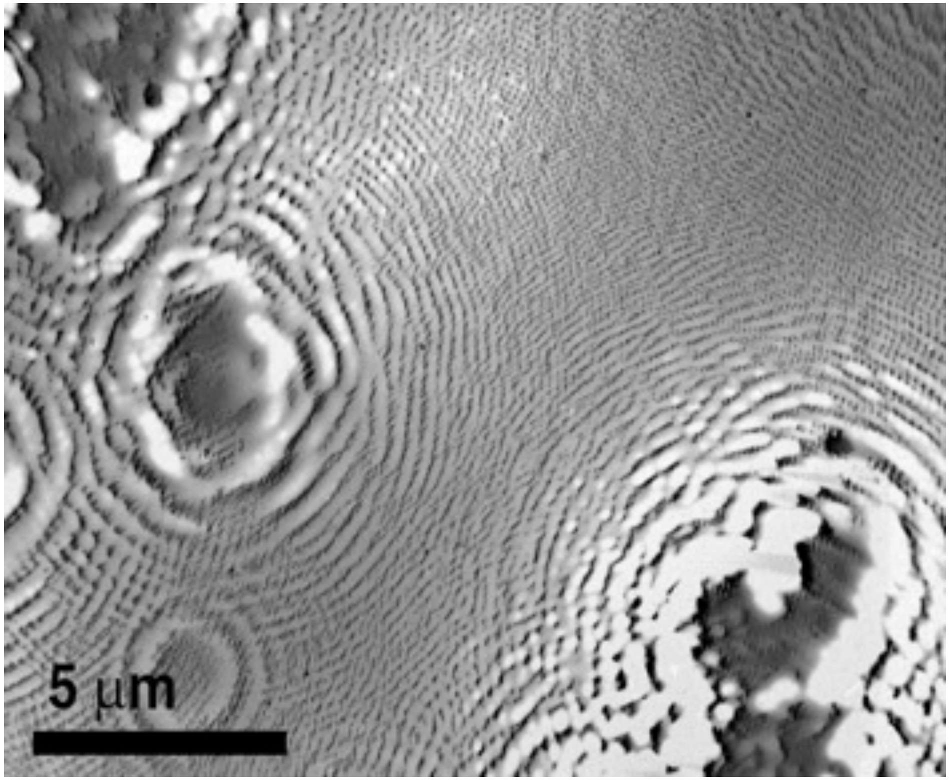



Fig. 2. (*a*) Original micrograph, 1·4 mm. diameter. (*b*) Micrograph, directly photographed through the same optical system which is used for the reconstruction (*d*). Ap. 0·04. (*c*) Interference diagram, obtained by projecting the micrograph on a photographic plate with a beam diverging from a point focus. The letters have become illegible by diffraction. (*d*) Reconstruction of the original by optical synthesis from the diagram at the left. To be compared with (*b*). The letters have again become legible

# X-ray holography predates X-ray Free Electron Lasers, and Diffraction Limited Storage rings

First proposal: Baez, *Nature* **169**, 963 (1952)

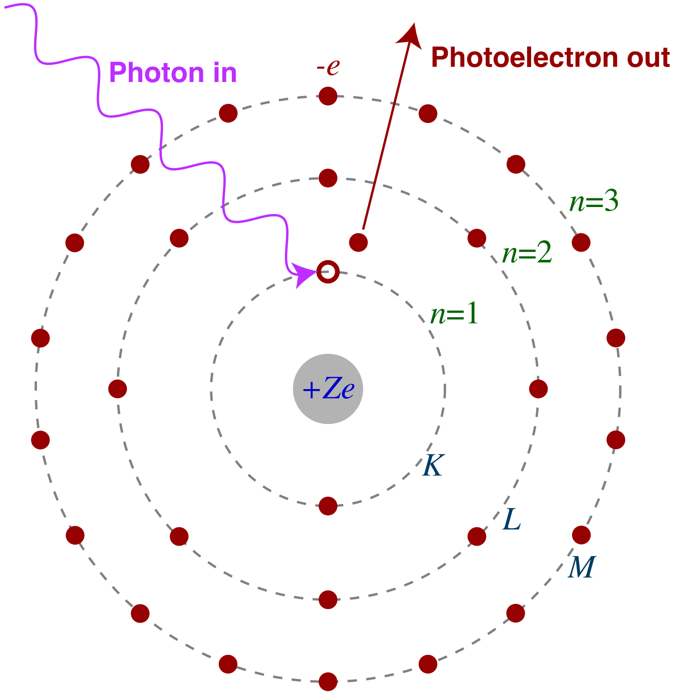
First demonstration: Aoki *et al*, *Japanese J. Appl. Phys.* **11**, 1857 (1972)




This data: see e.g., Howells *et al.*, *Science* **238**, 514 (1987); Jacobsen *et al.*, *J. Opt. Soc. Am.* **A 7**, 1847 (1990); Lindaas *et al.*, *J. Opt. Soc. Am.* **A 13**, 1788 (1996).

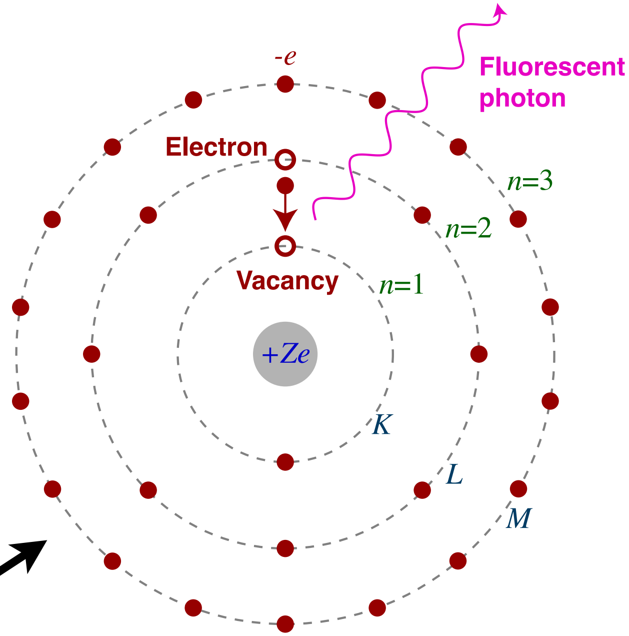
Anilao, Philippines, 17-Oct-2010

# X-ray fluorescence

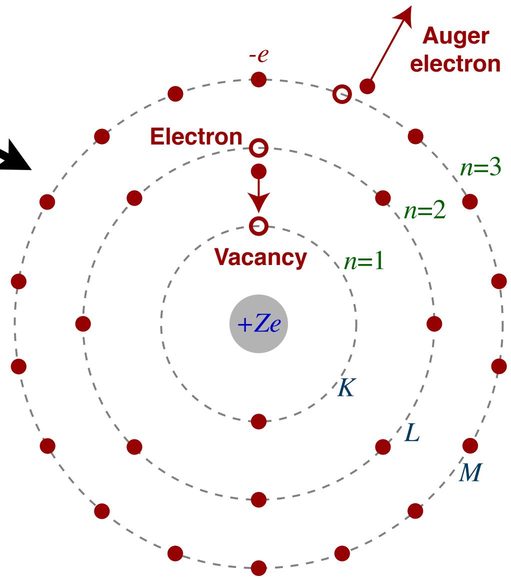



Absorb a photon;
create an inner-shell vacancy

Either/or




Fluorescence




Auger


Silverman Hall
Northwestern University
H
C
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Cu
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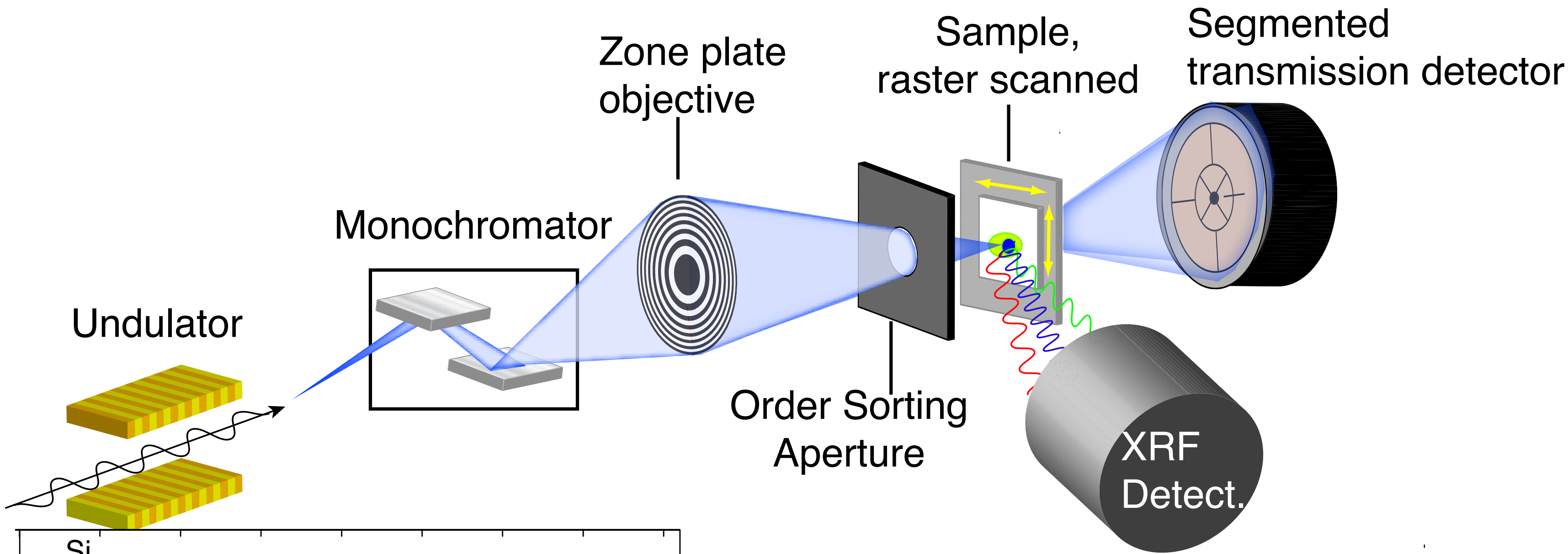
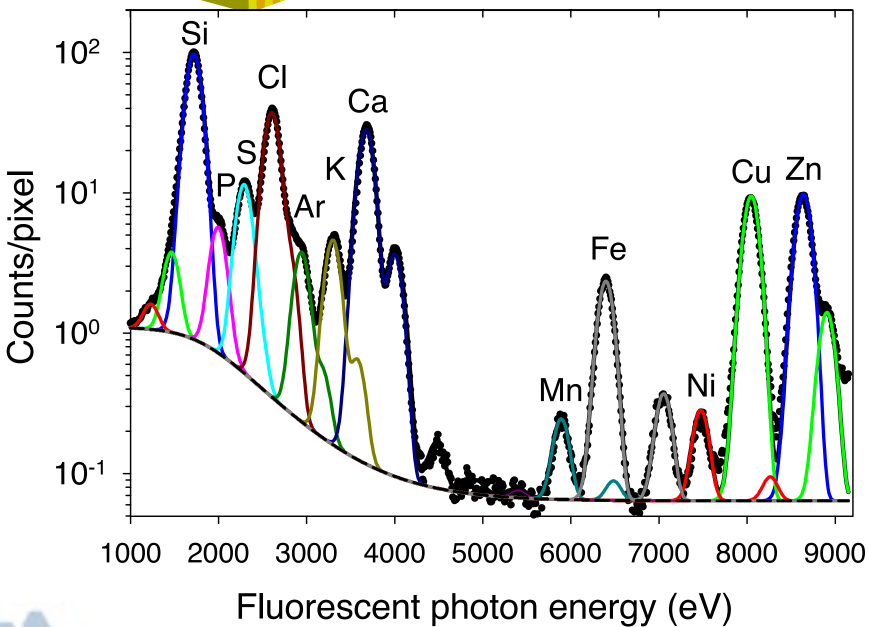
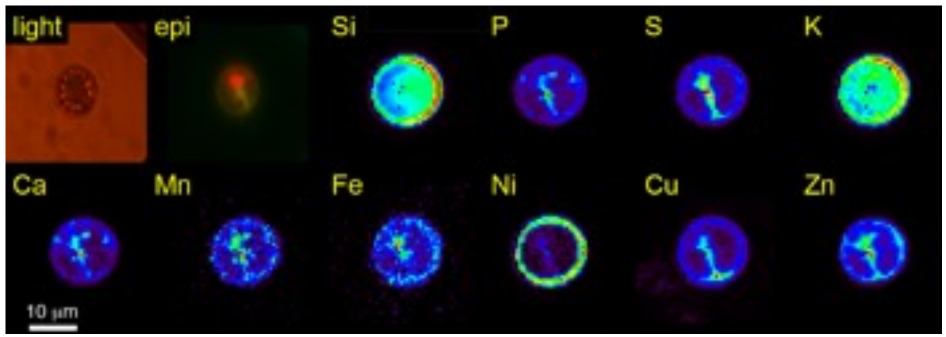
Tc
Ag
Pt
Gd

# Scanned nanofocused beam spots: fluorescence



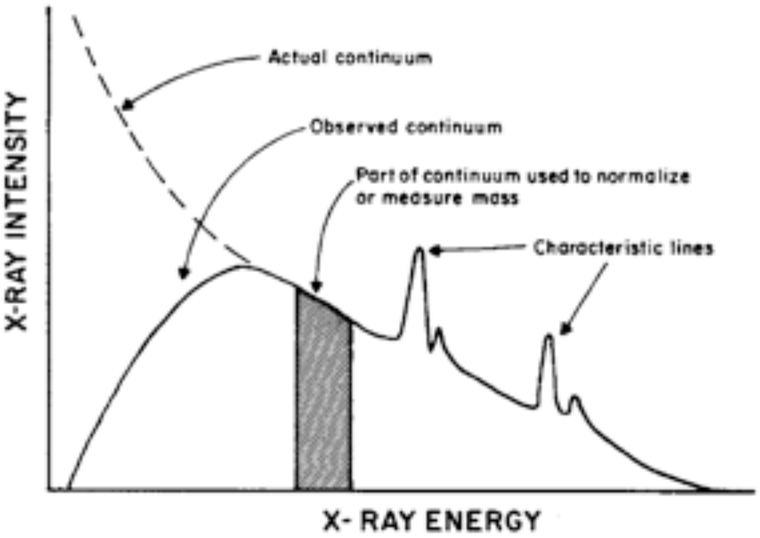



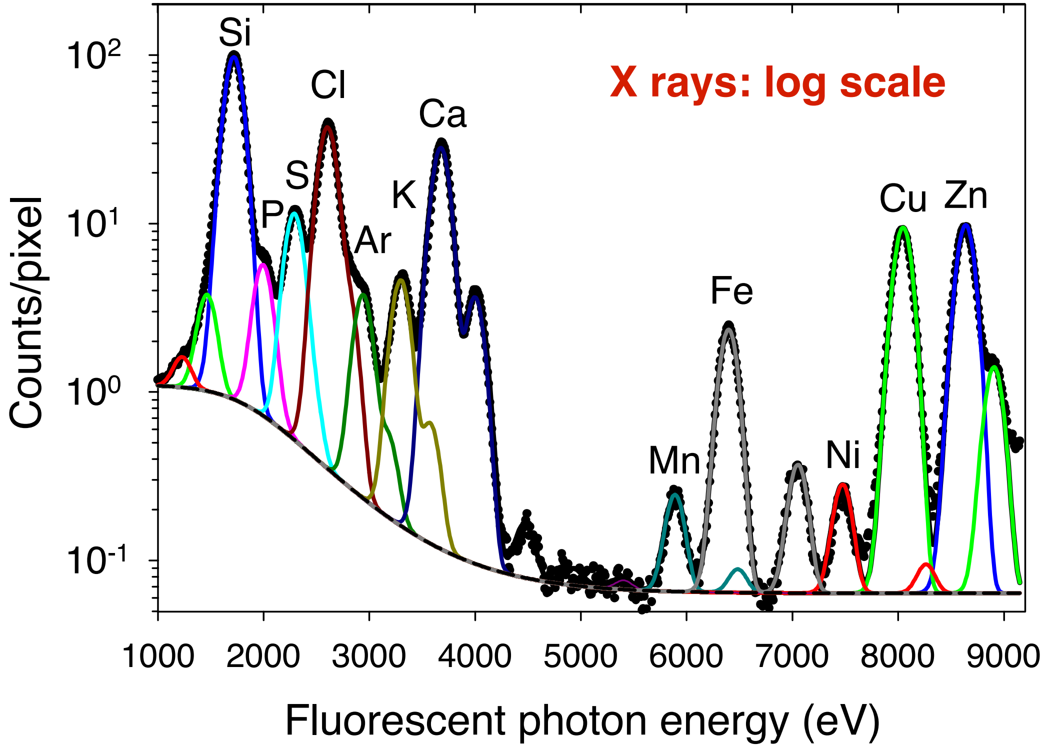

B. Twining, S. Baines, N. Fisher, J. Maser, S. Vogt, C. Jacobsen, A. Tovar-Sanchez, and S.Sañudo-Wilhelmy, *Anal.. Chem.* **75**, 3806 (2003)

# Exciting x-ray fluorescence

X rays and protons produce a dramatically lower continuum background, increasing sensitivity (but proton microprobes induce much more damage)

Electrons: linear scale

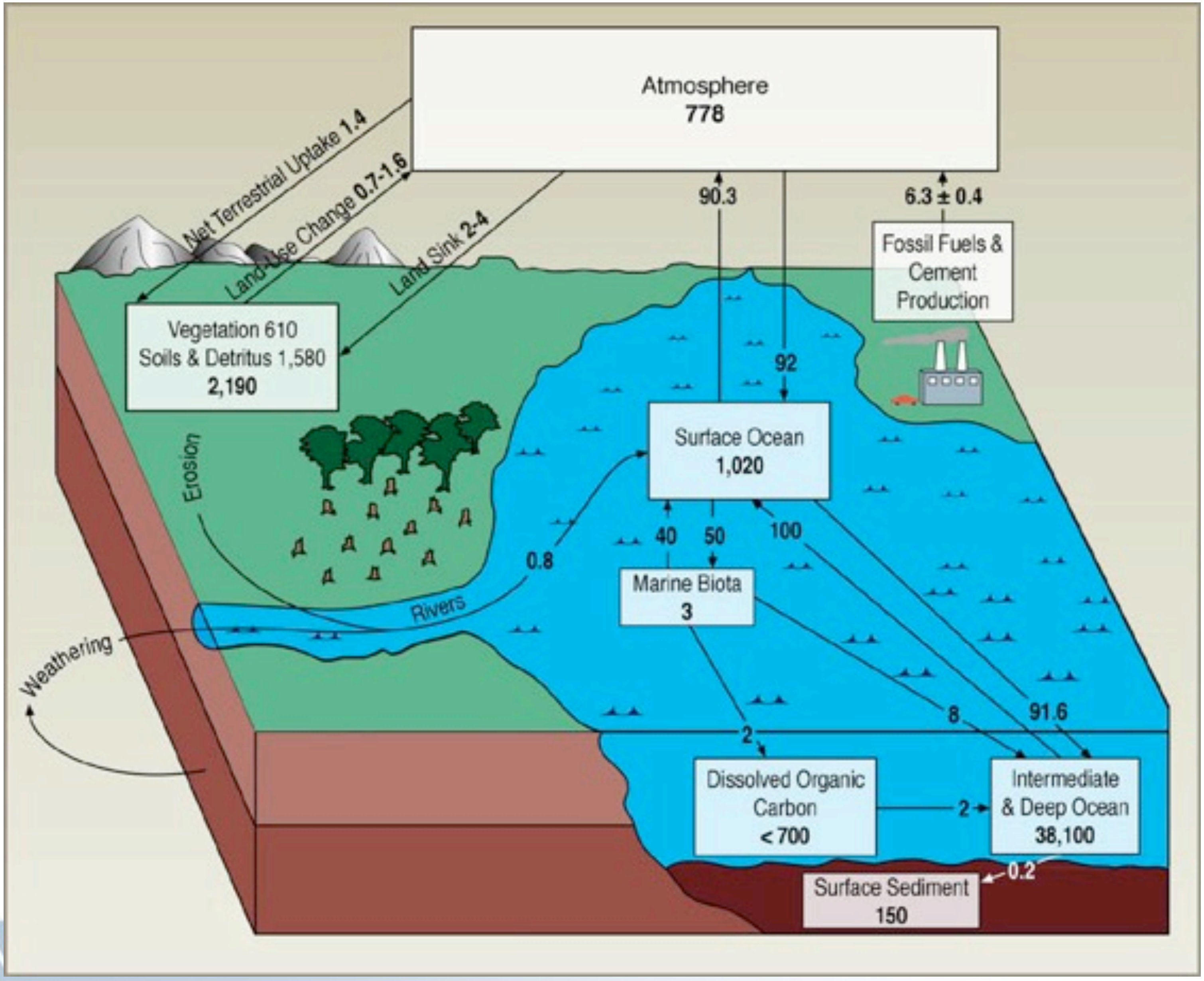



LeFurgey and Ingram, *Environmental Health Perspectives* **84**, 57 (1990)

Twining *et al.*, *Anal. Chem.* **75**, 3806 (2003). Analysis approach: Vogt, Maser, and Jacobsen, *J. Phys. IV* **104**, 617 (2003).

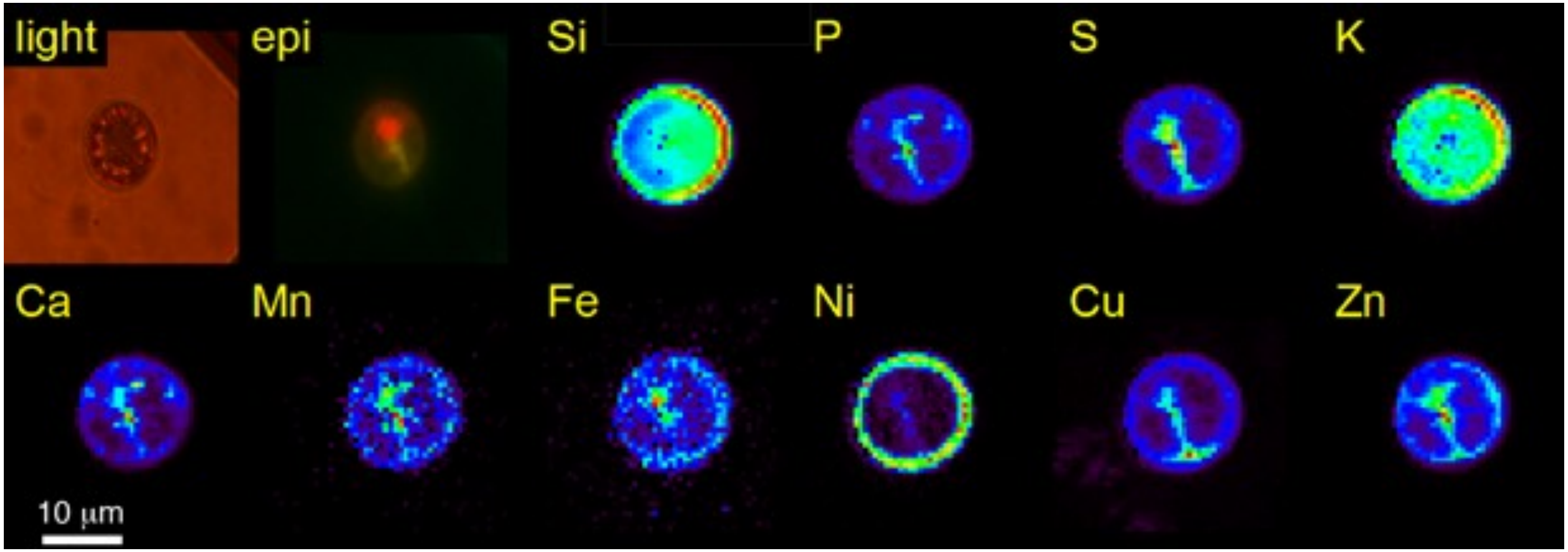
# Global carbon cycle




petagrams, petagrams/year (climatescience.gov)

# Iron and carbon in the ocean

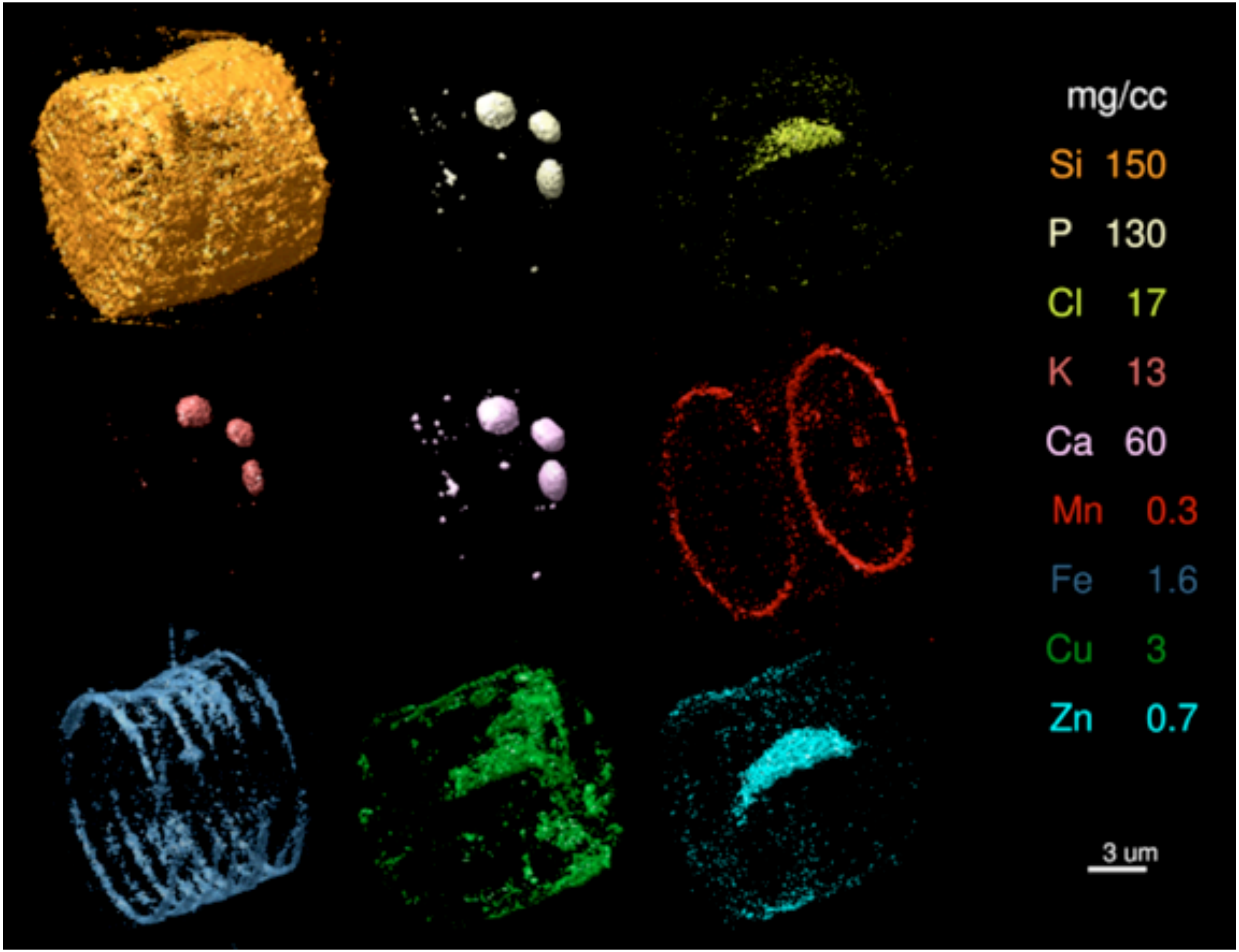
- Seed Southern Pacific with bioavailable iron to increase $CO_2$ uptake?
- Requires understanding of iron and carbon uptake in phytoplankton; combine fluorescence with phase contrast.


B. Twining, S. Baines, N. Fisher, J. Maser, S. Vogt, C. Jacobsen, A. Tovar-Sanchez, and S.Sañudo-Wilhelmy, *Anal.. Chem.* **75**, 3806 (2003)

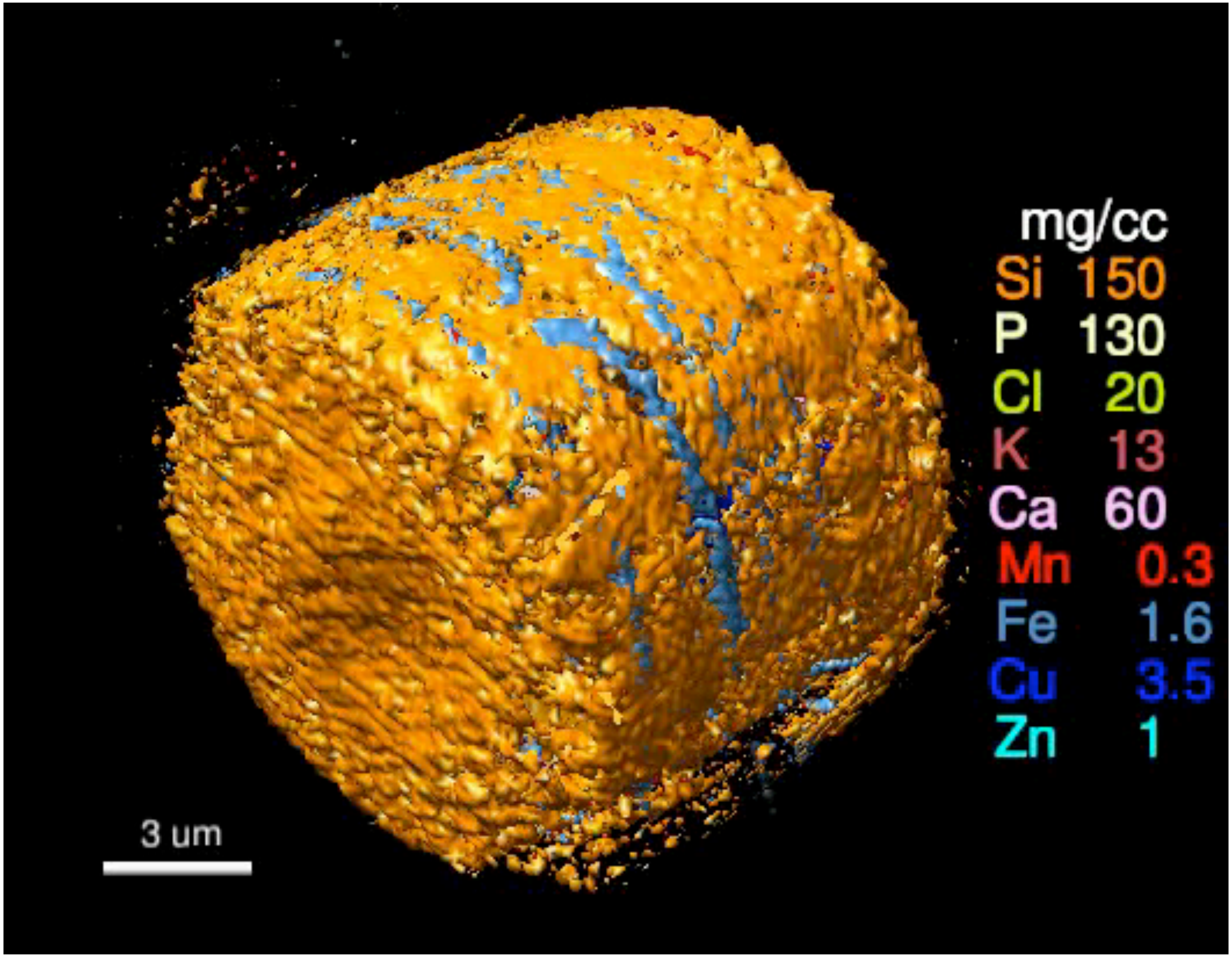
# Cruising the Southern Pacific

# Quantitative 3D fluorescence of a diatom



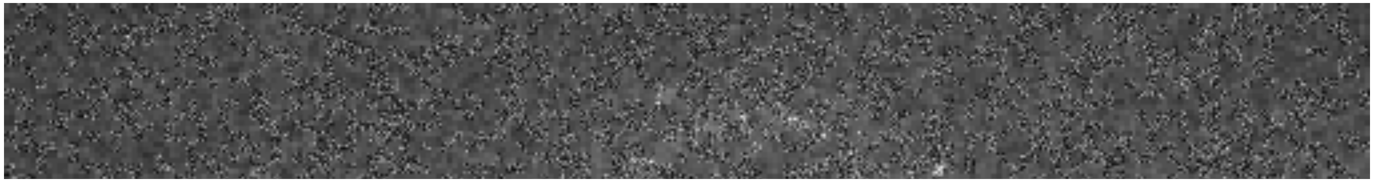

M. de Jonge, C. Holzner, S. Baines, B. Twining, K. Ignatyev, J. Diaz, D. Howard, A. Miceli, I. McNulty, C. Jacobsen, S. Vogt, *Proc. Nat. Acad. Sci.* **107**, 15676 (2010)

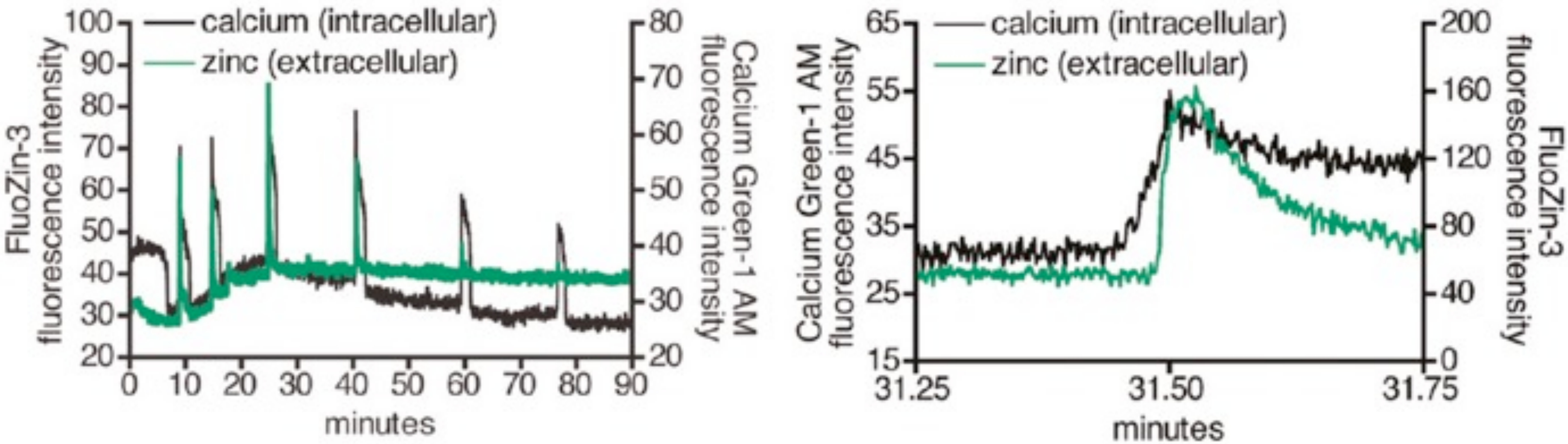
# Fluorescence tomography

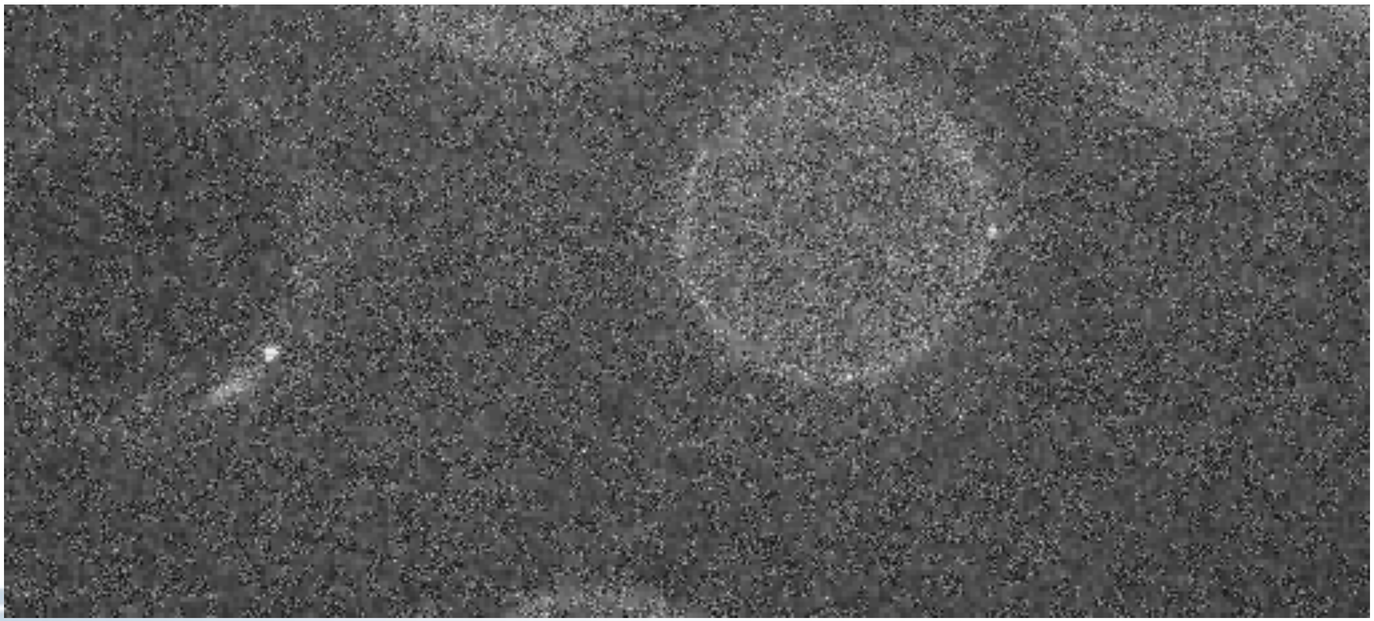



de Jonge *et al.*, *Proc. Nat. Acad. Sci.* **107**, 15676 (2010).
36 hours of data acquisition

# Zinc sparks



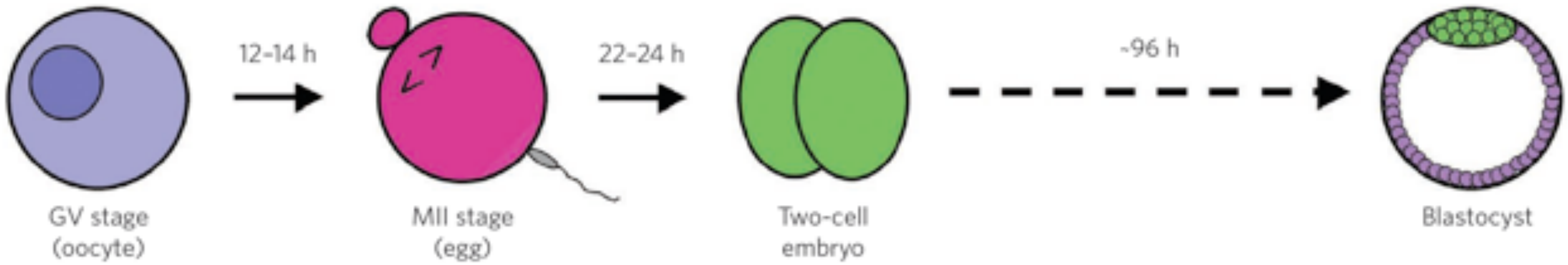


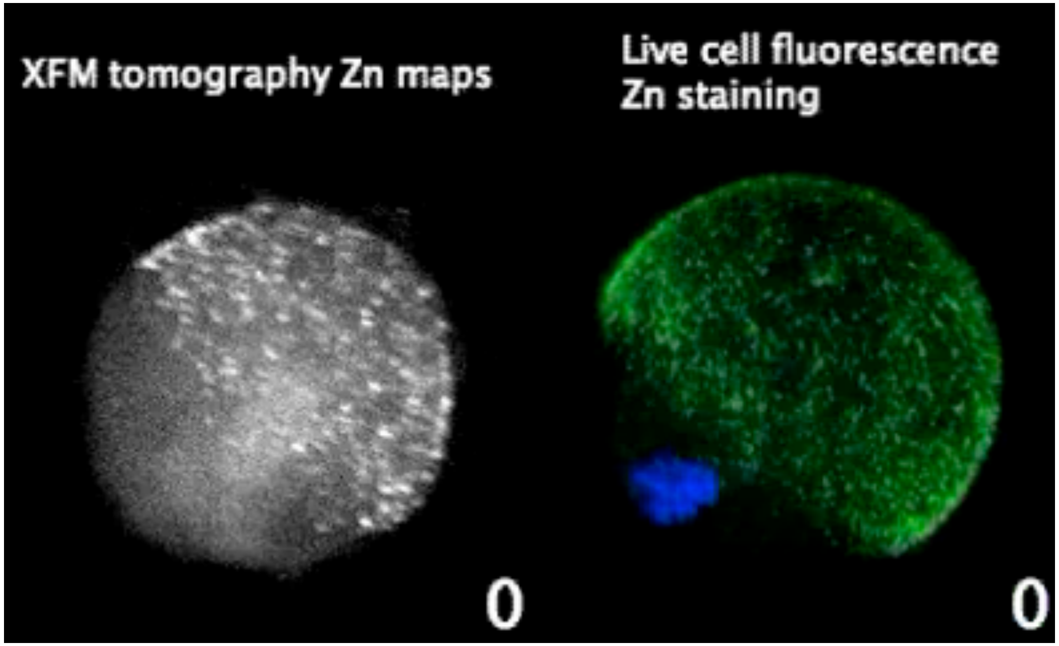
(crab-eating macaque).

- Real time: ~20 minutes.
- Kim *et al.*, *ACS Chem. Bio.* **6**, 716 (2011).

# Zinc sparks




- Zinc is collected ($10^{10}$ atoms!) during metaphase II arrest, before fertilization.
- Chelation (tying zinc up) halts division.
- Oocyte supplies zinc bolus as maternal legacy to the embryo?
- X-rays show *all* zinc; visible fluorescence depends on binding affinities.
- Kim *et al.*, *Nature Chem. Bio.* **6**, 674 (2010).
- Que *et al.*, *Nature Chem.*




Oocytes: ~50 µm



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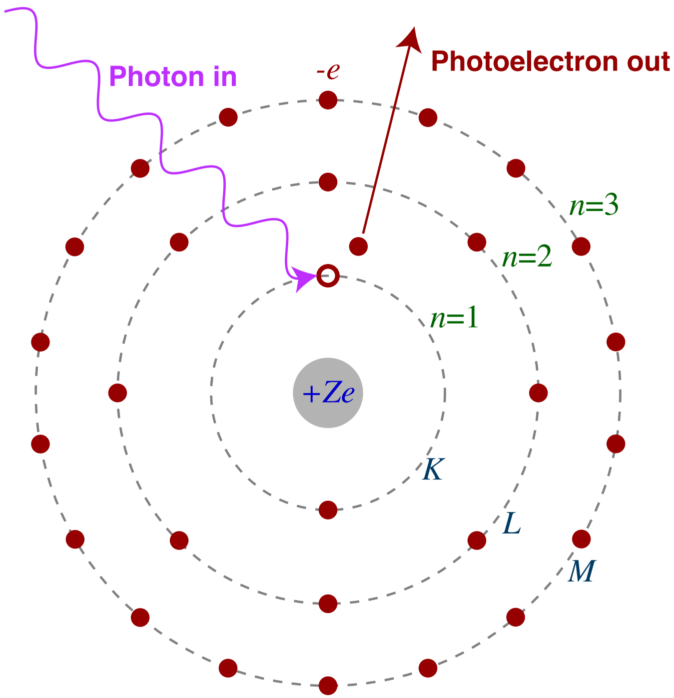
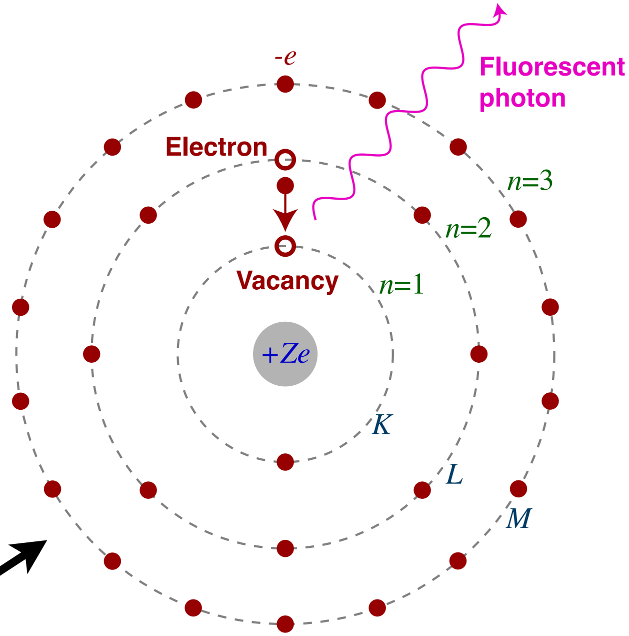
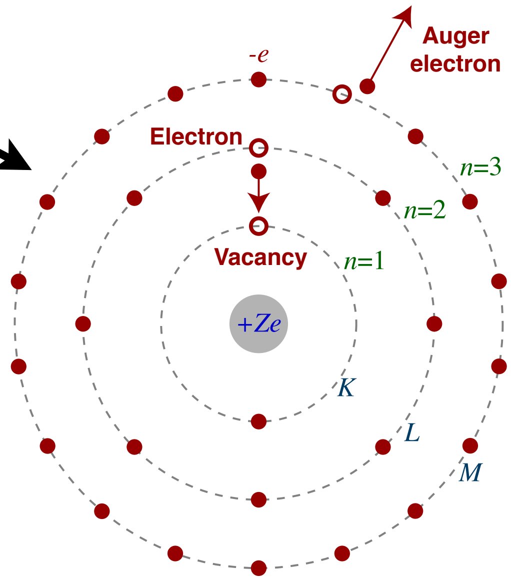
# X-ray fluorescence




Either/or




Fluorescence

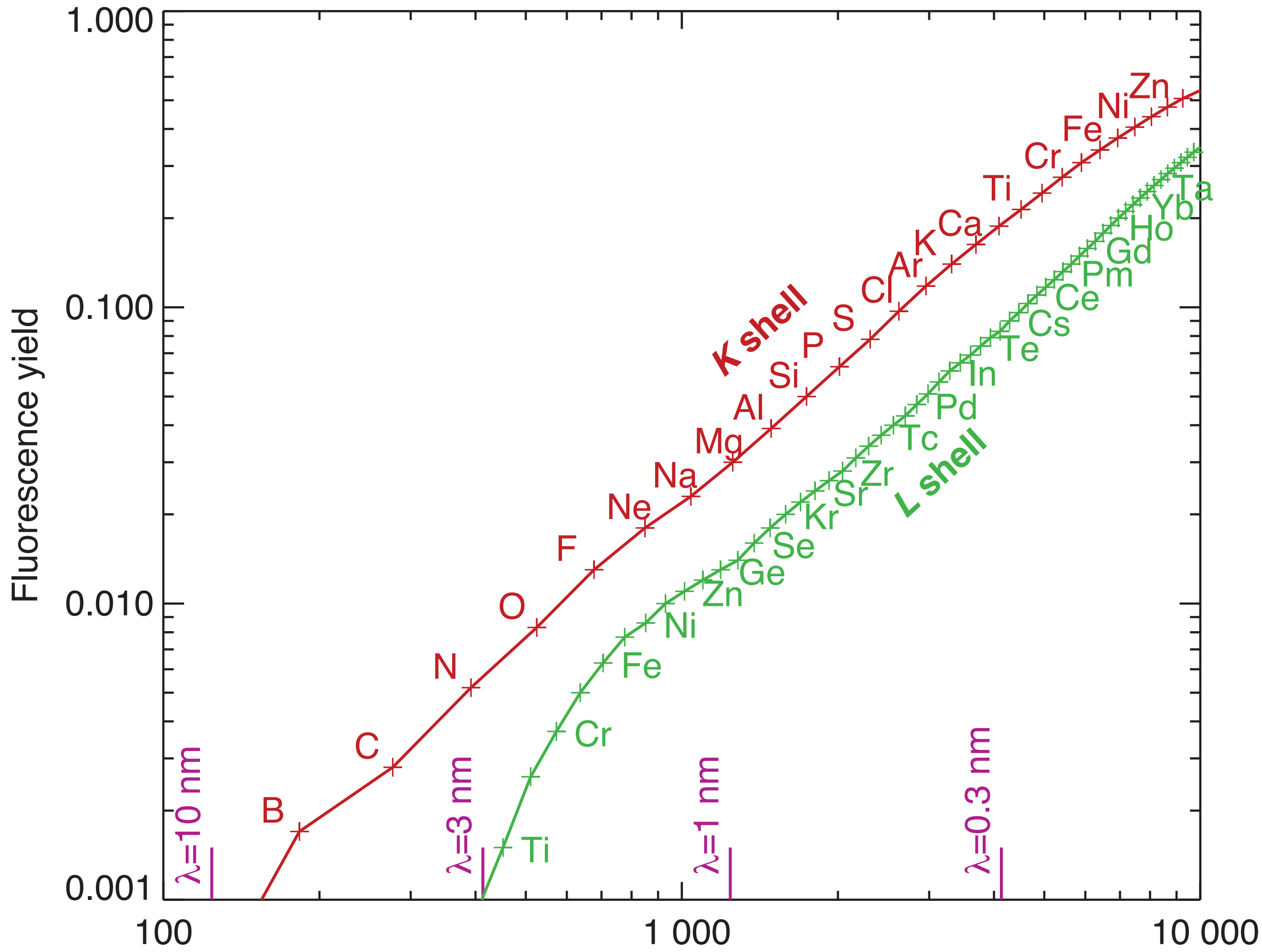



Auger

Absorb a photon;
create an inner-shell
vacancy

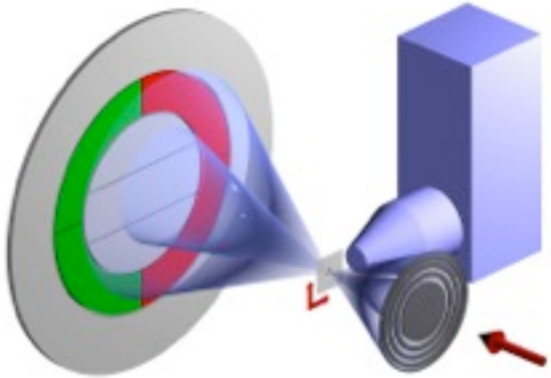
# Fluorescence versus Auger

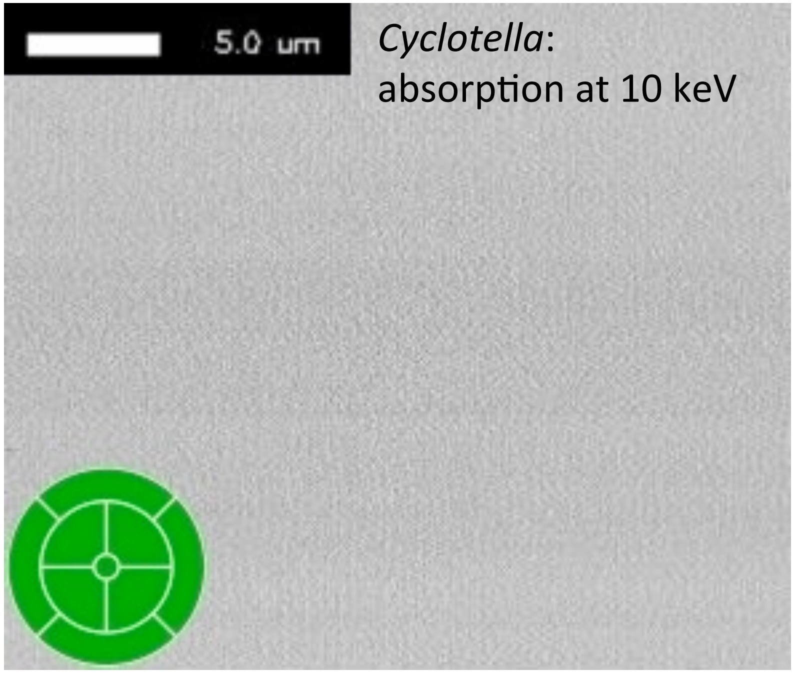
Fluorescence yield=fraction of time you get a fluorescent photon rather than an Auger electron

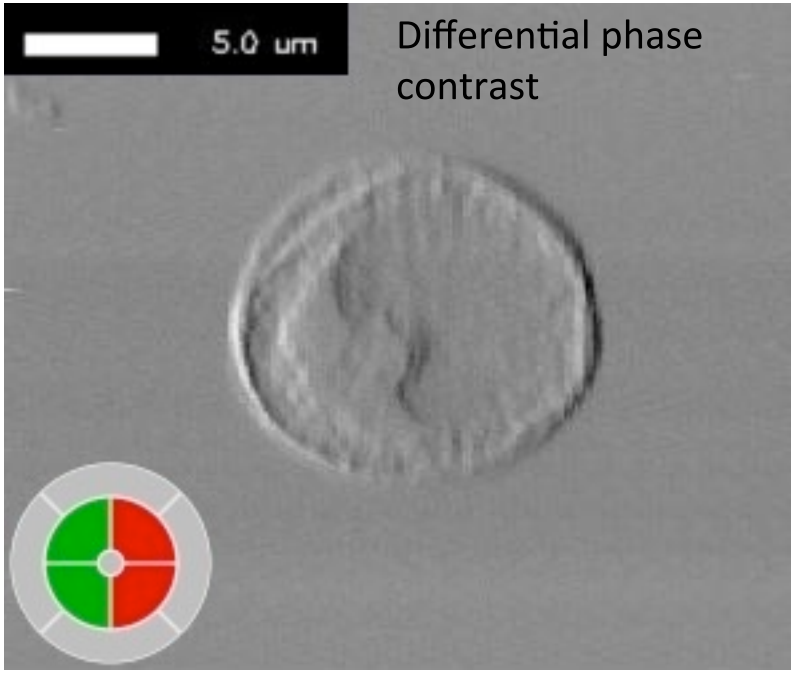


# What's missing? Phase contrast for low-Z

- Segmented x-ray detector.
- Acquire simultaneously with fluorescence
- Fourier filtering, Fourier integration for absolute phase contrast.
- Sensitivity: ~π/180.






Hornberger *et al.*, *Ultramic.* **107**, 644 (2007); Feser *et al.*, *Nucl. Inst. Meth. A* **565**, 841 (2006); de Jonge *et al.*, *Phys. Rev. Lett.* **100**, 163902 (2008)

# Scanned coherent beam spots: ptychography

## High-Resolution Scanning X-ray Diffraction Microscopy

Pierre Thibault,[1*] Martin Dierolf,[1] Andreas Menzel,[1] Oliver Bunk,[1] Christian David,[1] Franz Pfeiffer[1,2]

Coherent diffractive imaging (CDI) and scanning transmission x-ray microscopy (STXM) are two popular microscopy techniques that have evolved quite independently. CDI promises to reach resolutions below 10 nanometers, but the reconstruction procedures put stringent requirements on data quality and sample preparation. In contrast, STXM features straightforward data analysis, but its resolution is limited by the spot size on the specimen. We demonstrate a ptychographic imaging method that bridges the gap between CDI and STXM by measuring complete diffraction patterns at each point of a STXM scan. The high penetration power of x-rays in combination with the high spatial resolution will allow investigation of a wide range of complex mesoscopic life and material science specimens, such as embedded semiconductor devices or cellular networks.

SCIENCE VOL 321 18 JULY 2008 379

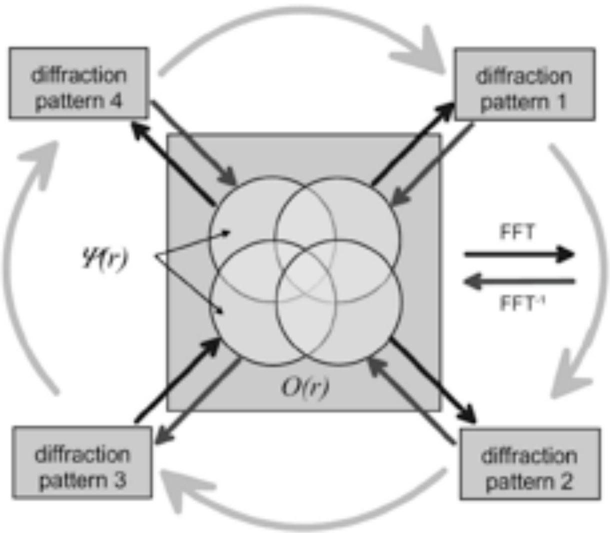
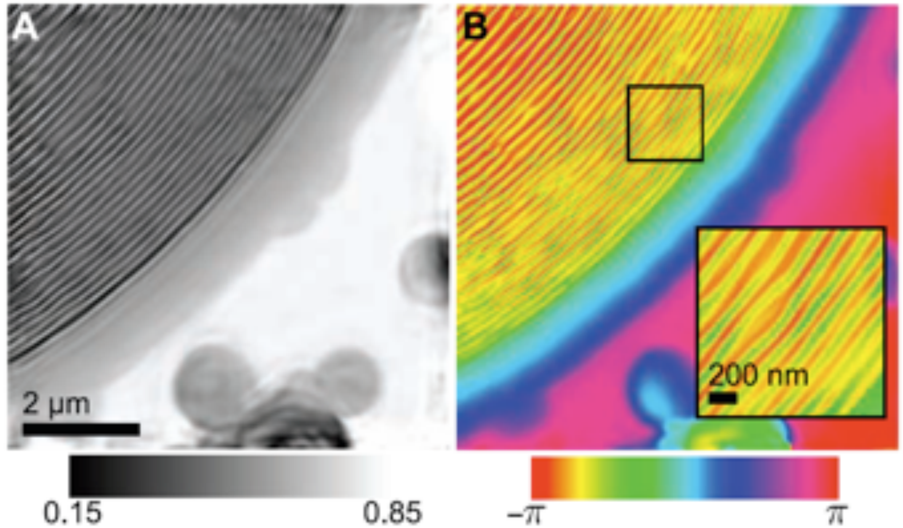
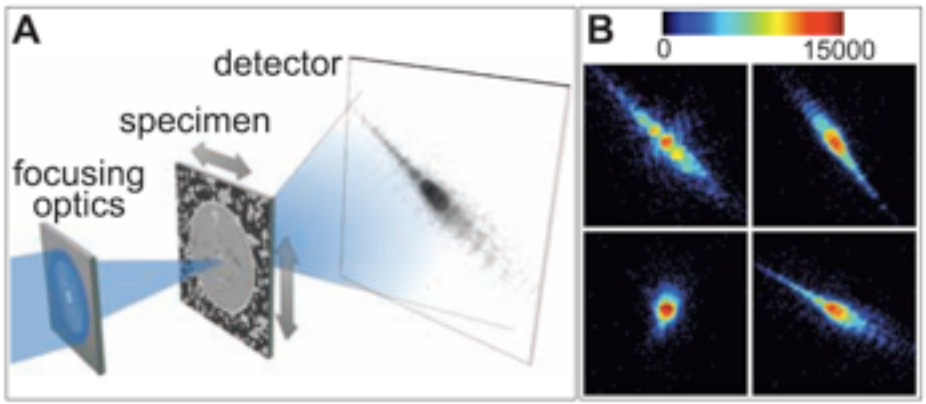



FIG. 2. Diagram of the phase-retrieval algorithm. The outer circular arrows indicate the position stepping within one iteration. The arrows within indicate (inverse) Fourier transforms and the desired input-output information.




Hegerl, ; Rodenburg *et al.*, *Phys. Rev. Lett.* **98**, 034801 (2007)



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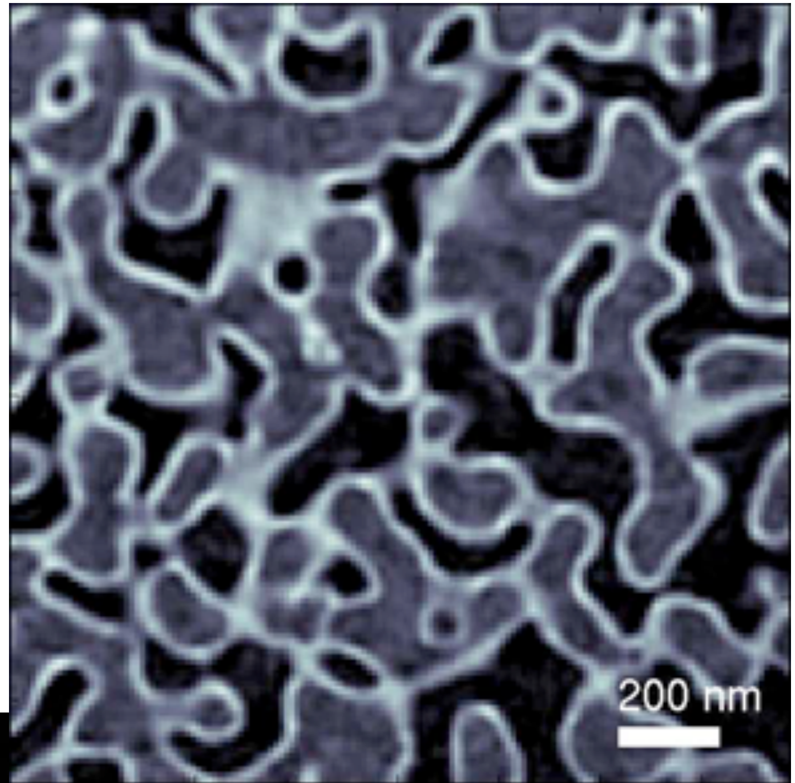
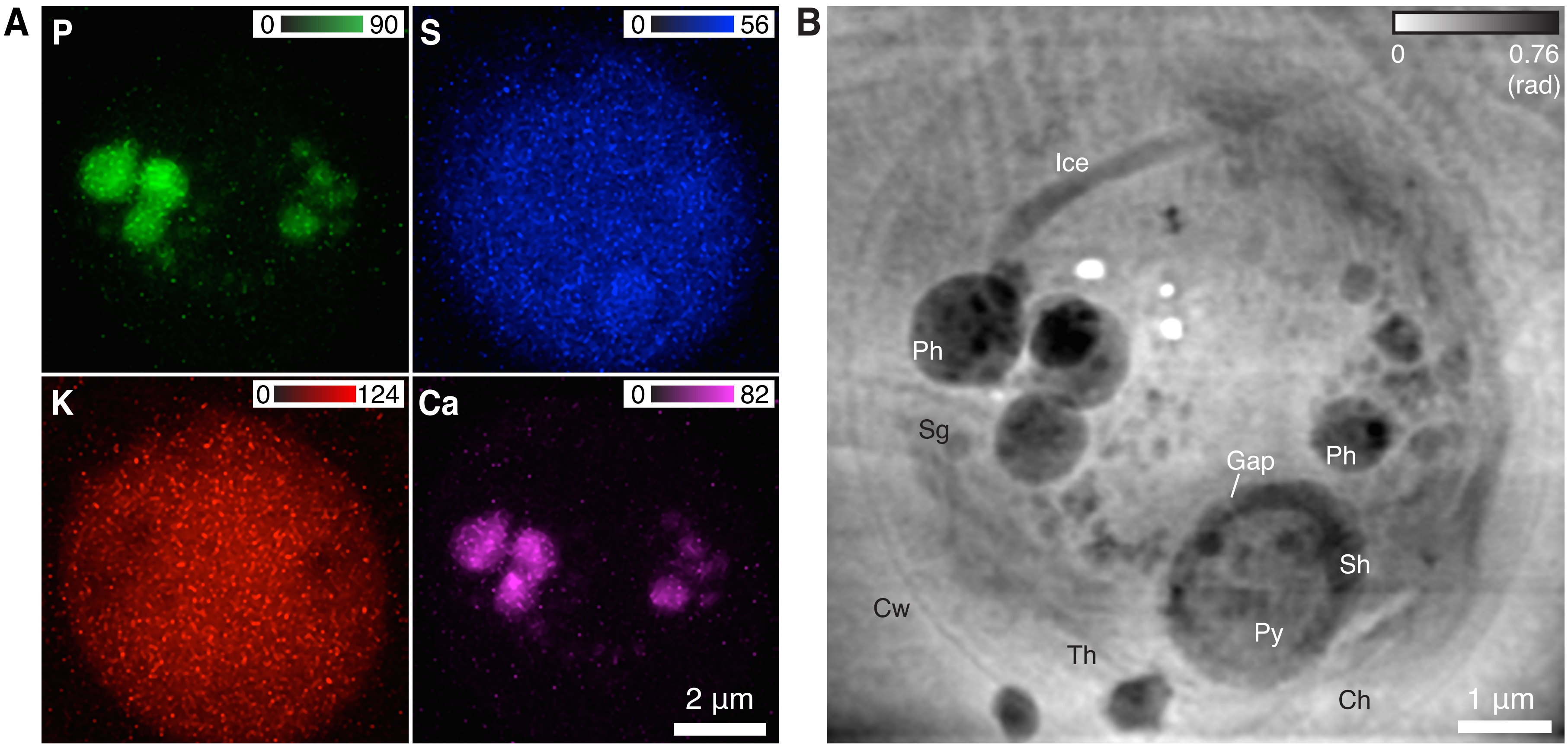
# X-ray coherent imaging: from prehistoric, to futuristic

- Holler *et al.*, *Scientific Reports* **4**, 3857 (2014); C-SAXS at Swiss Light Source.
- 56 hours for 720 projections at 6.2 keV.
- $Ta_2O_5$ on nanoporous glass at 16 nm in 3D



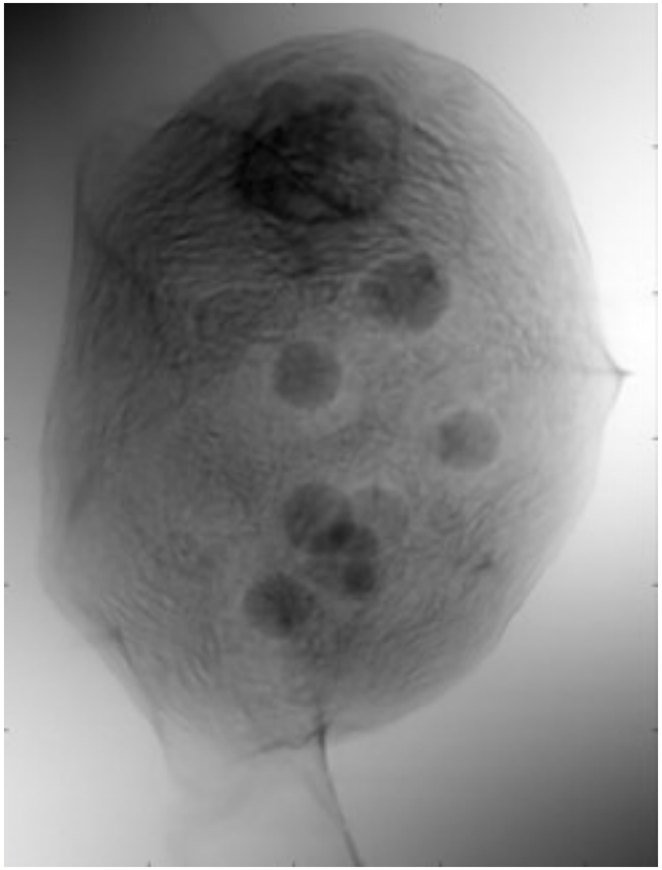

# Combined fluorescence and ptychography of *Chlamydomonas reinhardtii*

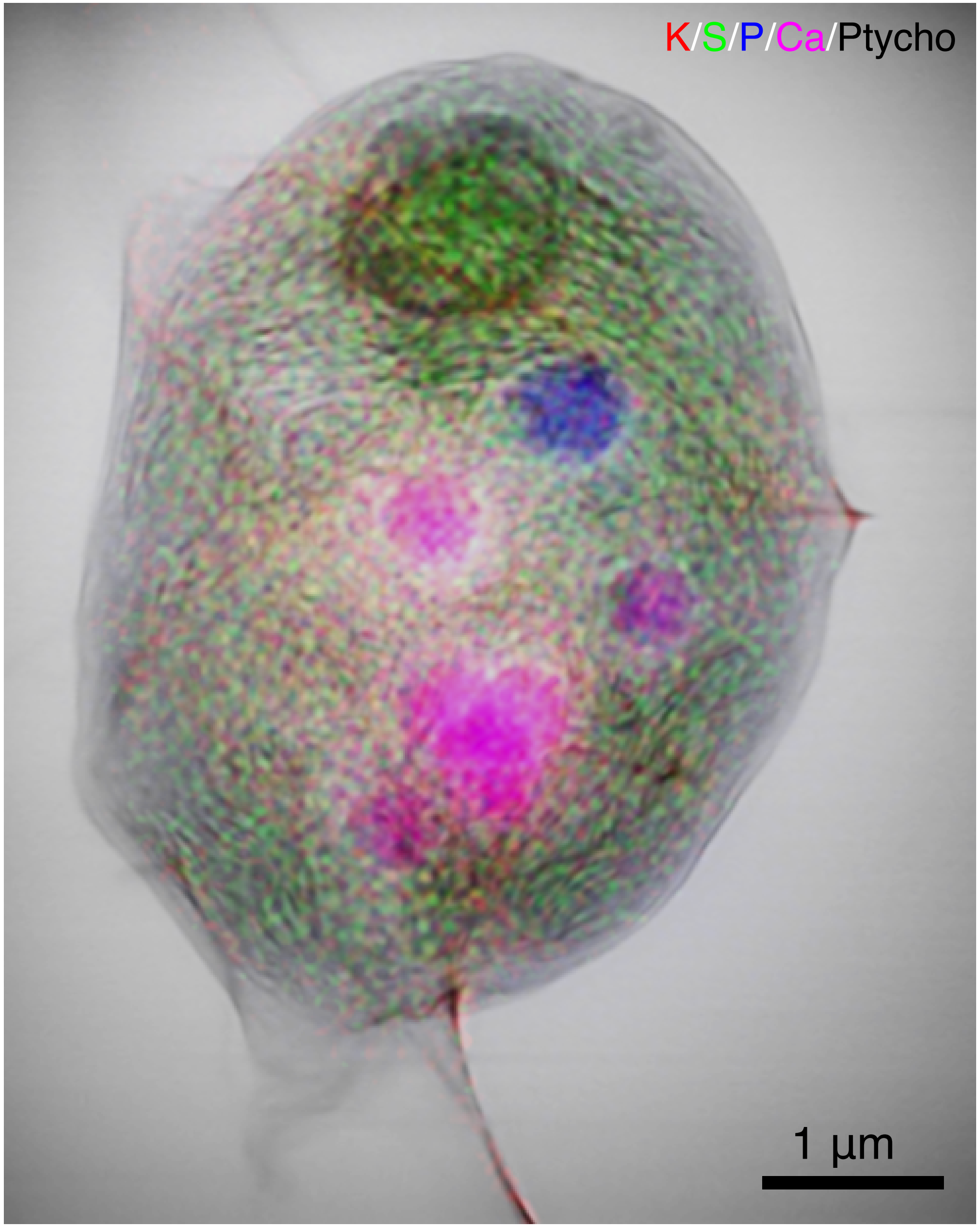
Deng *et al.*, *PNAS* **112**, 2314 (2015)



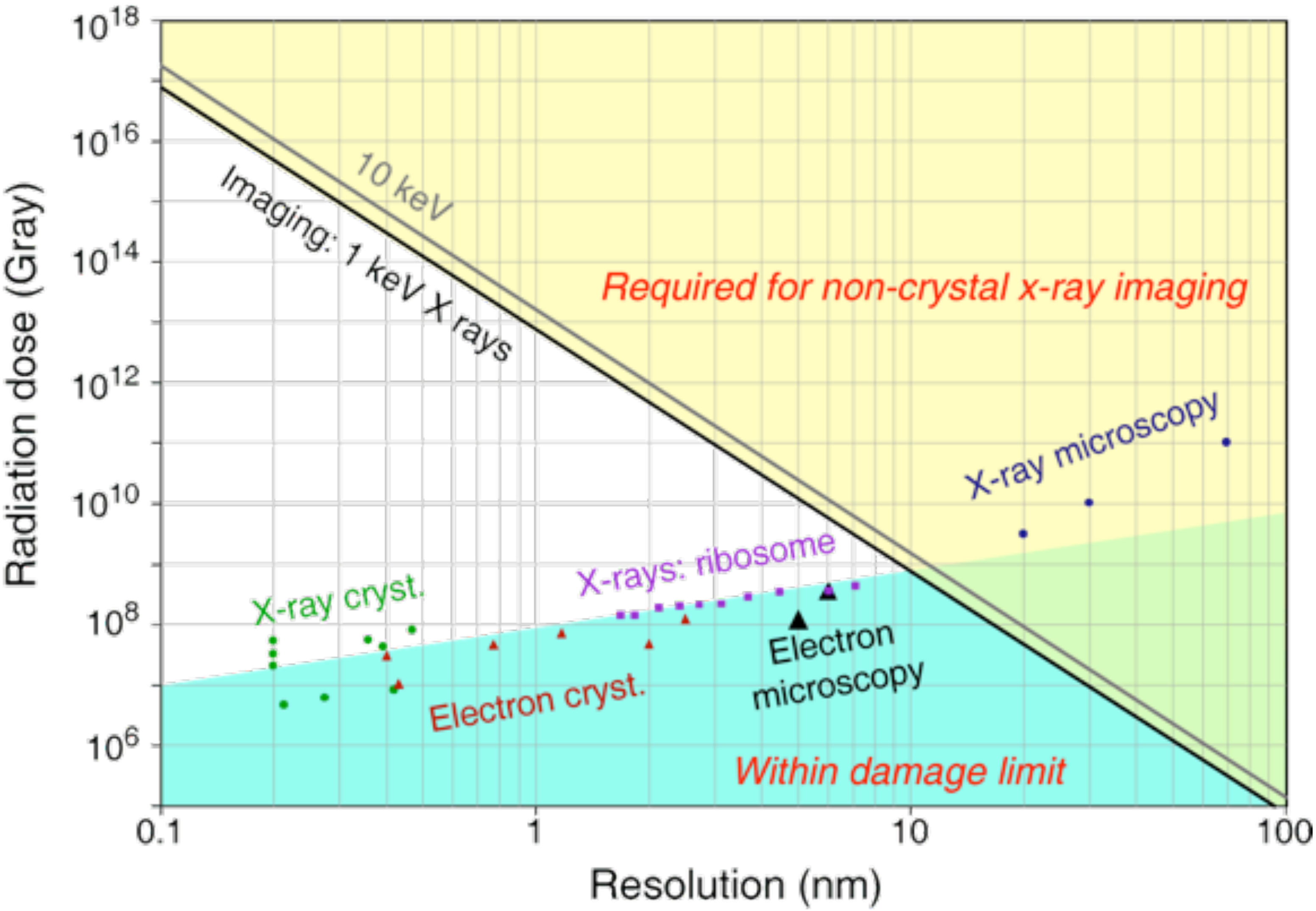
# Recent example

- *Chlamydomonas reinhardtii*, frozen in <0.1 msec from the living state, imaged under cryogenic conditions.
- Junjing Deng *et al.*





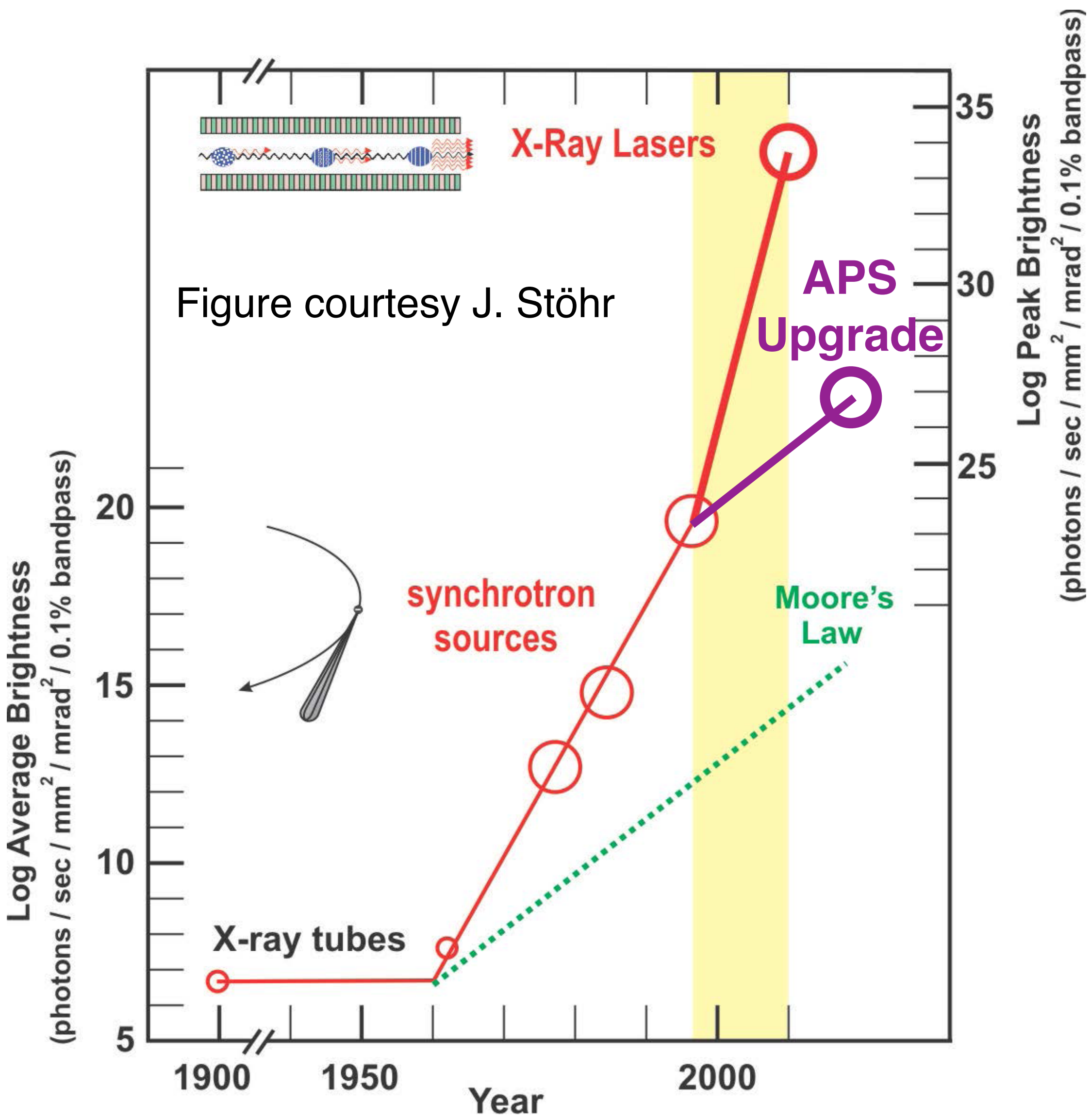
# Ultimate limits for biological samples: sub 10 nm




Assumption: 100% efficient microscopes! This plot: Howells *et al.*, *J. Electr. Spectr. Rel. Phen.* **170**, 4 (2009). See also Shen *et al.*, *J. Sync. Rad.* **11**, 432 (2004).

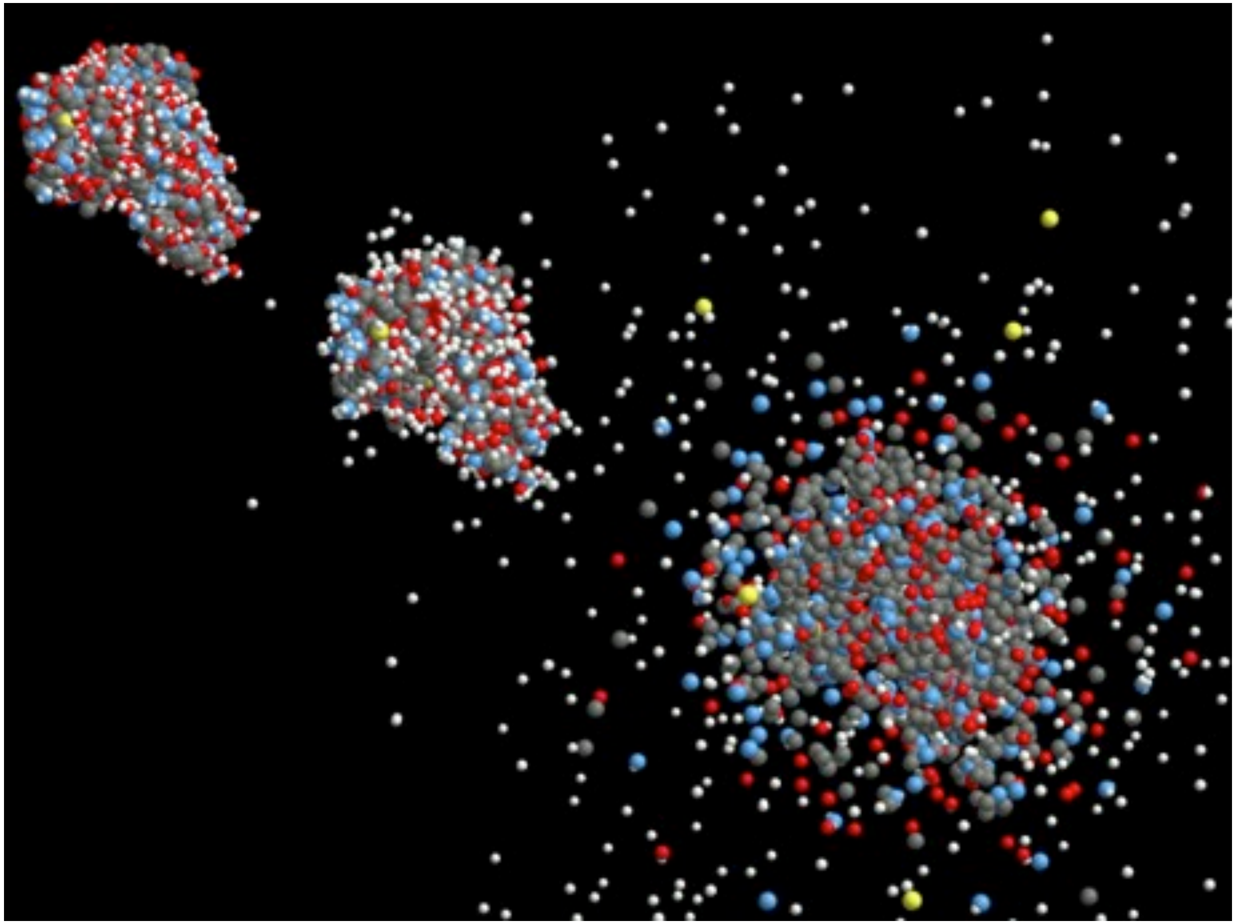
# X-ray brightness: beyond Moore's law in computing

- Synchrotron light sources deliver high time-averaged brightness, for many experiments simultaneously.
- X-ray free electron lasers (XFELS) deliver high instantaneous brightness in <100 fsec (sample-destroying) pulses, for one or a few experiments simultaneously.



# How does Lysozyme react to an XFEL pulse?

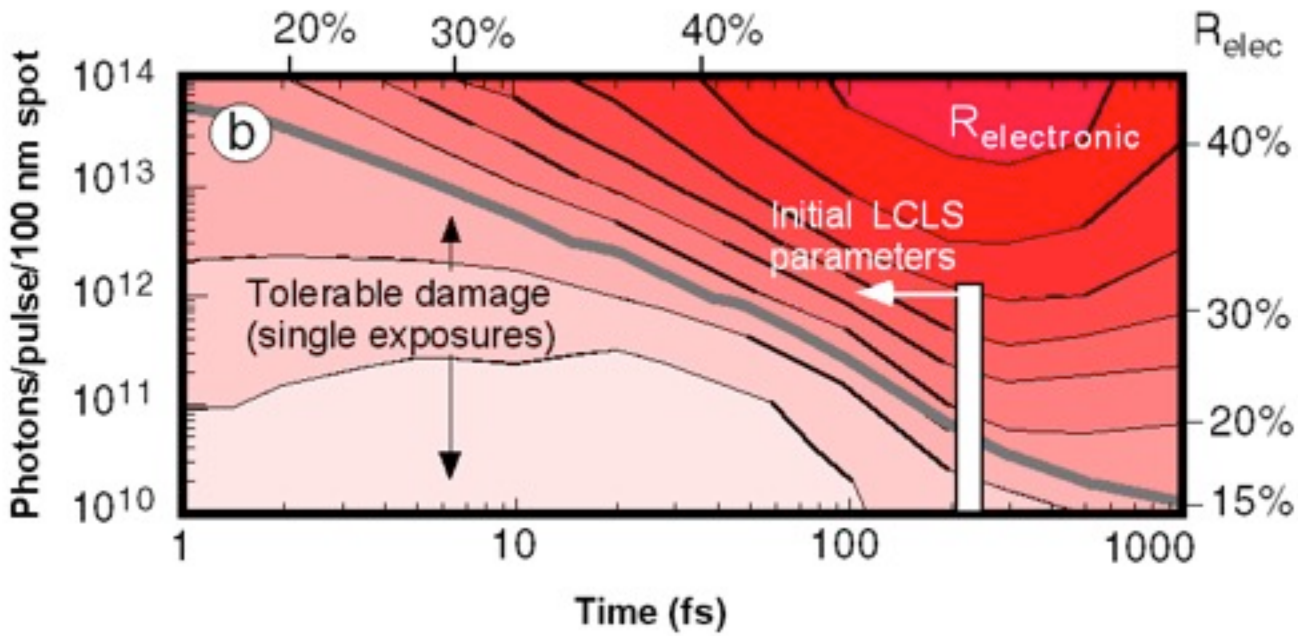
- **Violently!**
- Extension of GROMACS molecular dynamics program, with electrons removed by x rays
- Does not include any electron recombination.
- Lysozyme explodes in ~50 fsec
- R. Neutze *et al.*, *Nature* **406**, 752 (2000)



# Single molecule imaging: what's needed?

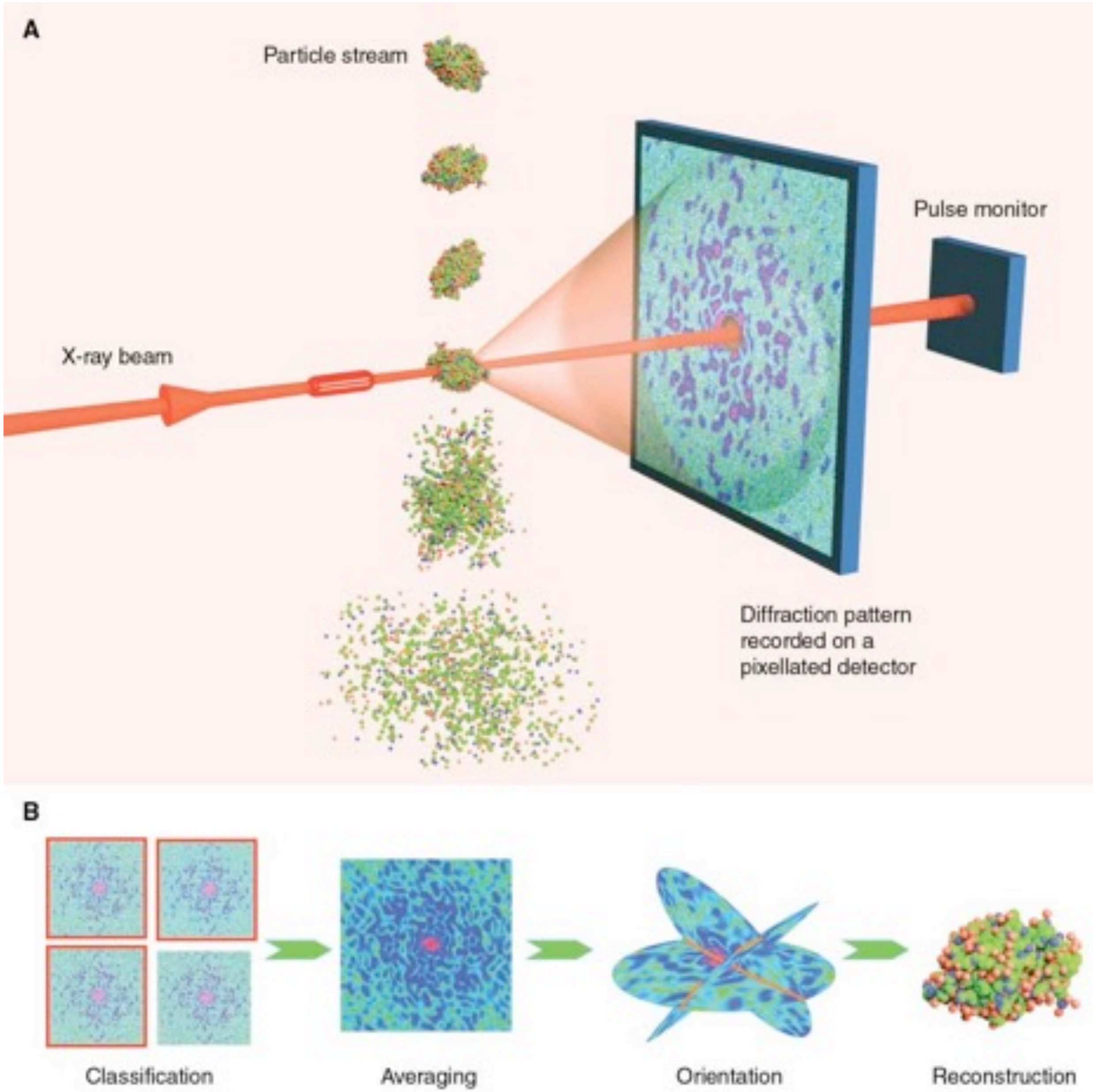
- Lots of coherent photons in a short pulse! 50 fsec is OK; 150 fsec is not.
- LCLS (Stanford), TESLA (Hamburg) X-FEL experiment proposals led by J. Hajdu (Uppsala)

$$R = \frac{\left|\sqrt{I(t)} - \sqrt{I_0}\right|}{\sqrt{I_0}}$$



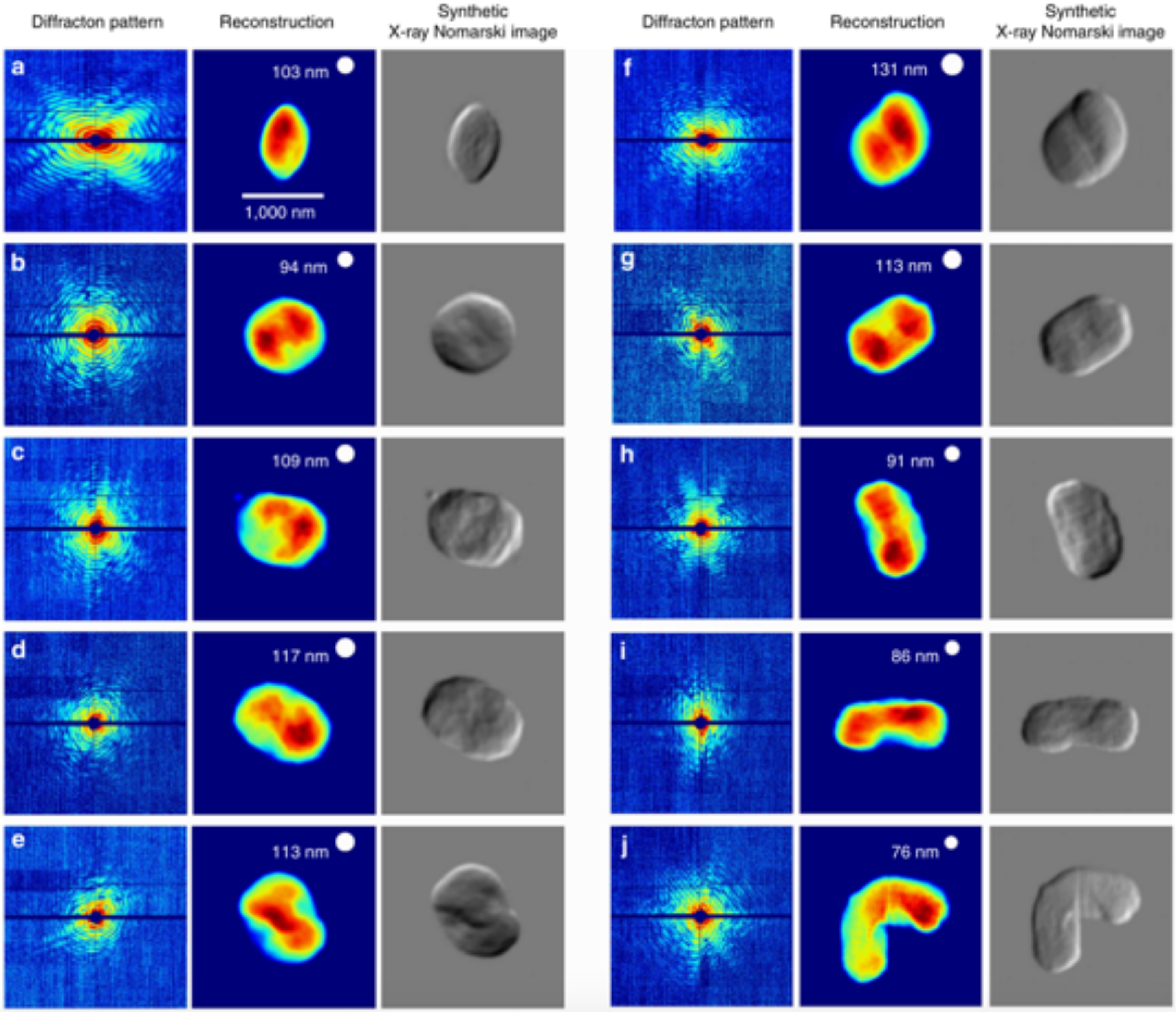
# XFEL imaging

- Requires identical objects (rigid viruses, molecules)
- To trace amino acid sequence into electron density, you need ~3 Å resolution.
- Neutze *et al.*, *Nature* **406**, 752 (2000); Huldt, Szoke, and Hajdu, *J. Struct. Bio.* **144**, 219 (2003); Gaffney and Chapman, *Science* **316**, 1445 (2007)



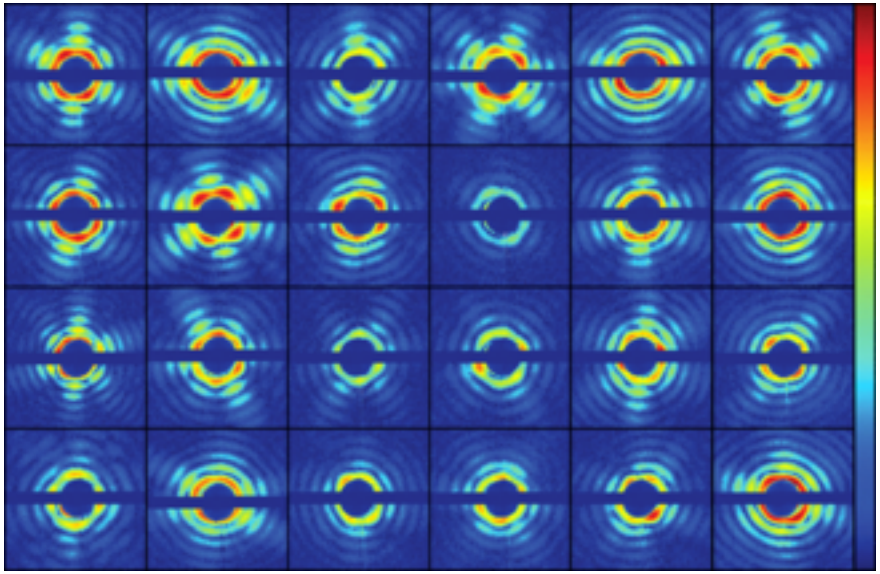
# XFEL imaging of cyanobacteria

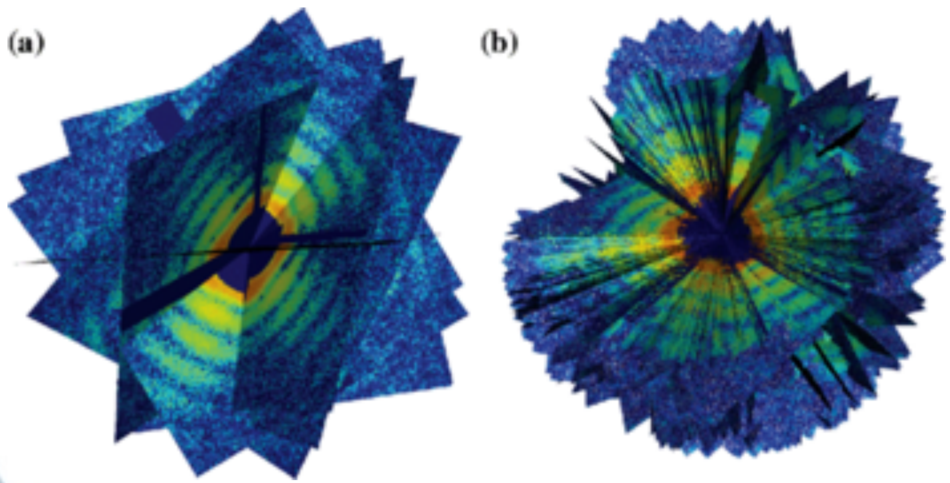
- van der Schot *et al.*, *Nature Comm.* **6**, 1 (2015)
- Context:
  - –light microscopy at 200 nm resolution, or ~50 nm using stochastic imaging of selected fluorophores.
  - –cryo electron microscopy at 5 nm resolution in 3D for samples below 500 nm thick (archaebacteria, some bacteria, thin peripheral regions of eukaryotic cells).
  - –cryo x-ray microscopy at 20-40 nm resolution in 3D for samples up to ~30 μm thick.

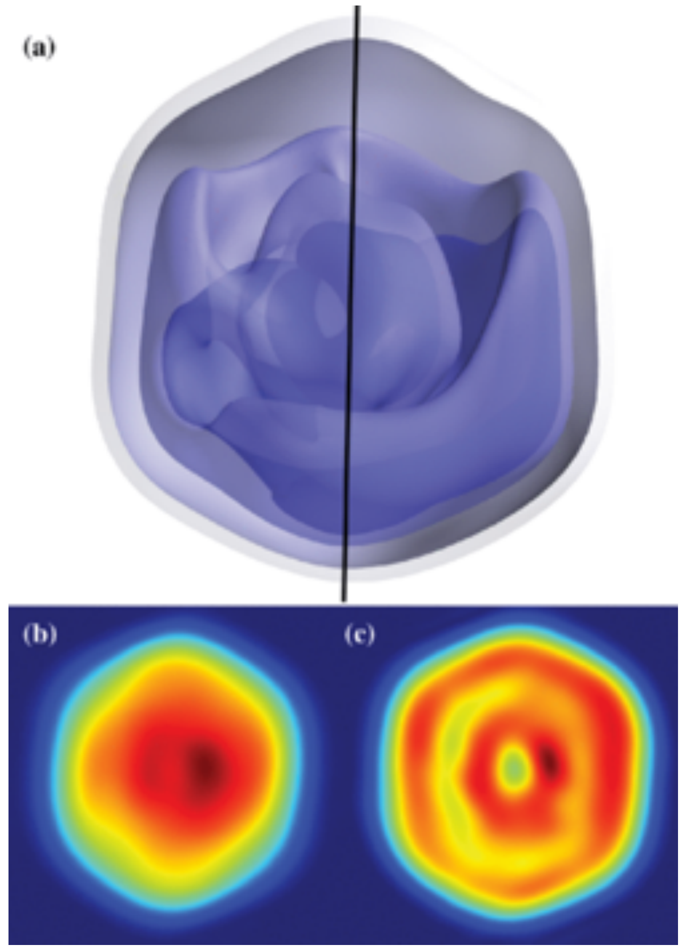


# XFEL imaging of mimivirus

- Eckeberg *et al.*, *Physical Review Letters* **114**, 098102 (2015)





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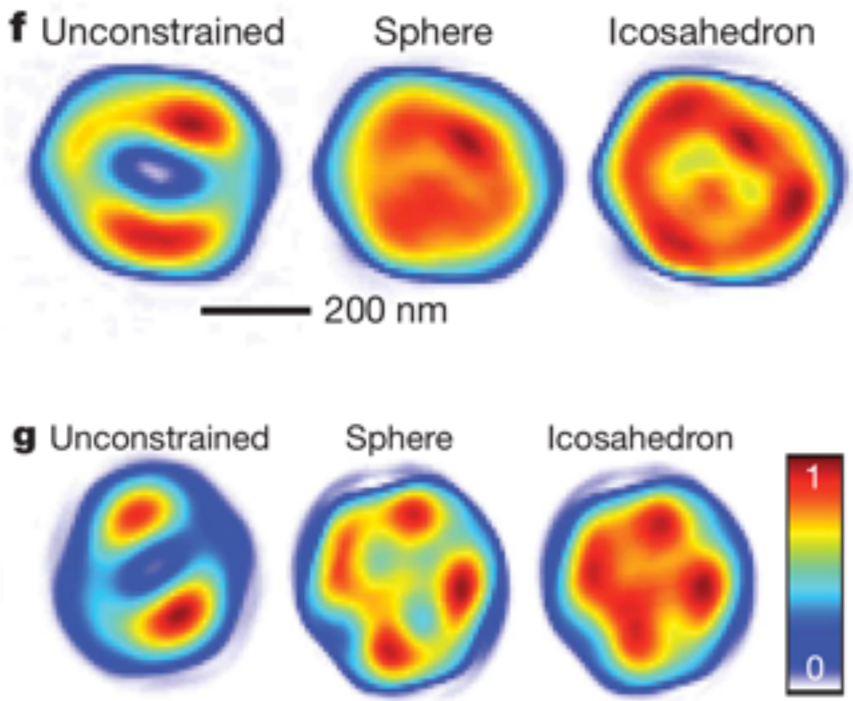
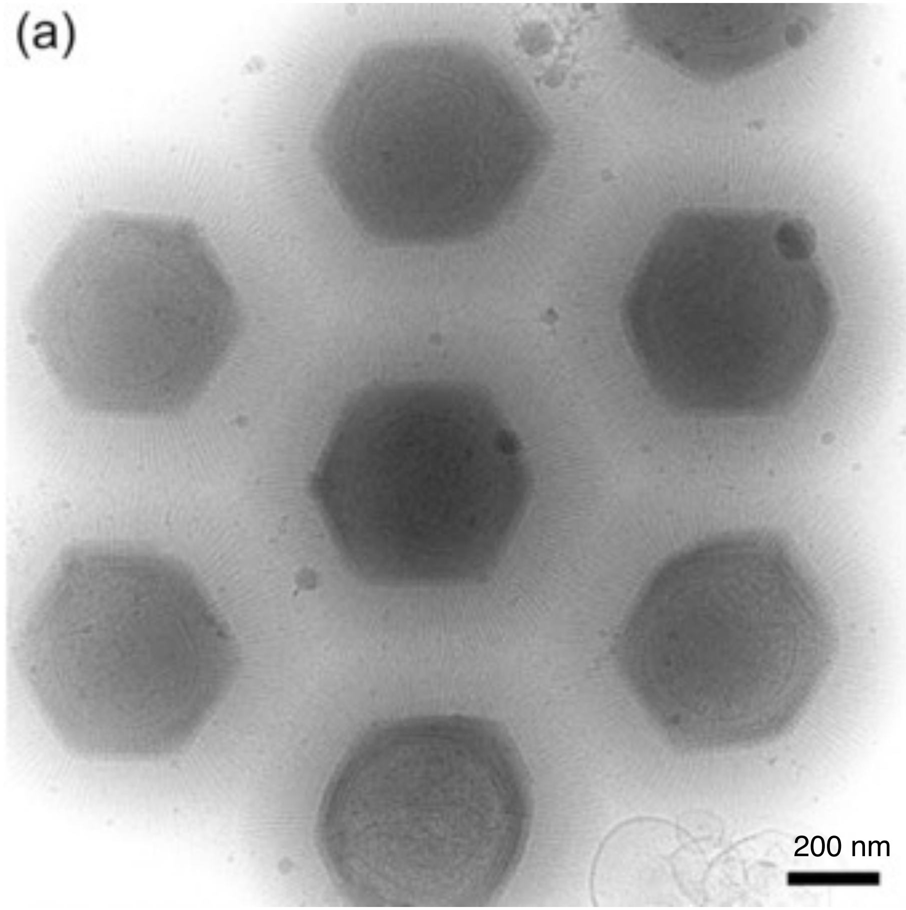
# Mimivirus

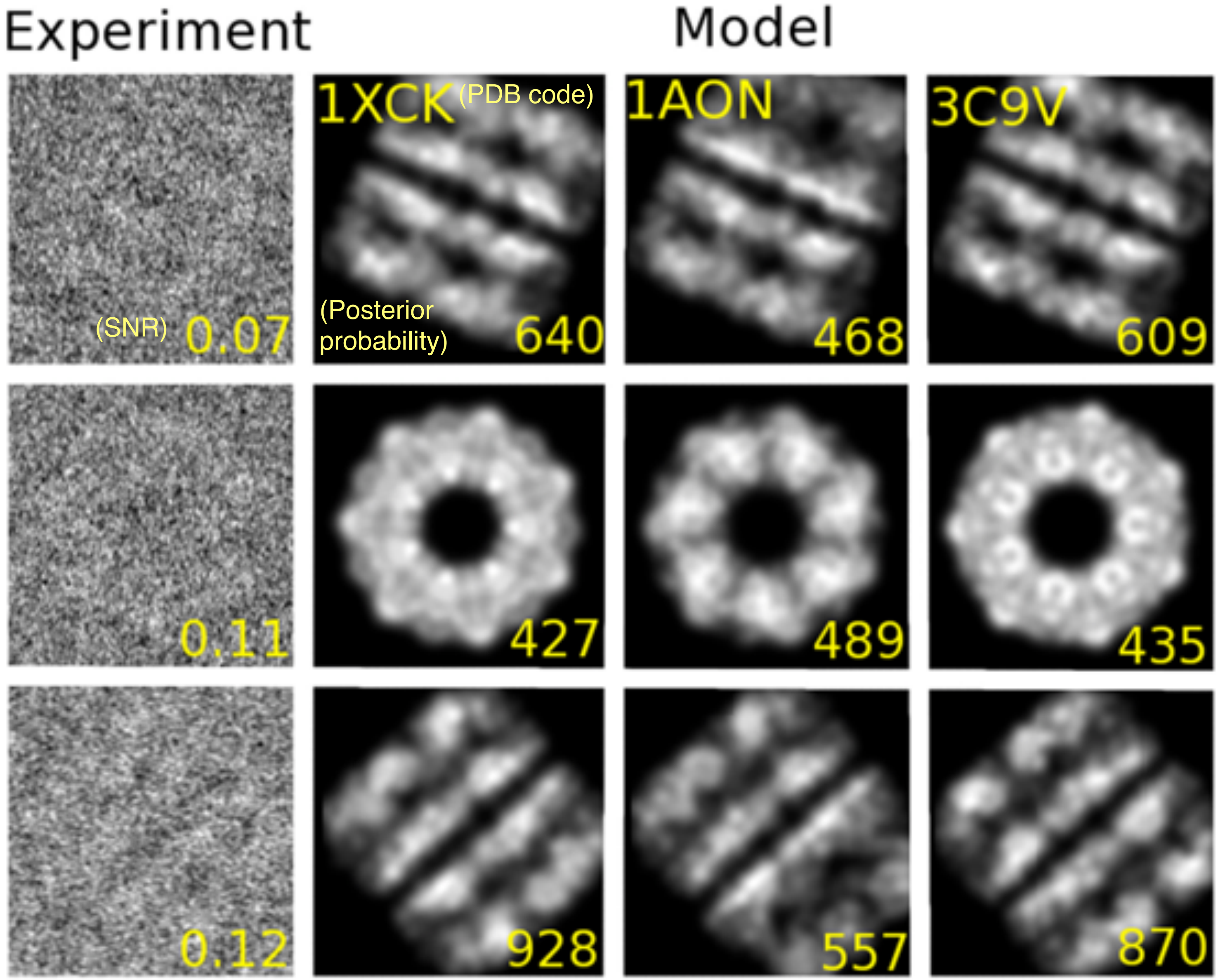



CDI at LCLS. Seibert *et al.*, *Nature* **470**, 78 (2011)




300 kV cryo EM. Xiao *et al.*, *J. Molecular Biology* **353**, 493 (2005)

# Conformational variants of GroEL (cryo electron microscopy




Cossio and Hummer, *J. Struct. Bio.* **184**, 427 (2013).



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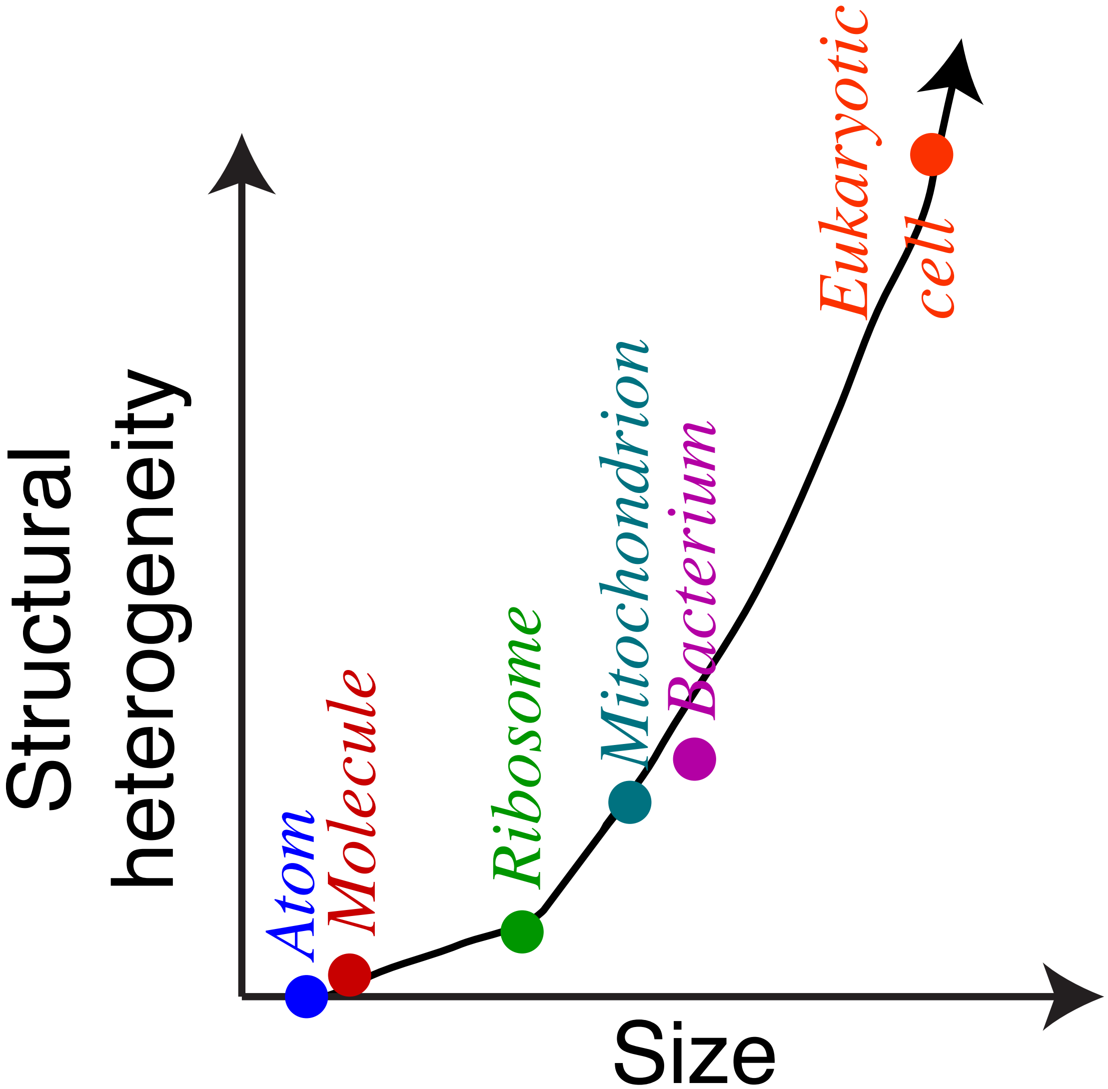
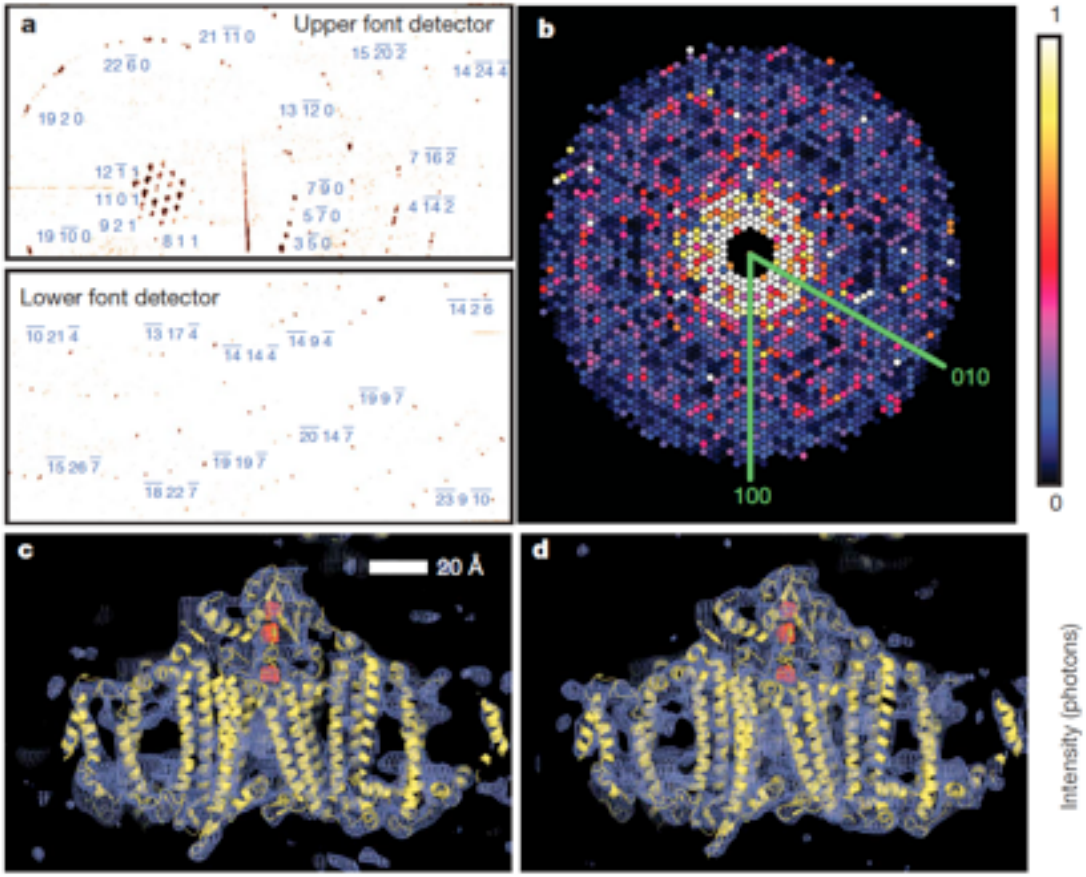
# The bigger you get, the more unique you are



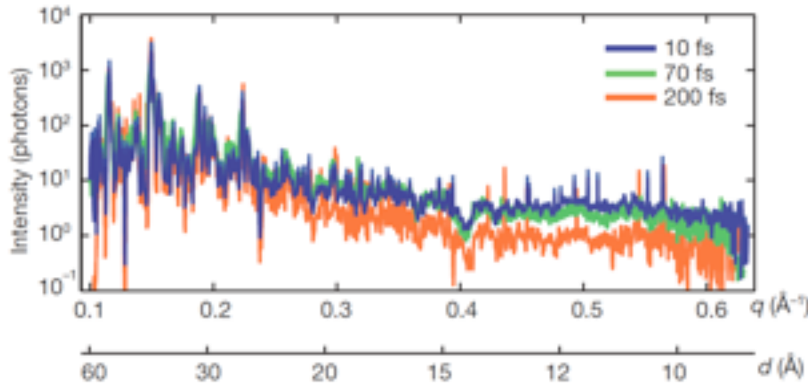
# Femtosecond nanocrystallography

- 1.8 keV (6.9 Å) LCLS XFEL: photosystem 1 (membrane protein)
- Chapman *et al.*, *Nature* **470**, 73 (2011)




XFEL reconstruction

Crystallography blurred to 8.5 Å



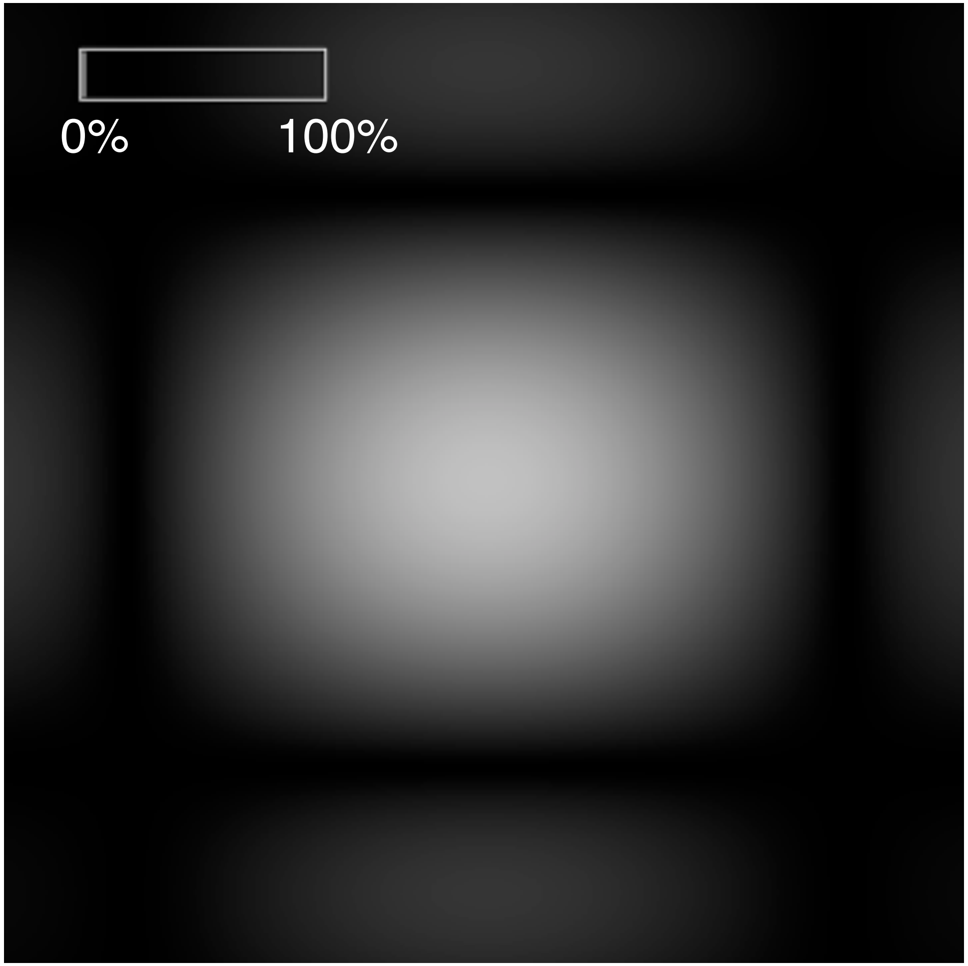
# We need large facilities for x-ray science; we need both diffraction-limited storage rings, and free electron lasers

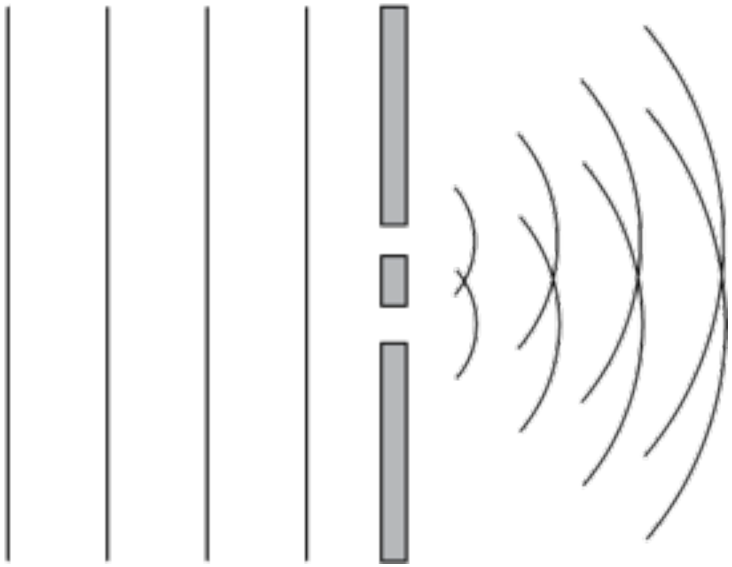
- Example: imaging the “wiring circuitry” of a whole mouse brain would take 3 months with a laboratory source, and half a day at today’s synchrotron light sources.
- Storage rings are what we want for multiple measurements on **unique** objects like individual biological cells:
  - Multiple rotation angles for 3D imaging via tomography
  - Spectroscopic imaging: trace elements via fluorescence, chemical binding states via absorption spectroscopy
- X-ray free electron lasers can be used for diffract-before-destroy studies of large numbers of **identical** objects
  - Serial crystallography of small (10x10x10 molecules?) crystals
  - Imaging of non-crystallizable macromolecules at beyond-electron-microscopy resolution?
- The future is bright!

# Supporting material

# Turn the coherence knob

Two slits, with variable degrees of phase correlation

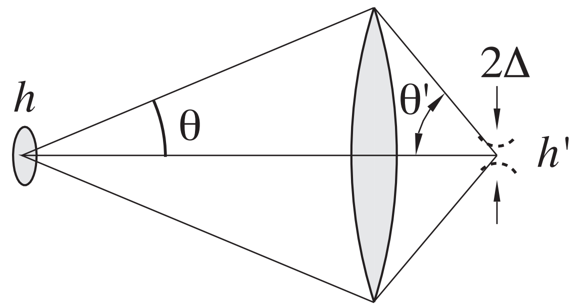


With a wide range of input wave directions, fringes get washed out.

# Photons and electrons

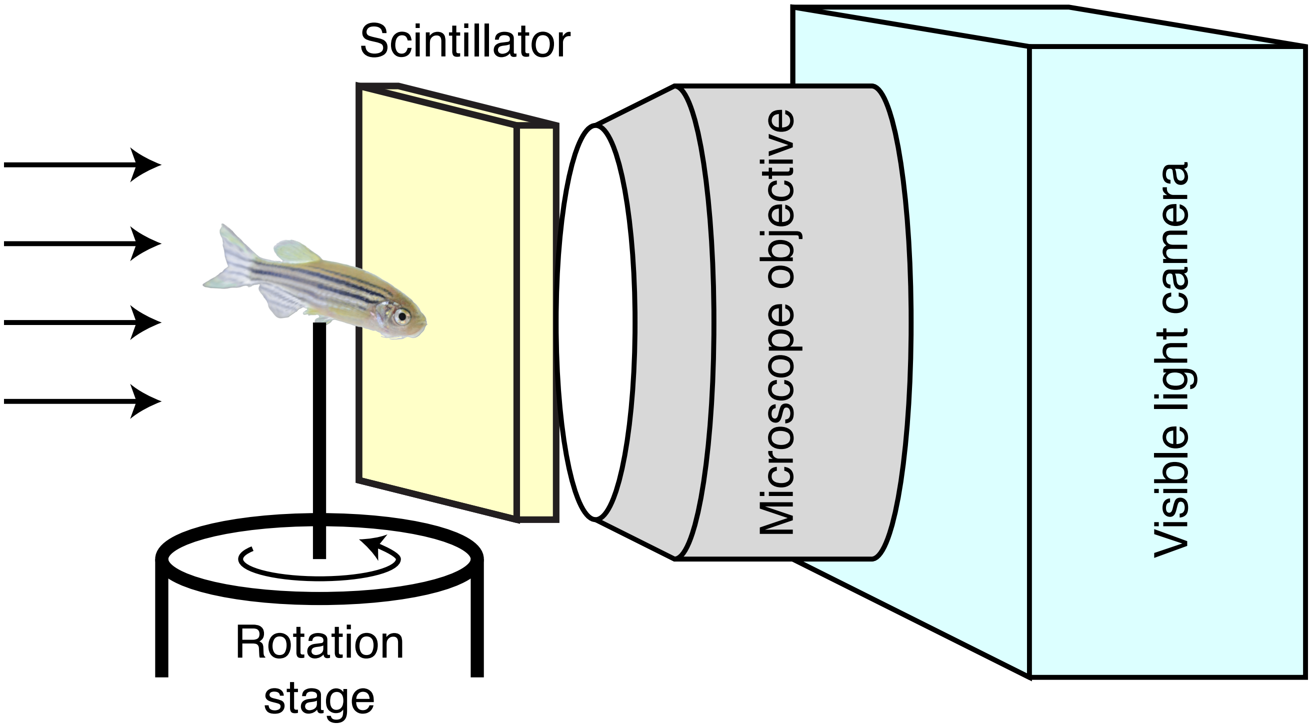
- A diffraction-limited focus from a lens requires that the illumination $h \cdot 2\theta$ be restricted to a 2D phase space area of $\sim\lambda^2$.
- The photons come from the electron beam, so ideally the electron beam 2D phase space should be restricted to $\sim\lambda^2$.




- Louiville's theorem in Hamiltonian mechanics says that phase space can be manipulated (tradeoff of size versus divergence), but not reduced.
- Coherent x-ray beams can only use the fraction of the electron beam that is within a 2D phase space $\sim\lambda^2$.
  - Answer 1: diffraction-limited storage rings (Borland talk)
  - Answer 2: free-electron lasers (several talks)

# X-ray tomography at the micrometer scale

- Resolution down to ~1 µm in 3D; limited by x-ray diffraction, visible light optics viewing scintillator.
- 3D Imaging times of 0.3-300 seconds at APS beamline 2-BM (X. Xiao and F. De Carlo).

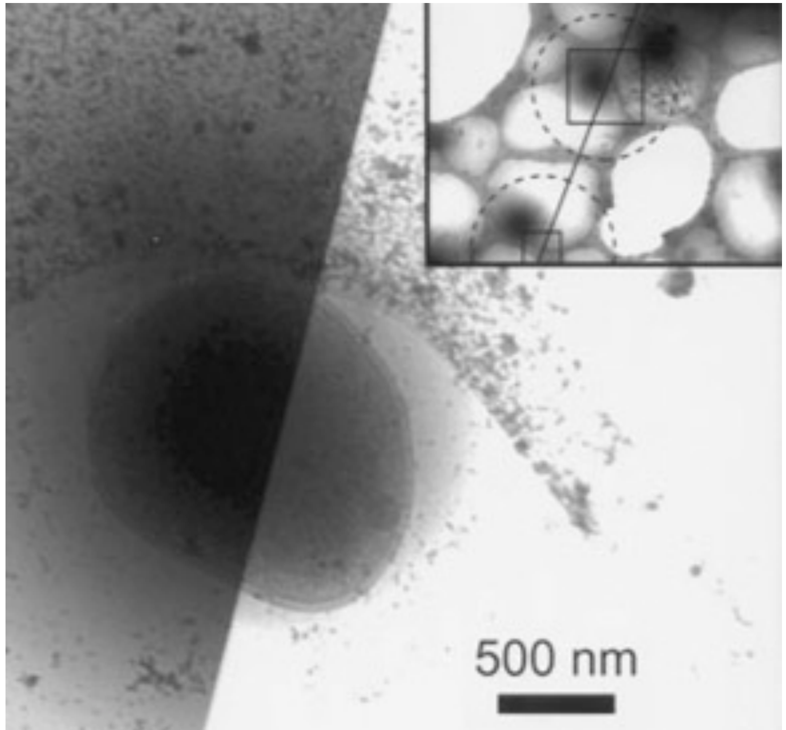


# Synchrotron X-ray tomography of Zebrafish

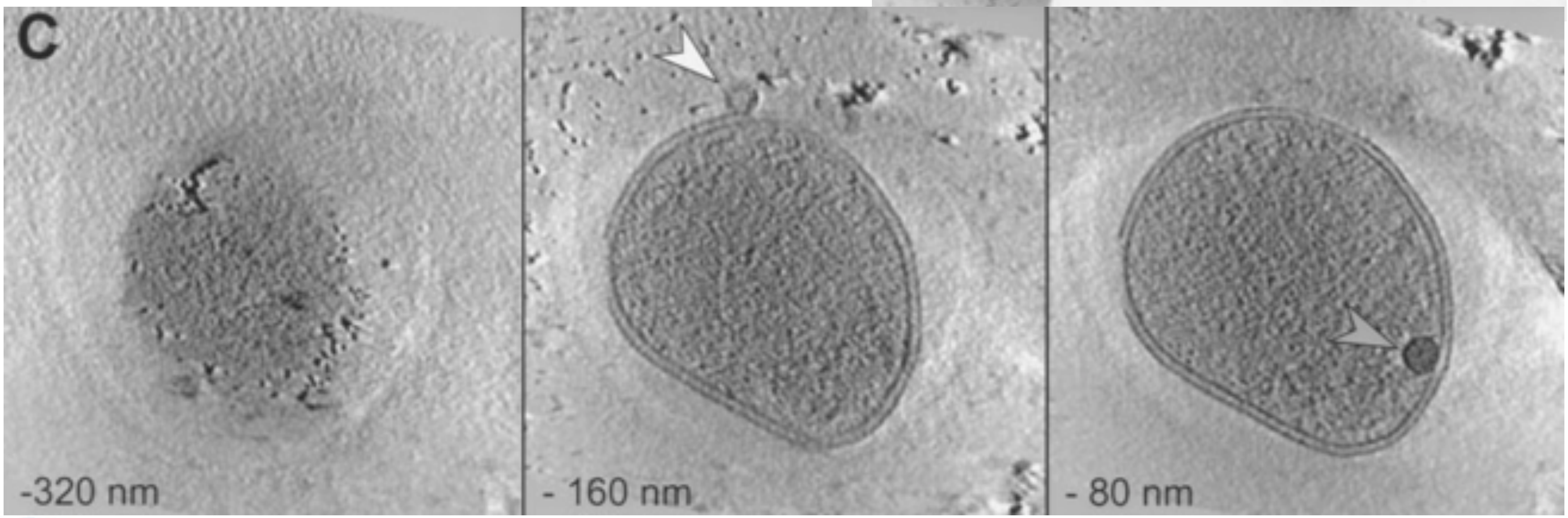
K. Cheng *et al.*, *Curr. Opin. Genetics & Devel.* **21**, 620 (2011)

# Tomography reveals what projections don't

- 3D imaging of complex objects: slices from tomography are *much* more revealing than single projections.
- Tomography requires multiple views of an unchanged specimen.




Grimm *et al.*, *Biophys. J.* **74**, 1031 (1998).



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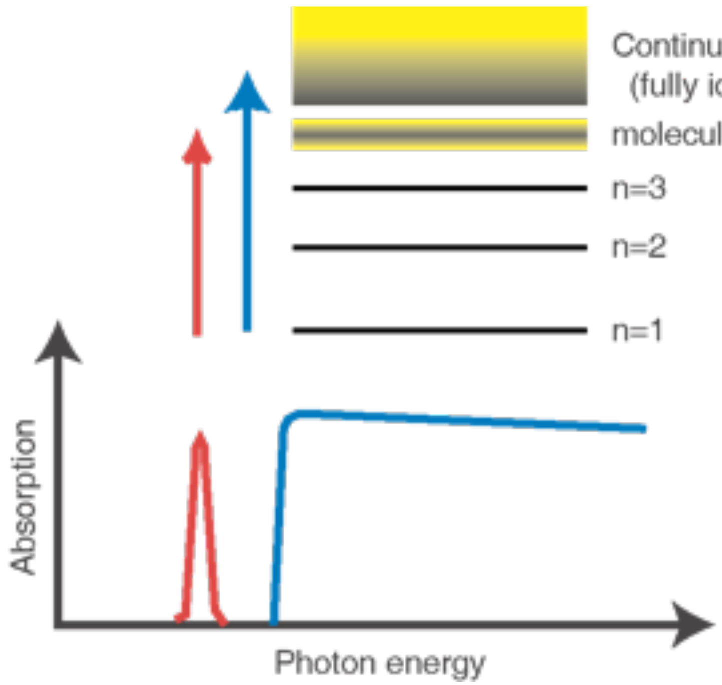
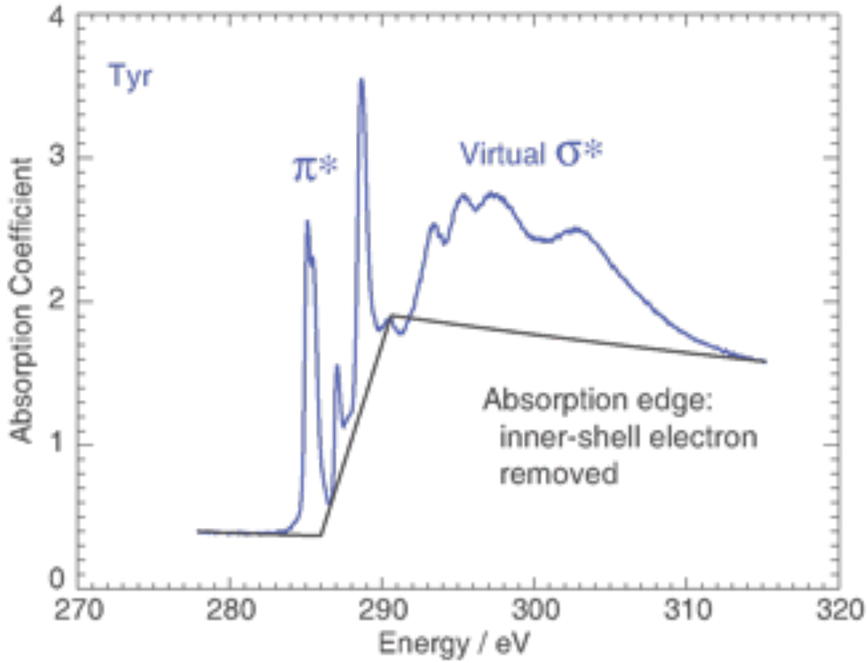
# Near-edge absorption fine structure (NEXAFS) or X-ray absorption near-edge structure (XANES)

- Fine-tuning of the x-ray energy near an atom's edge gives sensitivity to the chemical bonding state of atoms of that type
- First exploitation for chemical state transmission imaging: Ade, Zhang *et al.*, *Science* **258**, 972 (1992) – Stony Brook/X1A

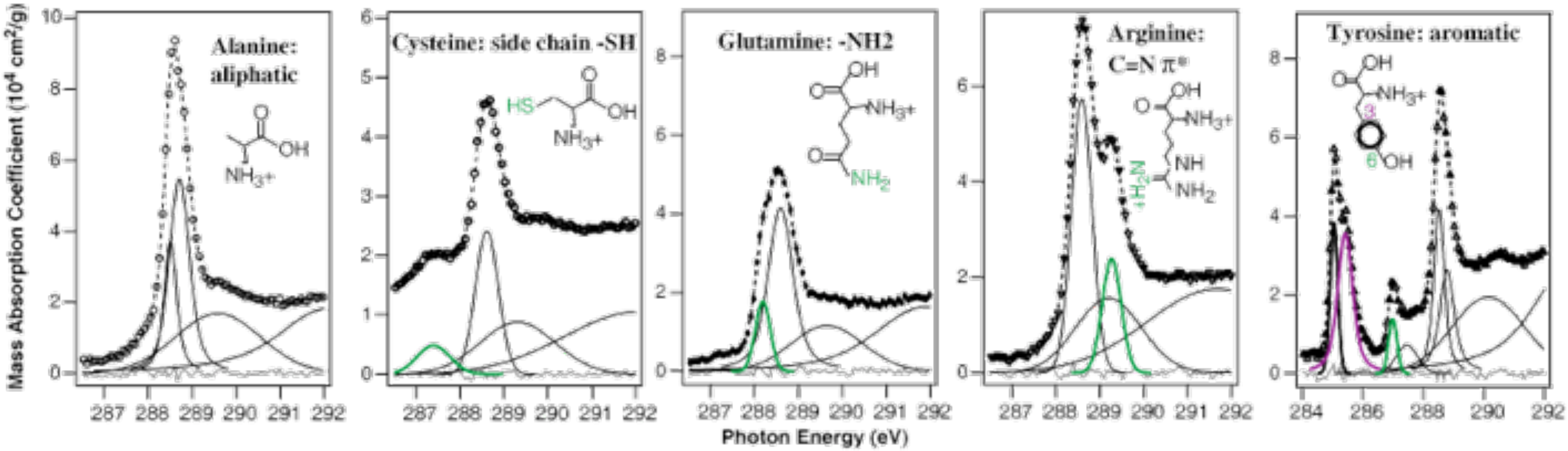



Compared with UV "tickling" of molecular orbitals, core-level electrons come from a single, well-defined state!

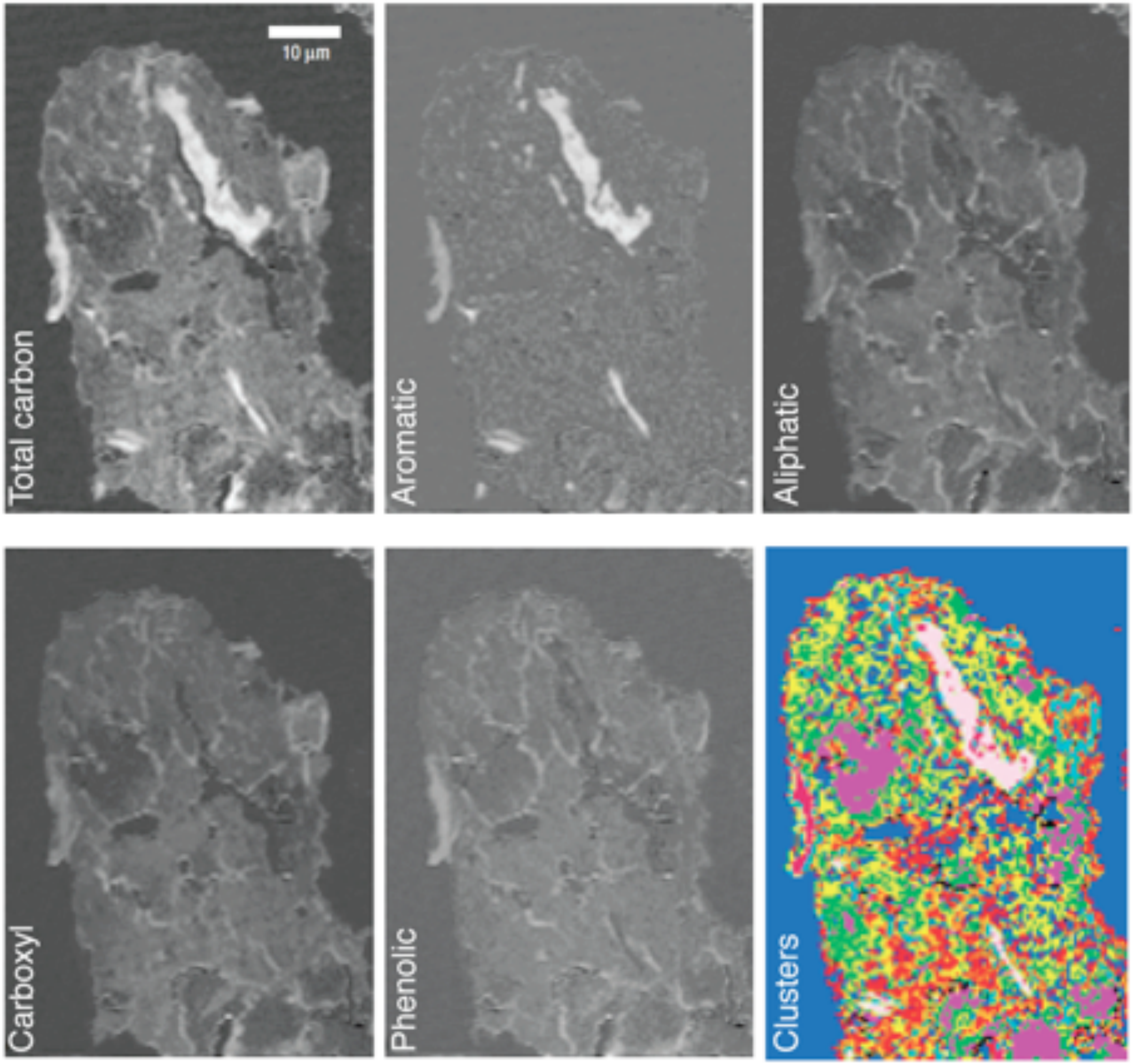
# C-XANES of amino acids

- K. Kaznacheyev *et al.*, *J. Phys. Chem.* **A 106**, 3153 (2002)
- Experiment: K. Kaznacheyev *et al.*, Stony Brook (now CLS)
- Theory: O. Plashkevych, H. Ågren *et al.*, KTH Stockholm; A. Hitchcock, McMaster




Polymers: see e.g., Dhez, Ade, and Urquhart, *JESRP* **128**, 85 (2003)

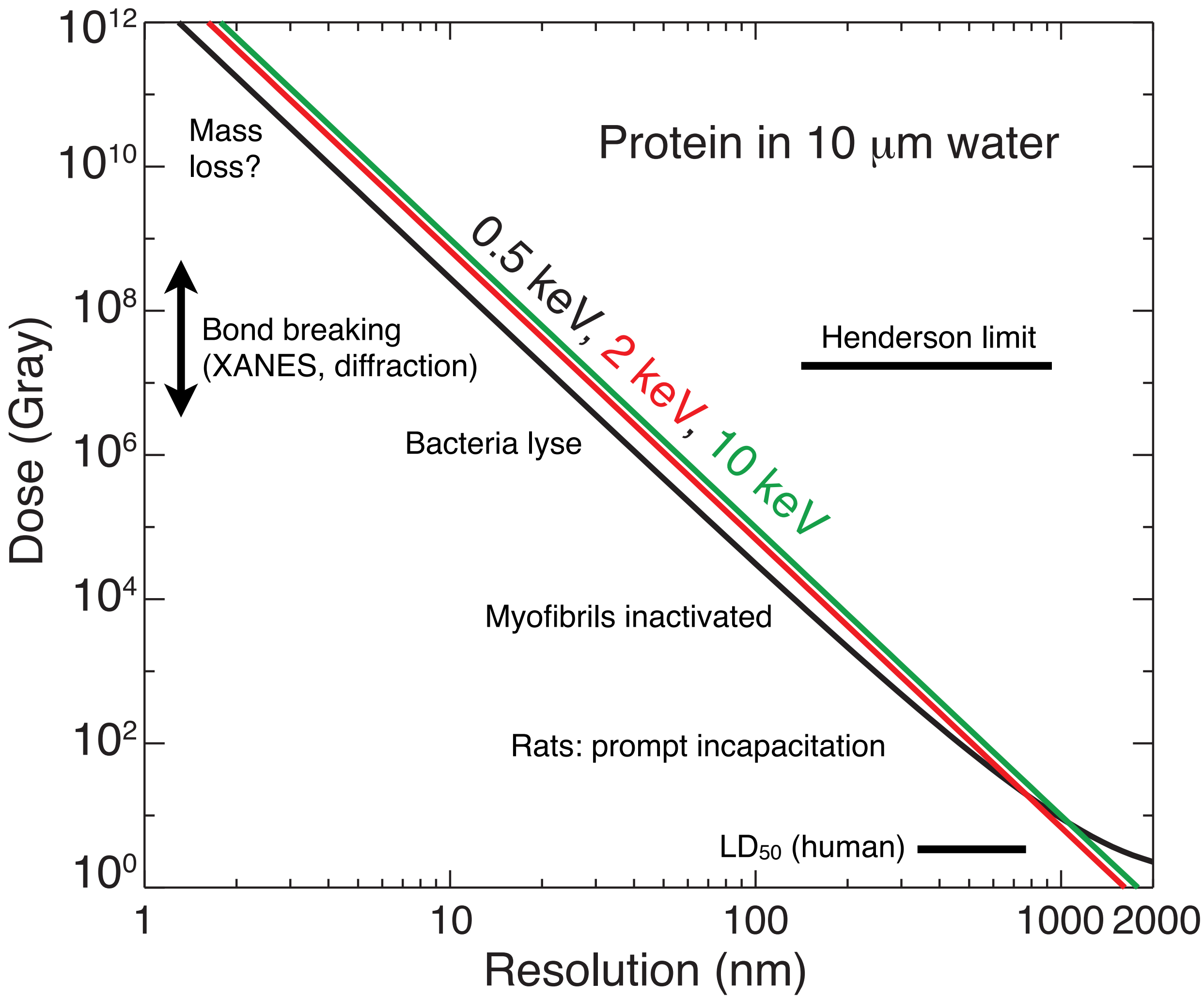
# Organic carbon in soils: C-XANES imaging




J. Lehmann, D. Solomon, J. Kinyangi, L. Dathe, S. Wirick, and C. Jacobsen, *Nature Geoscience* **1**, 238 (2008)

# Dose versus resolution for wet soft materials

- Calculation of radiation dose using best of phase, absorption contrast and 100% efficient imaging.
- In a 3D world, high resolution structures are also thin, with lower contrast.



# Coherence and nanoprobes

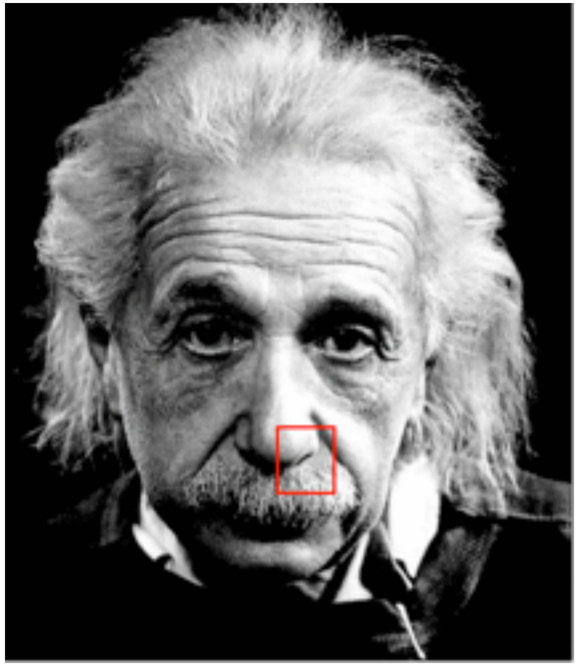
- You can only reach the diffraction limit (as opposed to the source-limited limit) of focusing from a lens when you accept a single coherent mode with phase space area ~1λ in each direction.
- If the phase space of your source is larger, you must throw away the incoherent modes!

| Parameter | electron beam | photon beam | MBA Upgrade combination | today |
|---|---|---|---|---|
| Horizontal size | $\sigma_x = 21.5\ \mu m$ | $\sigma_r = 5.5\ \mu m$ | $\Sigma_x = 22.2\ \mu m$ | $275.0\ \mu m$ |
| Horizontal divergence | $\sigma'_x = 3.1\ \mu rad$ | $\sigma'_r = 3.6\ \mu rad$ | $\Sigma'_x = 4.8\ \mu rad$ | $12.1\ \mu rad$ |
| Vertical size | $\sigma_y = 4.0\ \mu m$ | $\sigma_r = 5.5\ \mu m$ | $\Sigma_y = 6.8\ \mu m$ | $10.7\ \mu m$ |
| Vertical divergence | $\sigma'_y = 1.7\ \mu rad$ | $\sigma'_r = 3.6\ \mu rad$ | $\Sigma'_y = 4.0\ \mu rad$ | $6.2\ \mu rad$ |
| Phase space parameter $p_x$ | $(2.35\Sigma_x)(2.35\Sigma'_x)/\lambda$ | | 4.69 at 10 keV | 148.53 |
| Phase space parameter $p_y$ | $(2.35\Sigma_y)(2.35\Sigma'_y)/\lambda$ | | 1.20 at 10 keV | 2.95 |
| $p_x \cdot p_y/\lambda^2$ | | | 5.7 | 438.1 |

# Seeing the whole picture

- Changes a heroic day-long measurement (common in fluorescence tomography, for example) into just another 15 minute measurement.  Go from single observations to statistical significance!
- Lets you see the whole picture, rather than just 1% of it:

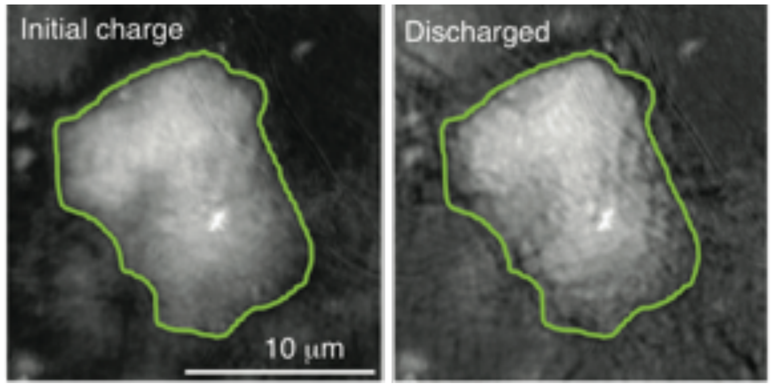
1% of what?



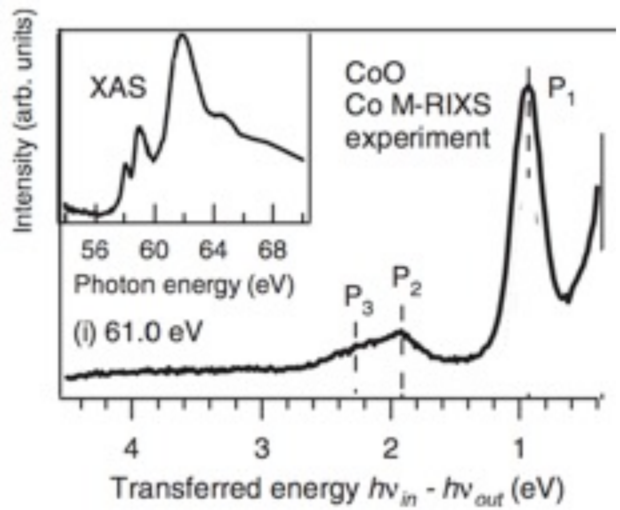
100% of Einstein

# Inelastic nanoprobe to image lithium batteries?

- Lightweight batteries are crucial for transportation (e.g., Chevy Volt), portable electronics (cell phones).
- Inelastic x-ray scattering combined with scanning probe would enable you to maps Lithium specifically in a thick battery *in situ* or *in operando*.
- Discussions with Yue Sun.



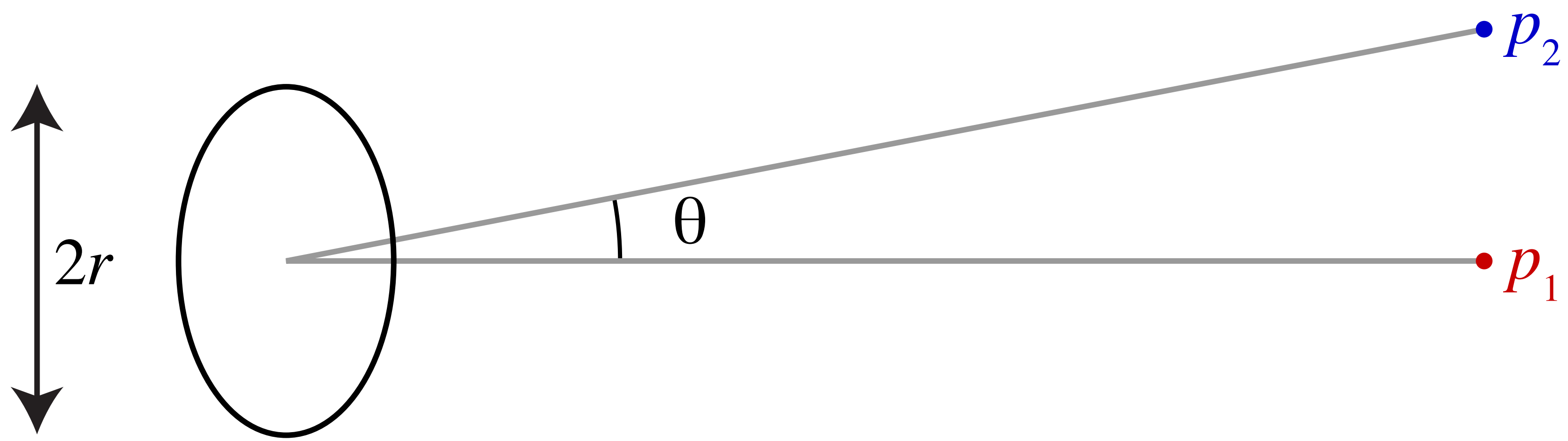

Sulfur/Super-P carbon black particle in a Li-S battery after one discharge cycle, imaged at 6 keV. J. Nelson *et al.*, *JACS* **134**, 6337 (2012).




Demonstration of RIXS at a energy near the Li *K* edge (in this case, the Co *M* edge). Chiuzbăian *et al.*, *Phys. Rev. B* **78**, 245102 (2008).

# van Cittert-Zernike Theorem

- Incoherent source of diameter $2r$
- Degree of mutual coherence (fringe visibility) between points 1 and 2 is $|\mu_{1,2}| = \frac{2J_1(\nu)}{\nu}$ where $\nu = \frac{2\pi\, r\, \theta}{\lambda}$
- The square is the Airy pattern for the intensity distribution of diffraction from a pinhole



# van Cittert-Zernike Theorem

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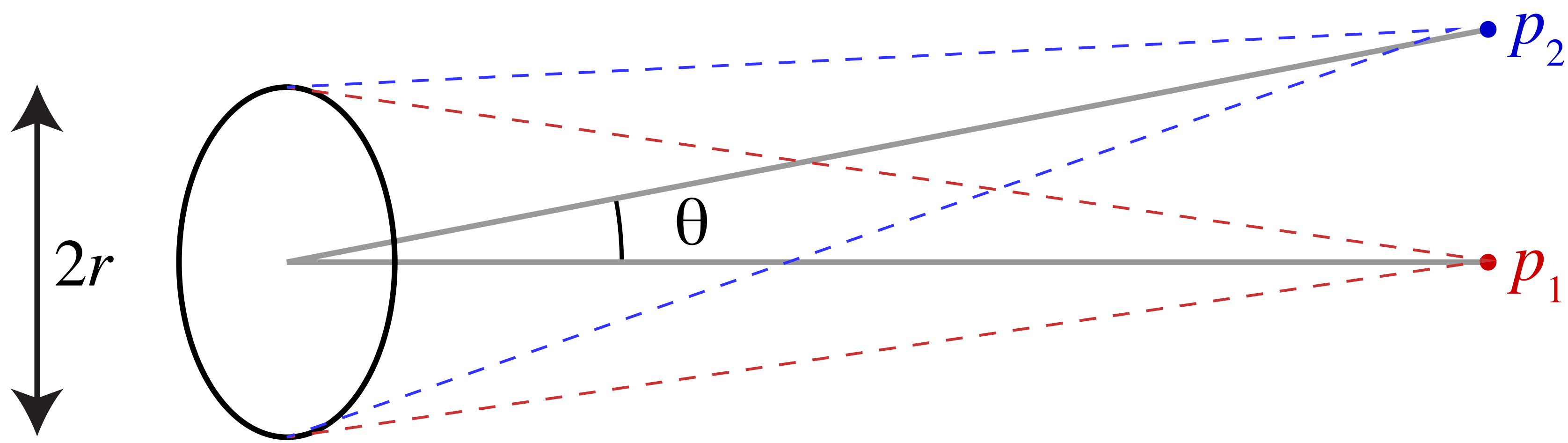


# Coherent phase space

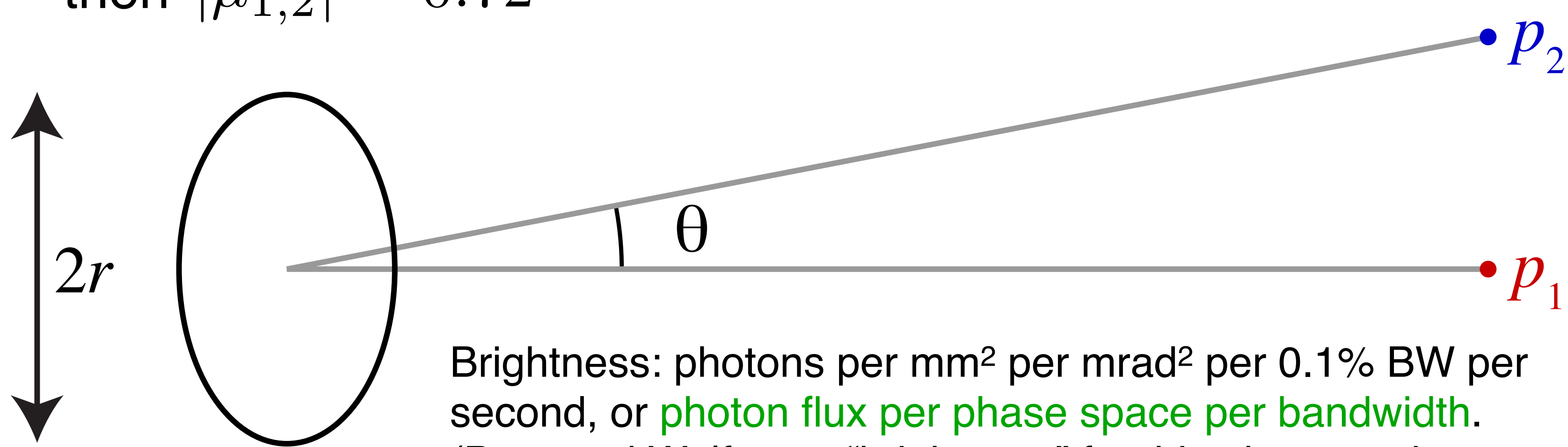
- Degree of mutual coherence (fringe visibility) between points

  1 and 2 is $|\mu_{1,2}| = \frac{2J_1(\nu)}{\nu}$ where $\nu = \frac{2\pi\, r\, \theta}{\lambda}$

- When $2\theta=\lambda/(2r)$, then $\nu = \frac{2\pi\, r\, \lambda}{\lambda \cdot (4r)} = \frac{\pi}{2}$ and $\frac{2J_1(\pi/2)}{\pi/2} = 0.72$

- In other words, when (full diameter)•(full angle accepted)=$\lambda$

  then $|\mu_{1,2}| = 0.72$

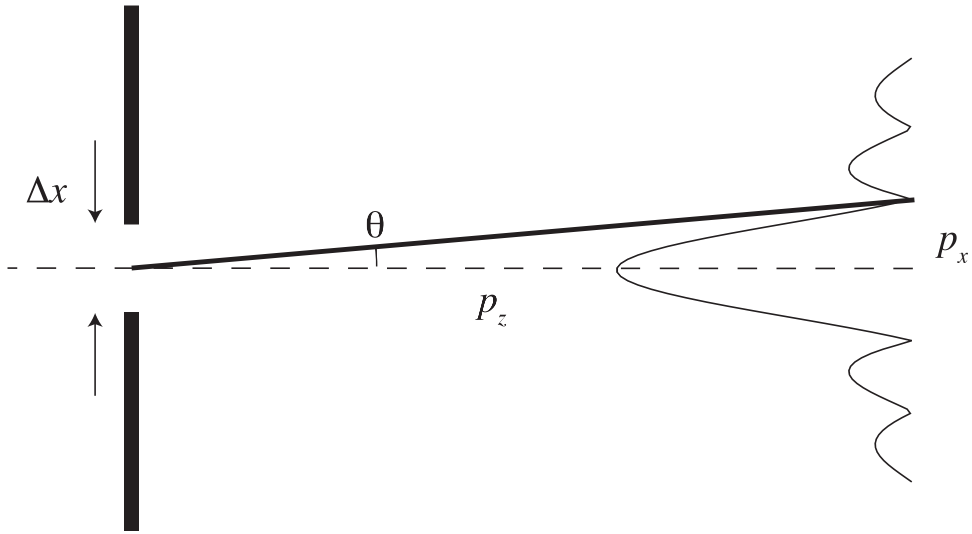



Brightness: photons per mm² per mrad² per 0.1% BW per second, or photon flux per phase space per bandwidth. (Born and Wolf uses "brightness" for this photometric quantity; APS has often used "brilliance" for the same thing).

# Phase space, quantum mechanics, and coherence

- Liouville's theorem in classical mechanics: $(\Delta p)\cdot(\Delta q)$=constant in a constant Hamiltonian $\mathcal{H} = T + V$
- Measuring the $\hat{x}$ momentum of a particle restricted to a position $\Delta x$ means it will be diffracted by the slit with a semi-angle θ of λ/($\Delta x$) giving

$$\Delta p_x = p_z \sin\theta = \frac{h}{\lambda}\frac{\lambda}{\Delta x} = \frac{h}{\Delta x}$$




- Thus $(\Delta x)\cdot(\Delta p_x) = h$ for zero mutual coherence (or $\nu$=1.22π or $\nu$=3.83 with circular apertures).
- Heisenberg uncertainty principle of $(\Delta x)\cdot(\Delta p_x) = \hbar$ corresponds to $\nu$=0.61 and $|\mu_{1,2}| = 0.95$

# Atomic resolution imaging: electrons or photons?

**10 keV photons**

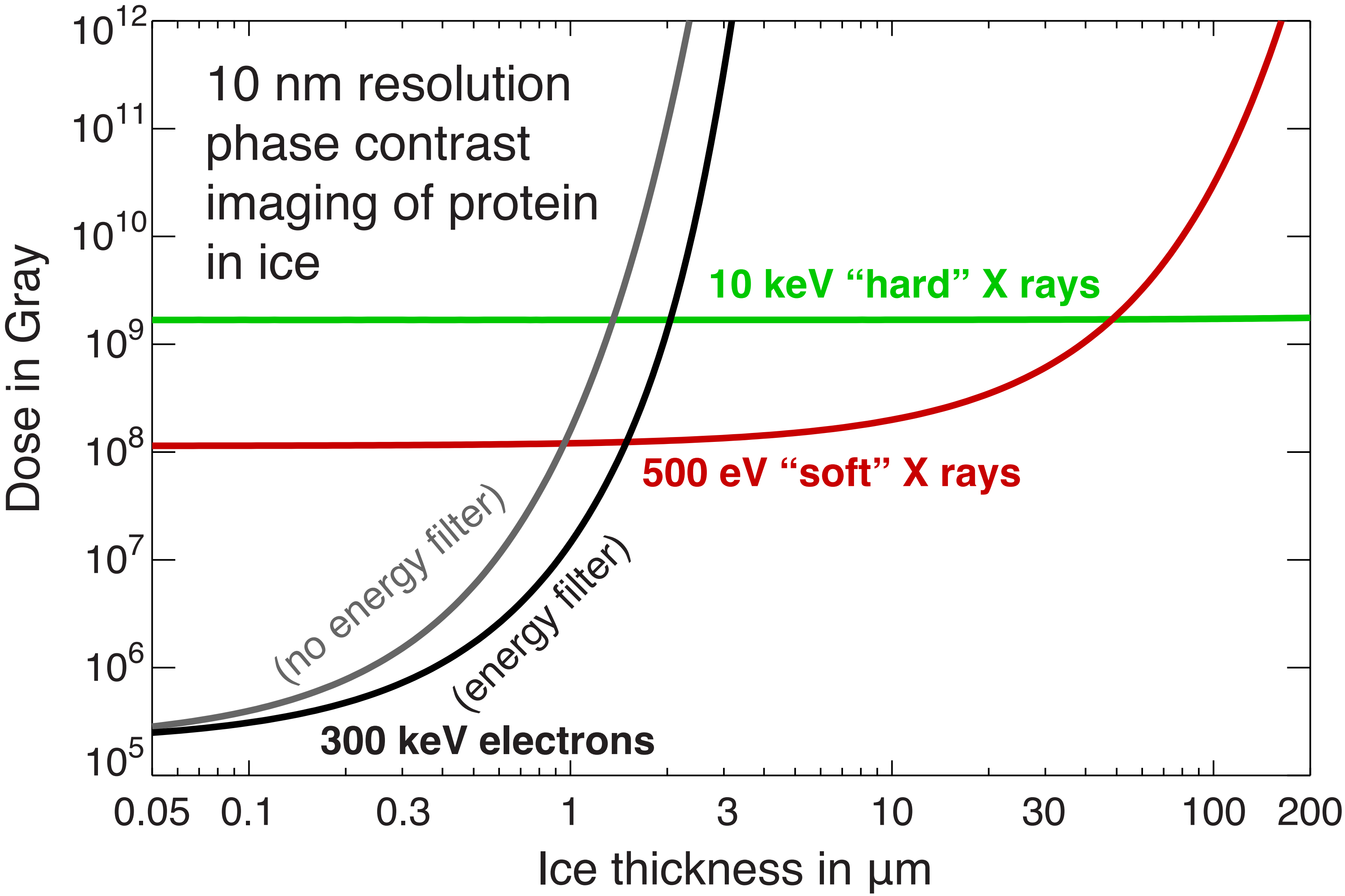
- About 100 absorption events per elastic scatter
- About 10 keV deposited per absorption
- Therefore about $10^6$ eV deposited per elastic scatter
- A thousand scattered photons: $10^3 \cdot 10^6$ eV into (2 Å)$^3$, or $2\times10^{13}$ Gray

**100 keV electrons**

- About 2.5 inelastic scatters per elastic scatter
- About 45 eV deposited per inelastic scatter
- Therefore about $10^2$ eV deposited per elastic scatter
- A thousand scattered electrons: $10^3 \cdot 10^2$ eV into (2 Å)$^3$, or $2\times10^9$ Gray

- Electrons are better than photons for atomic resolution imaging: J. Breedlove and G. Trammel, *Science* **170**, 1310 (1970); R. Henderson, *Q. Rev. Biophys*. **28**, 171 (1995).
- X-ray crystallography's answer: spread the dose out over many identical unit cells
- X-ray Free Electron Lasers: get image in <100 fsec, before damage

# X rays and electrons: another look

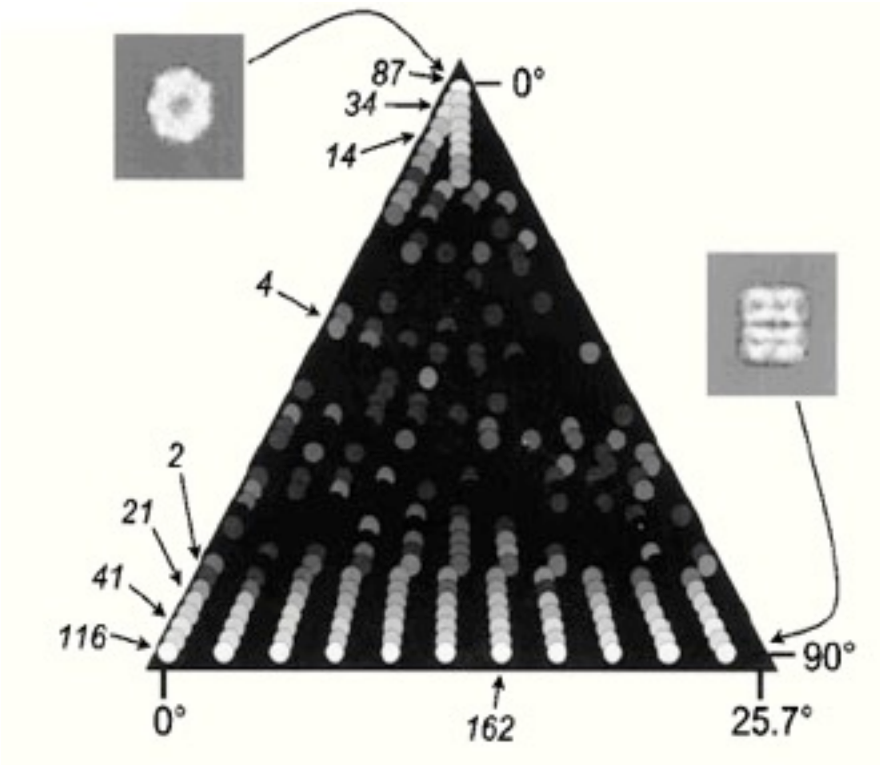


# Forming a tomographic dataset

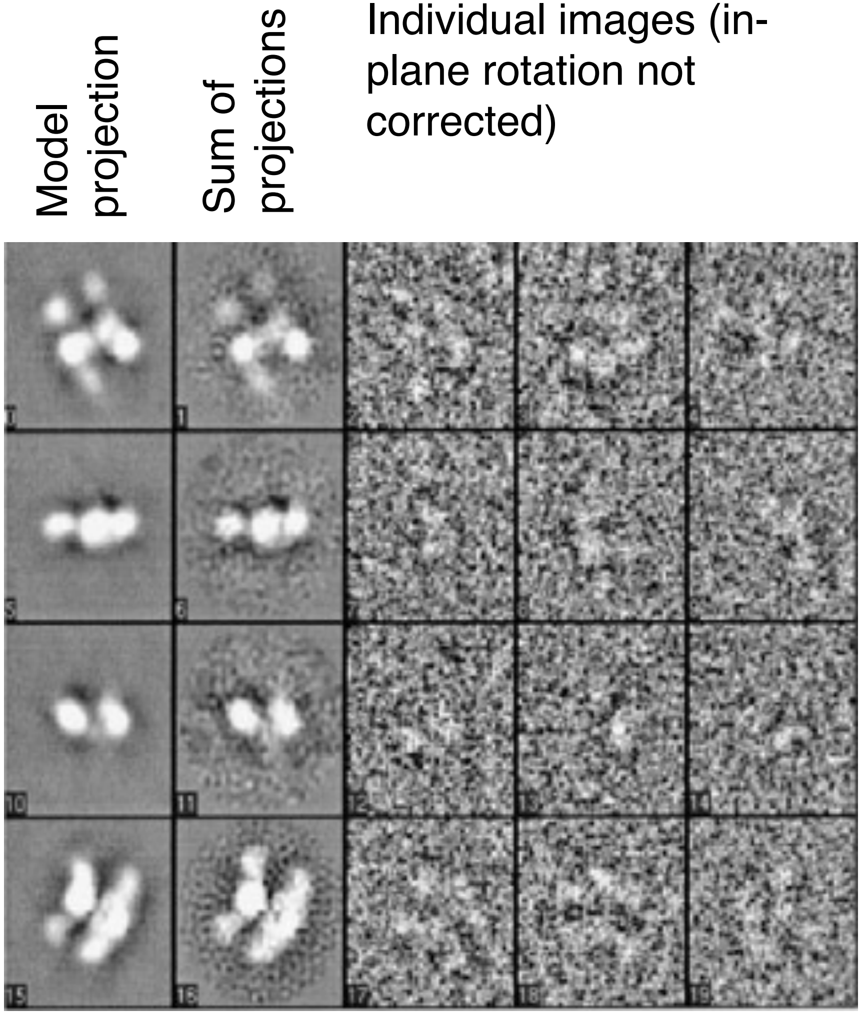
Group similar projections, then iterate:

1. Correlate data to a view of a model
2. Tomographic reconstruction of data to obtain new model

Individual images (in-plane rotation not corrected)



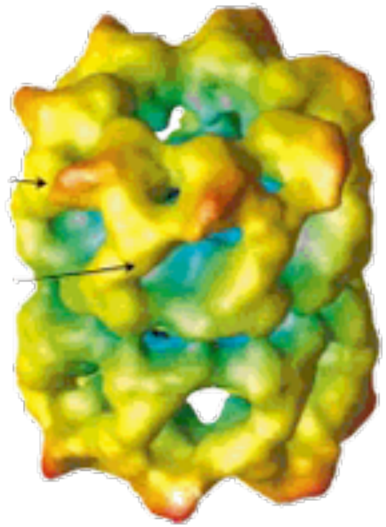

Ludtke *et al.*, *J. Mol. Bio*. **314**, 253 (2001)



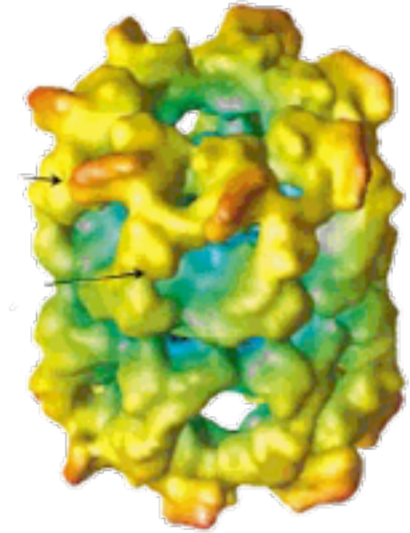

Brink *et al.*, *PNAS* **99**, 138 (2002)

# Single particle imaging example

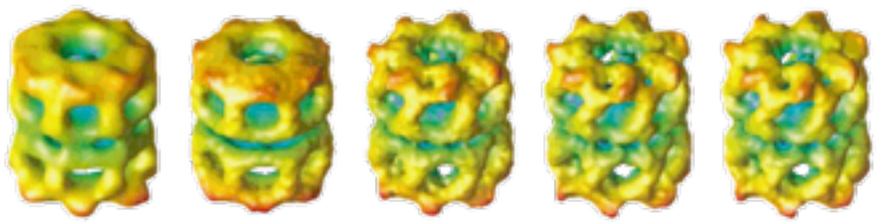
- GroEL: a molecular chaperone to promote protein folding (essentially an inner sanctuary, hidden from chemical environment of a cell). About 17 nm across.
- Ludtke *et al*., *J. Mol. Bio*. **314**, 253 (2001)



Cryo-EM



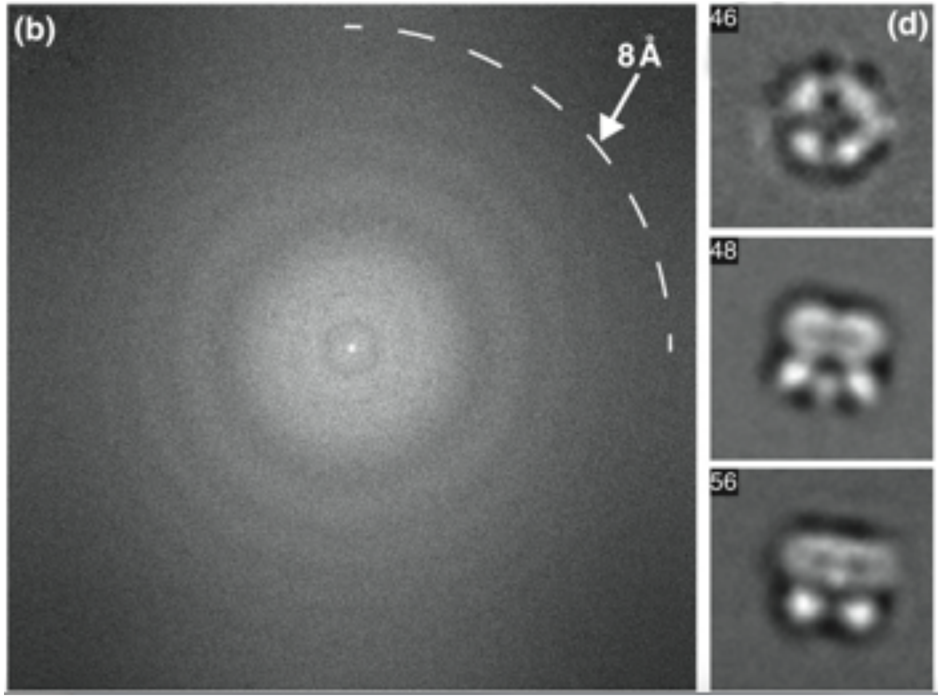
X-ray crystallography blurred to 1.2 nm



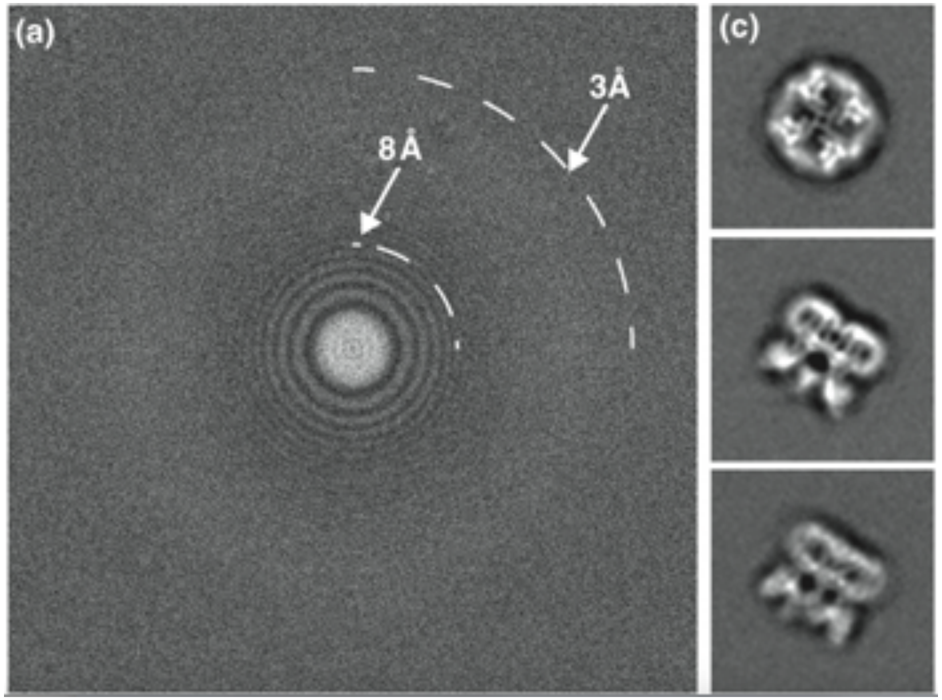
Iter 1 Iter 2 Iter 3 Iter 4 Iter 5

# Improving the raw data with direct electron detectors

Scintillator plus visible detection: slow time response




Fast framing and direct electron detection: cross-correlation to correct for drift and molecular motion




Liao, Cao, Julius, and Cheng, *Current Opinion in Structural Biology* **27**, 1 (2014). See also Li *et al.*, *Nature Methods* **10**, 584 (2013).

# Transient receptor potential V1 (TRPV1) at 3.4 Å

- TRPV1 is the receptor for capsaicin - hot chilis!
- As a membrane protein, it is difficult to crystalize.
- At ~3 Å, one can start fitting molecular models to the image.
- Liao, Cao, Julius, and Cheng, *Nature* **504**, 107 (2013)