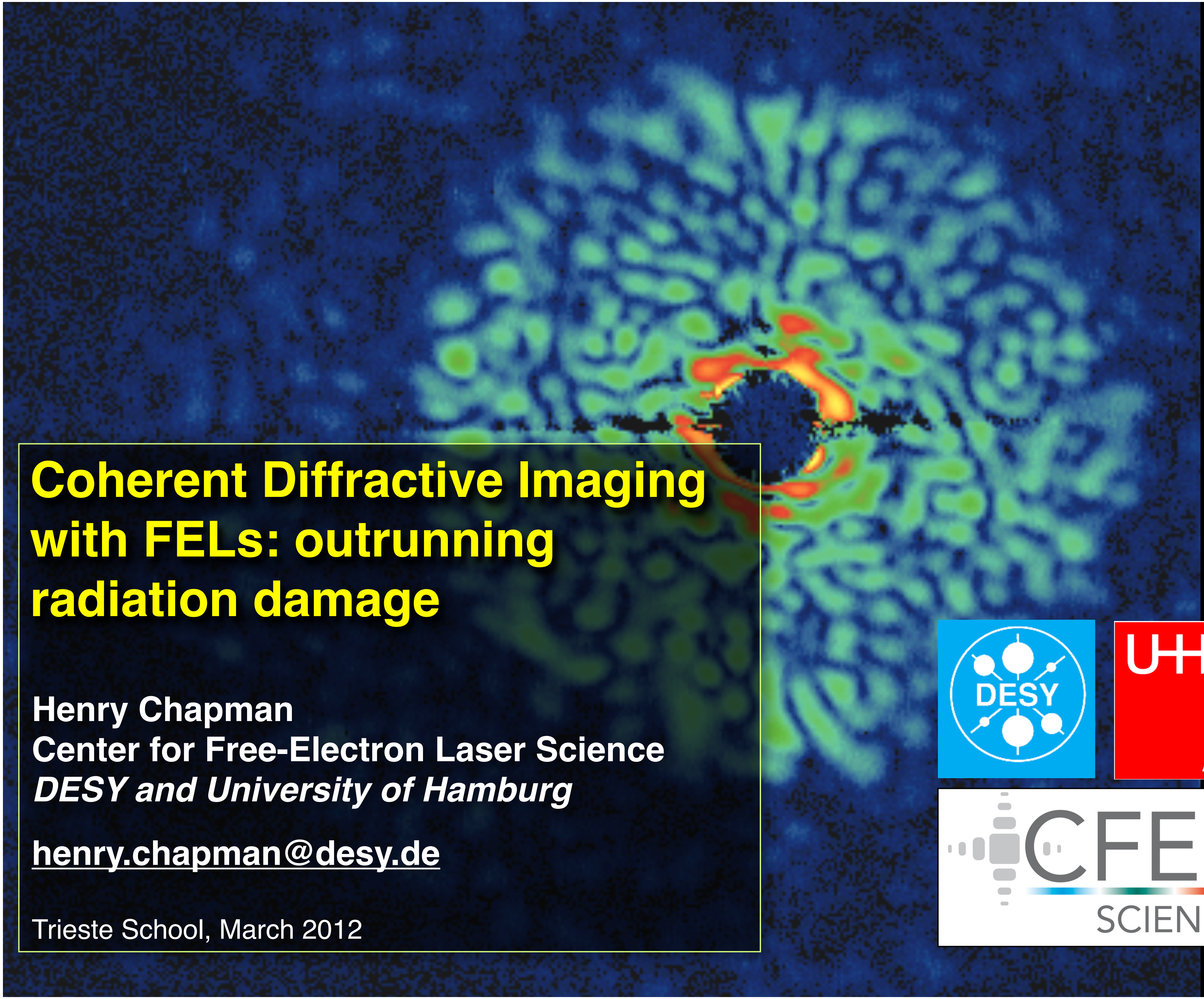
2332-24

School on Synchrotron and FEL Based Methods and their Multi-Disciplinary Applications

19 - 30 March 2012

Coherent Diffractive Imaging with FELs: outrunning radiation damage

Henry Chapman
DESY and University of Hamburg
Germany



Coherent Diffractive Imaging with FELs: outrunning radiation damage

Henry Chapman
Center for Free-Electron Laser Science
DESY and University of Hamburg

henry.chapman@desy.de

Trieste School, March 2012

Free electron lasers open up new frontiers in X-ray science

Unique properties

Ultrashort pulses
(20 - 200 fs)

Intense pulses
(10^{12} - 10^{13} photons/pulse)

X-ray radiation
(50eV - 12keV)
(32nm - 1Å)

High peak power
(200 μJ/pulse to 4 mJ/pulse in 25 fs)

Coherence
('Monochromatic',
transverse coherence)

Repetition rate: 120 Hz (LCLS)
27 kHz (XFEL)

Unique capabilities

- Beating radiation damage
- Freeze atomic motion
- Freeze electron states

- Single-shot studies
  (Variation in behaviour, not just the average)

- Penetrating power
- Spatial resolution
- Inner shell atomic physics

- New regimes in X-ray matter interaction

- X-ray diffraction
  (Coherent imaging, XPCS)
- Diffraction limited focus

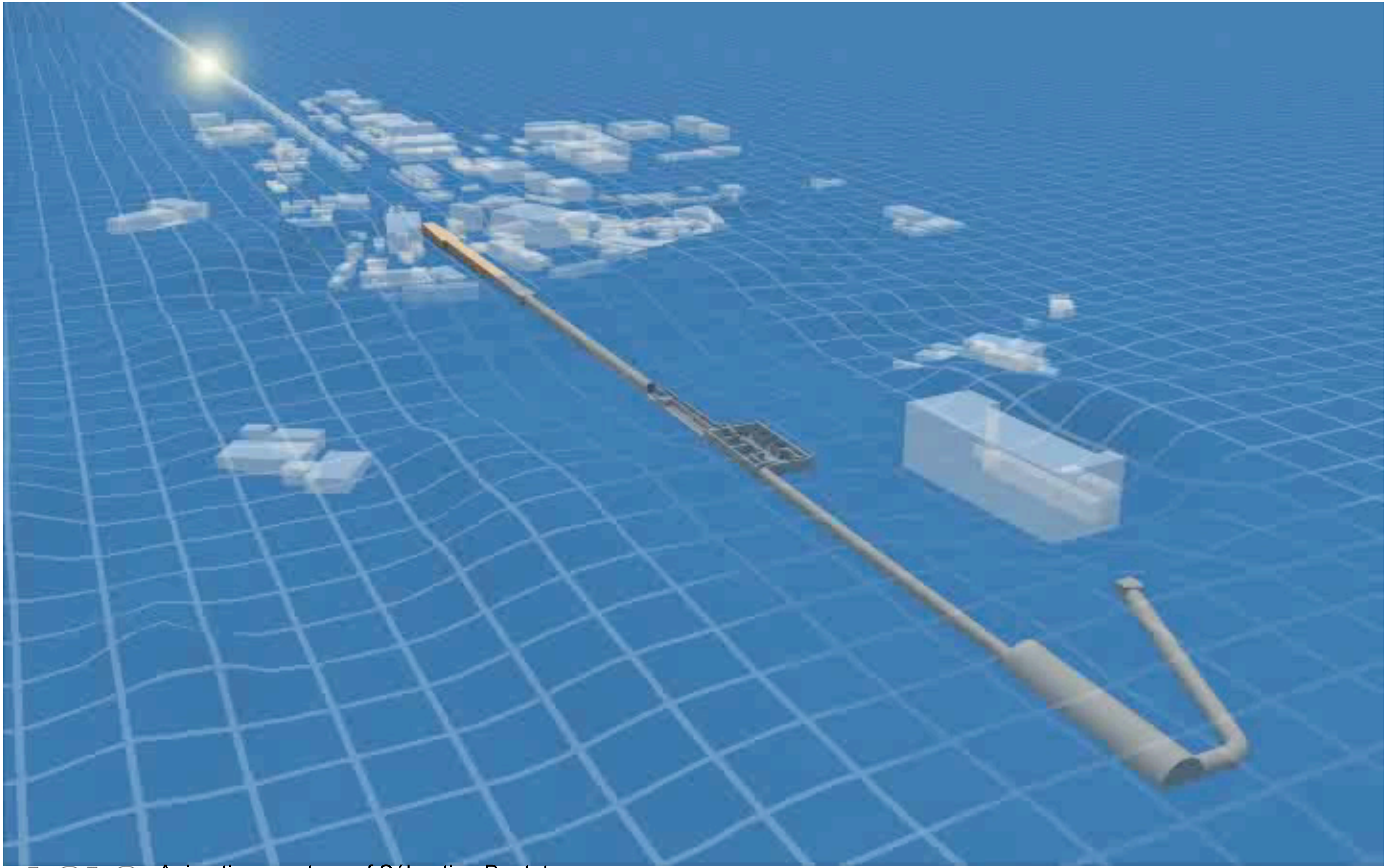
Repeat experiment millions of times

Unique applications

- Biological imaging
  (beating radiation damage)
- Ultrafast structural studies
  (where are the atoms?)
- Ultrafast dynamics
  (sub-ps density changes)
- Femtochemistry
  (valence electrons)
- Magnetism
  (electron spin)

- Ideal probe for:
  - Biomolecules
  - Electron dynamics
  - Molecular physics
  - Materials dynamics
  - Melting and recrystal.
  - Nucleation
  - Shocked materials
  - Solid state physics
  -

"Diffraction before destruction" imaging introduces a new sample into the beam on each FEL pulse



Animation courtesy of Sébastien Boutet,
CXI instrument scientist, SLAC

FLASH Experiments:

LLNL: A. Barty, M. J. Bogan, M. Frank, S. P. Hau-Riege, S. Marchesini, B. W. Woods, S. Bajt, W. H. Benner, R. London, R. W. Lee, E. Spiller, A. Szoke

U. Uppsala: J. Hajdu, S. Boutet, M. Bergh, C. Caleman, G. Huldt, M. M. Seibert, F. R. N. C. Maia, N. Timneanu, D. van der Spoel, M. Svenda, I. Andersson, J. Andreasson, D. Westphal, B. Iwan

DESY: E. Plonjes, M. Kuhlmann, R. Treusch, S. Dusterer, T. Tschentscher, J. R. Schneider

TU Berlin: T. Moller, C. Bostedt, M. Hoener

LCLS Experiments:

DESY: A. Barty, T. White, A. Aquila, J. Schulz, D. P. DePonte, A. Martin, K. Nass, F. Stellato, M. Liang, M. Barthelmess, C. Caleman, F. Wang, S. Bajt, L. Gumprecht, S. Stern, L. Galli, K. Beyerlein, G. Potdevin, H. Graafsma

Arizona State University: J. C. H. Spence, P. Fromme, R. Fromme, M. S. Hunter, R. A. Kirian, U. Weierstall, R. B. Doak, K. E. Schmidt, X. Wang, I. Grotjohann

U. Uppsala: F. R. N. C. Maia, J. Hajdu, N. Timneanu, M. M. Seibert, J. Andreasson, A. Rocker, B. Iwan, D. Westphal, O. Jonsson, M. Svenda, I. Andersson

Max Planck Society: I. Schlichting, L. Lomb, R. L. Shoeman, S. Epp, R. Hartmann, D. Rolles, A. Rudenko, L. Foucar, N. Kimmel, G. Weidenspointner, P. Holl, B. Rudek, B. Erk, C. Schmidt, A. Homke, C. Reich, D. Pietschner, L. Struder, G. Hauser, H. Gorke, J. Ullrich, S. Herrmann, G. Schaller, F. Schopper, H. Soltau, K.-U. Kuhnel, R. Andritschke, C. Schroter, F. Krasniqi, M. Bott, T. R. M. Barends, H. Hirsemann

SLAC: S. Boutet, M. Bogan, J. Krzywinski, C. Bostedt, M. Messerschmidt, J. Bozek, C. Hampton, R. Sierra, D. Starodub, G. J. Williams

LLNL; S. Hau-Riege, M. Frank

LBNL: J. M. Holton, S. Marchesini

European XFEL: N. Coppola, J. Schulz, A. Aquila

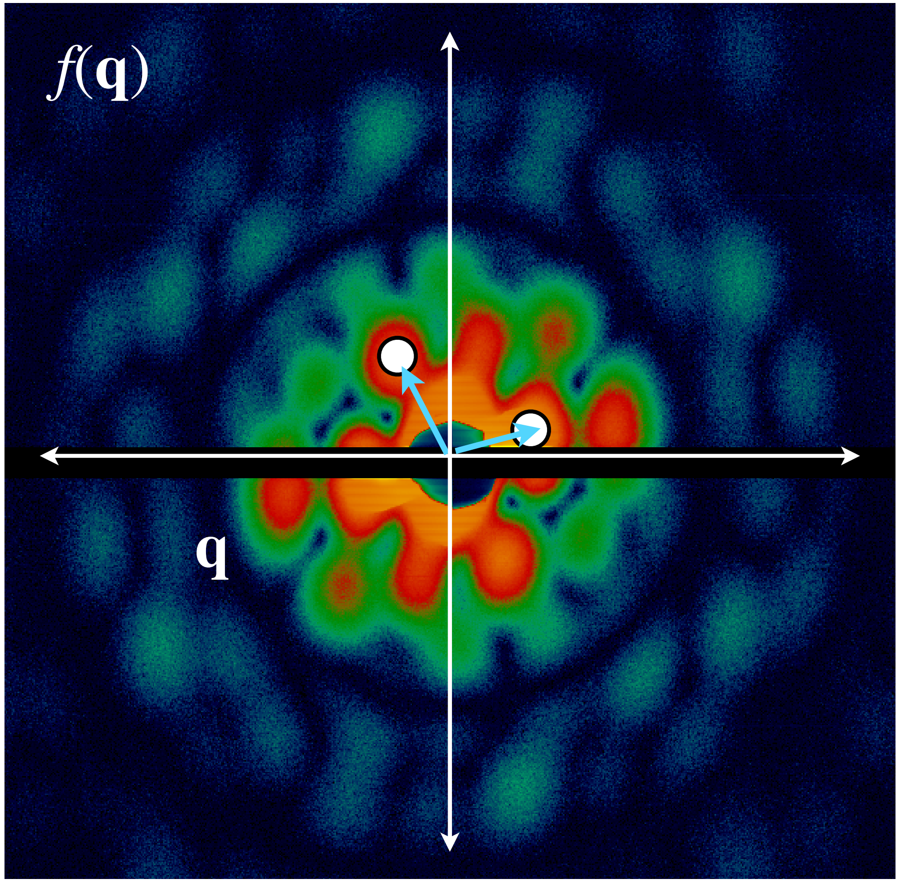
Gotheburg: R. Neutze

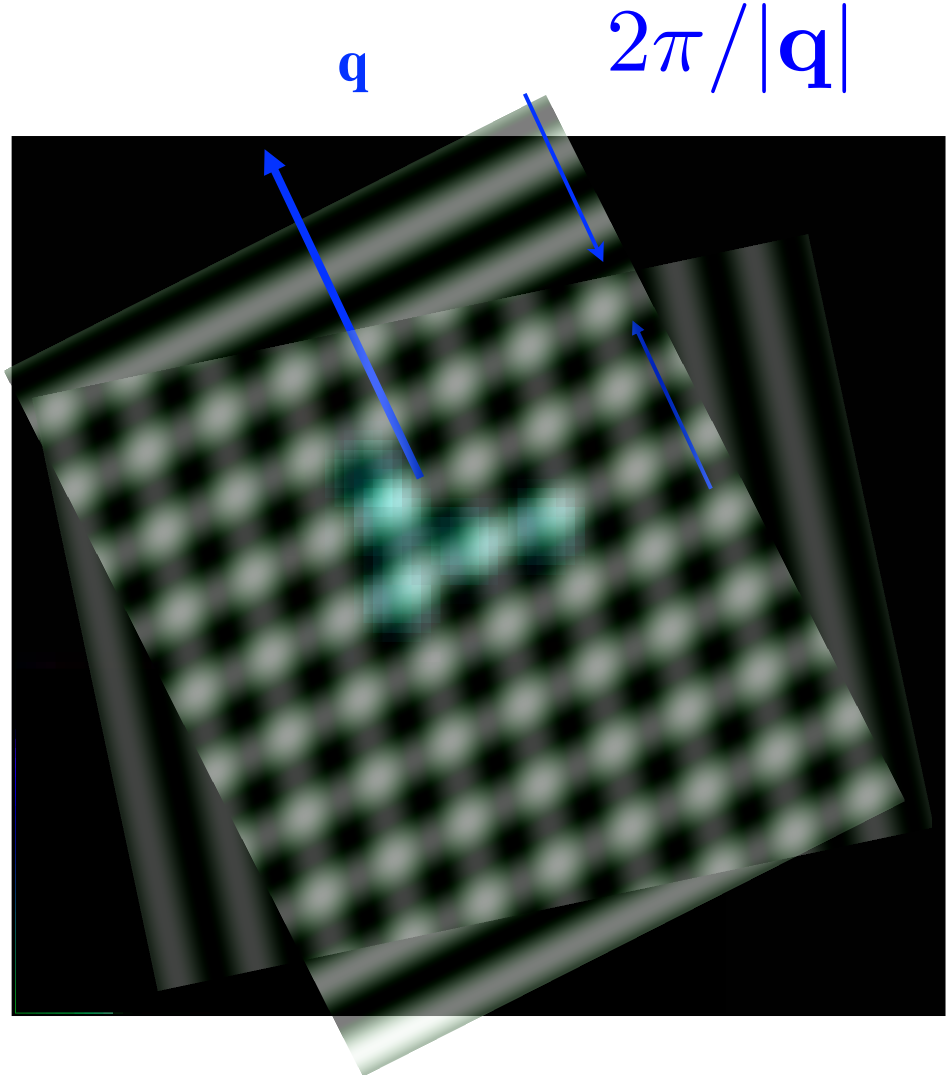
TU Berlin: S. Schorb, D. Rupp, M. Adolph, T. Gorkhover

U. Hamburg C. Betzel, L. Redecke

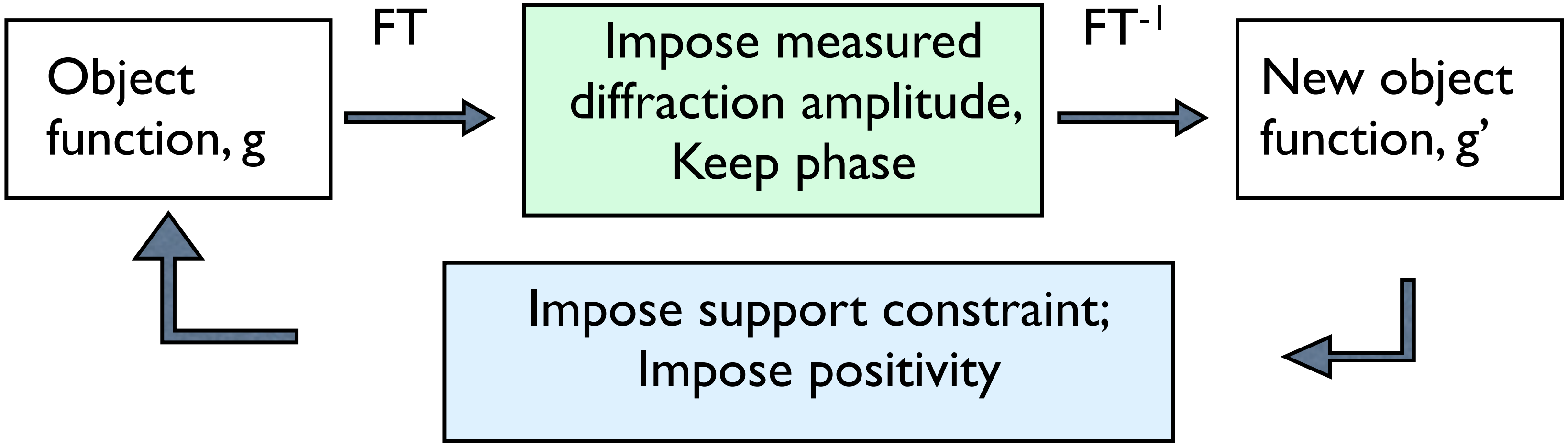
U. Tübingen: M. Duszenko, R.Koopman, K. Cupelli

Images are synthesized from the Fourier amplitudes





Phase retrieval can be accomplished with iterative transform algorithms



Object function, g

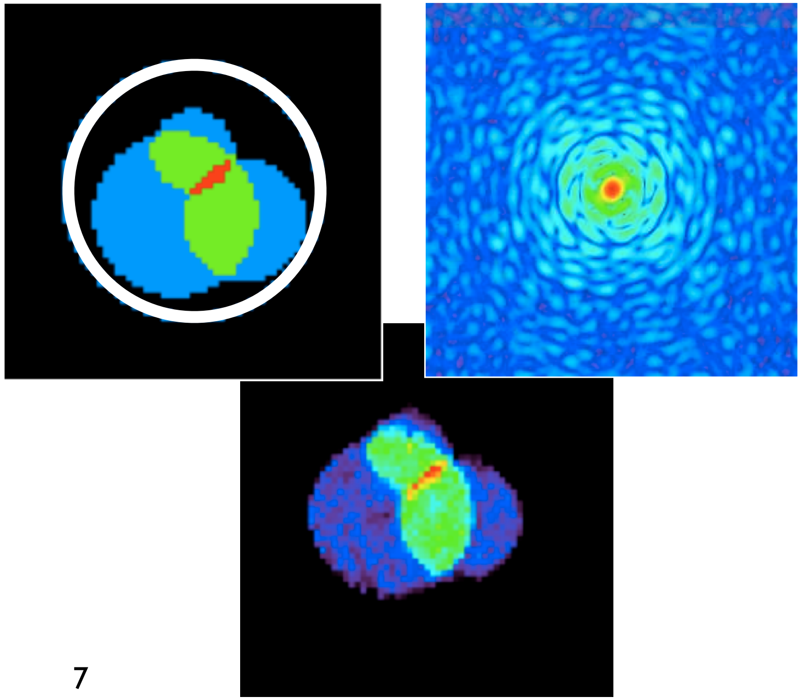
FT

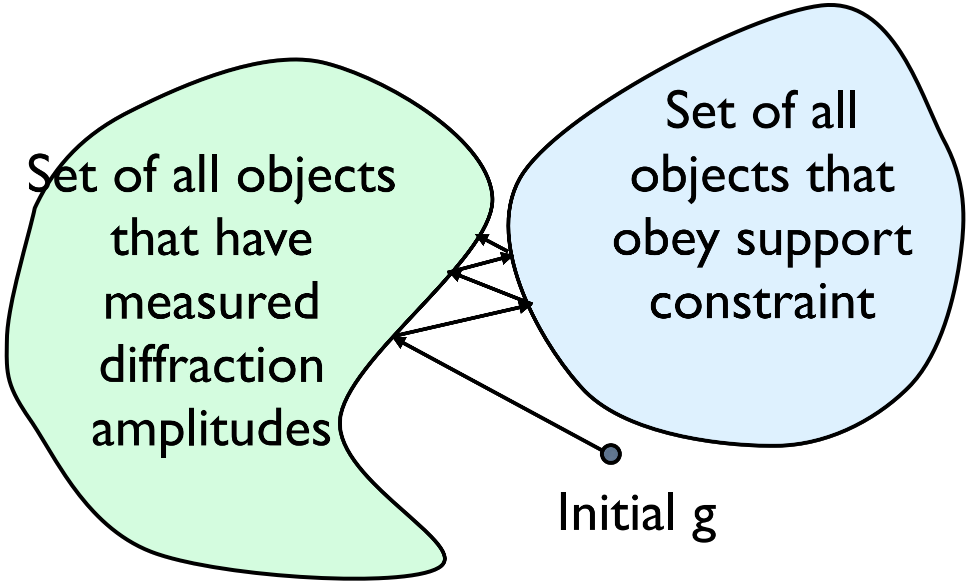
Impose measured diffraction amplitude, Keep phase

FT^{-1}

New object function, g'

Impose support constraint; Impose positivity



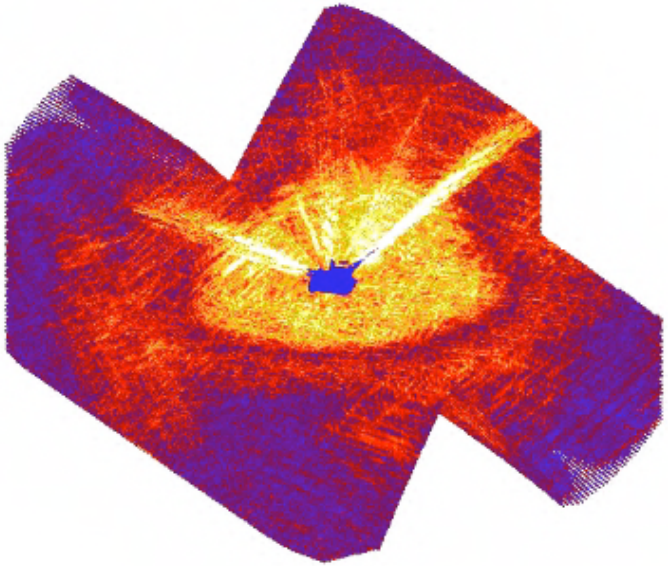


Set of all objects that have measured diffraction amplitudes

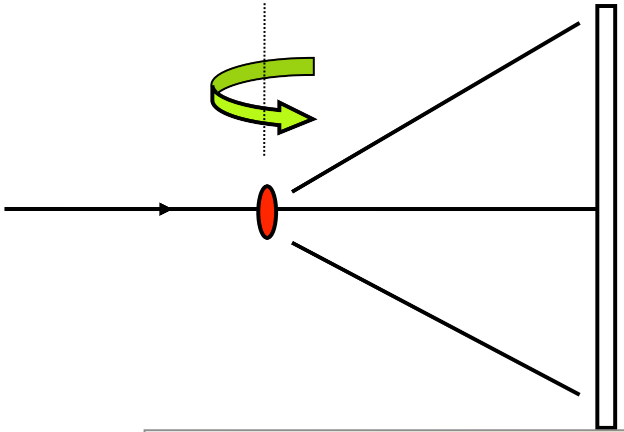
Set of all objects that obey support constraint

Initial g

We have reconstructed a 3D X-ray image of a non-crystalline object at 10 nm resolution

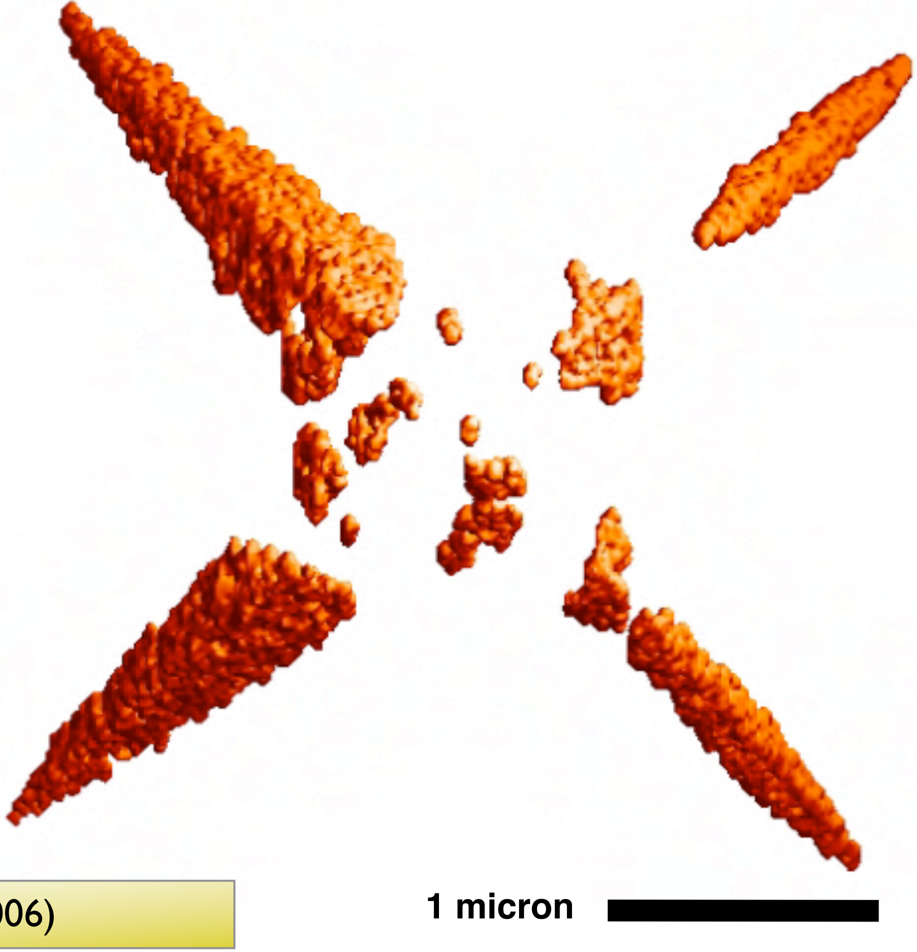


Coherent X-ray diffraction data, rotating the sample -70 to +70 degrees (5×10^8 data points)

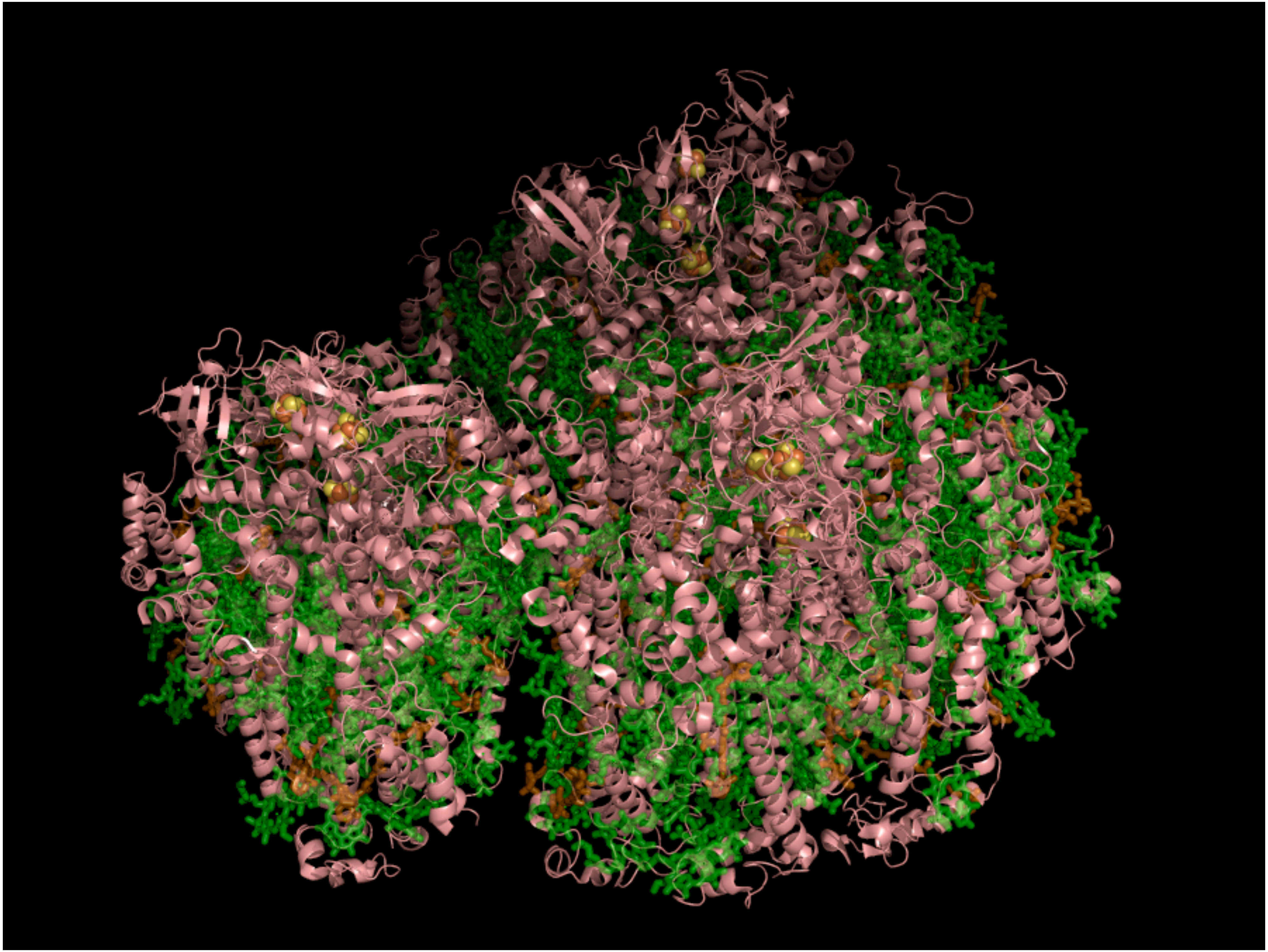


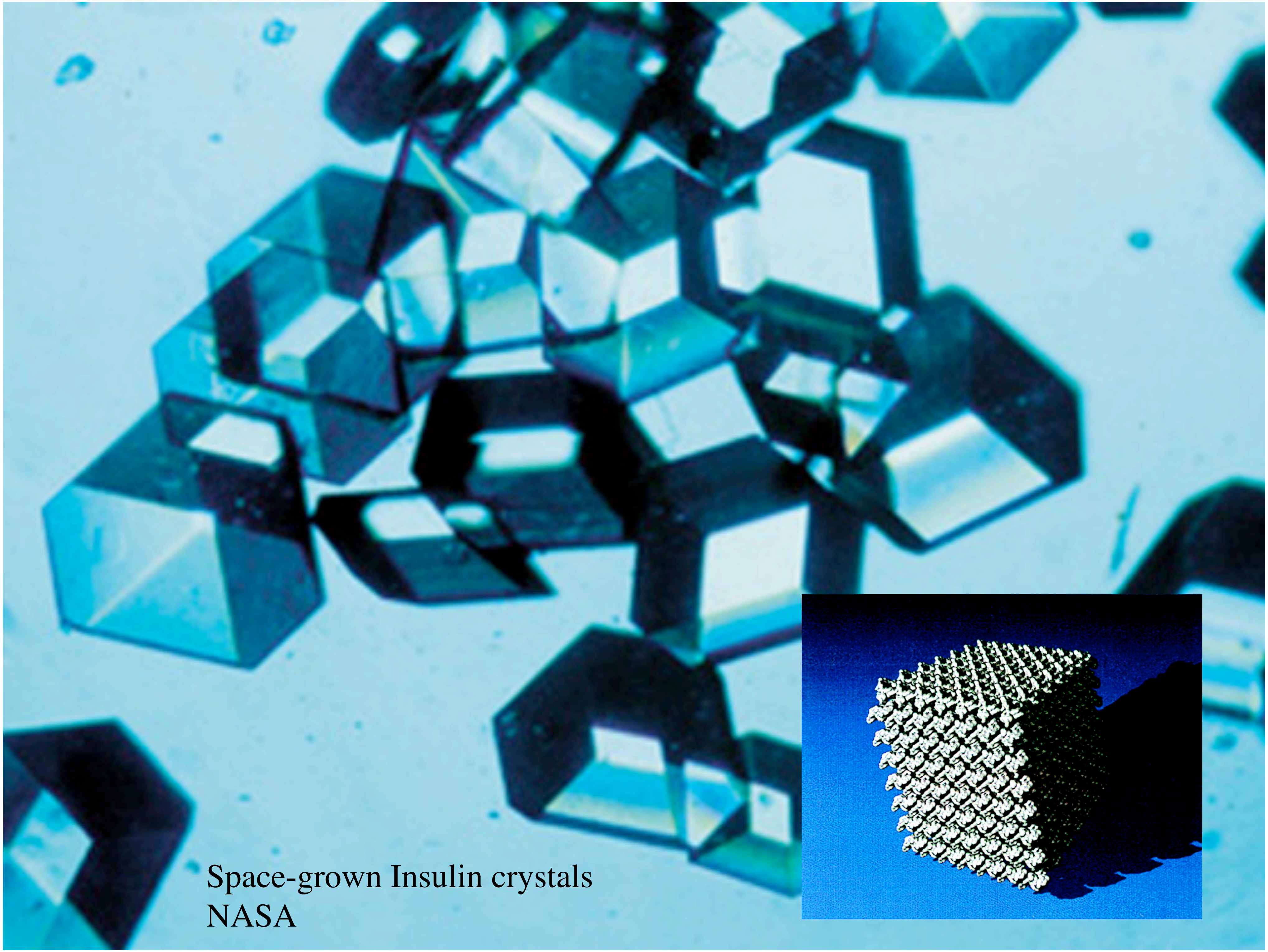
Coherent X-ray diffraction data λ =1.6 nm, from a sample of 50-nm gold spheres arranged on a pyramid on a ***synchrotron***

Complete image reconstruction achieved, without any prior knowledge, using our "**shrinkwrap**" algorithm, **parallelized** for 3D on 32-CPU cluster. Resolution = 10 nm



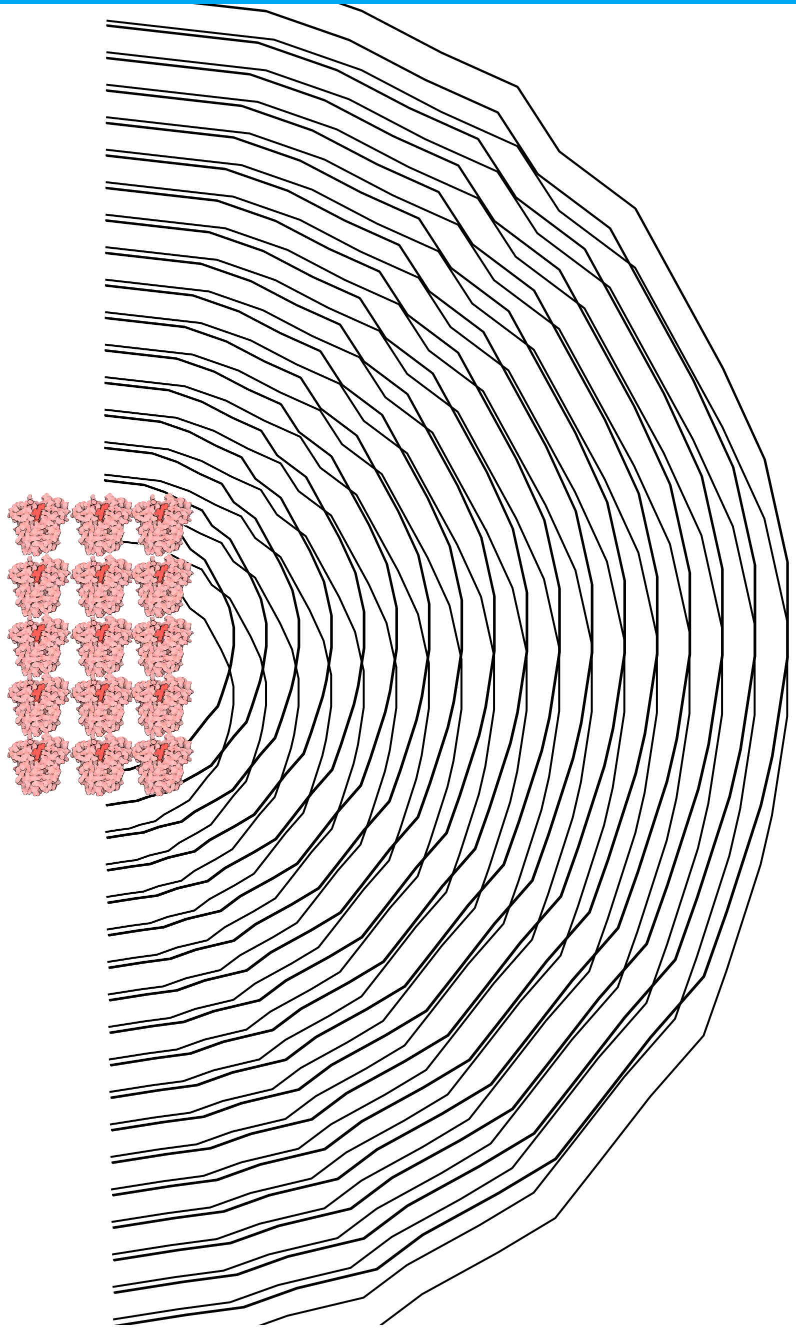
H. Chapman, et al., JOSA A **23** 1169 (2006)

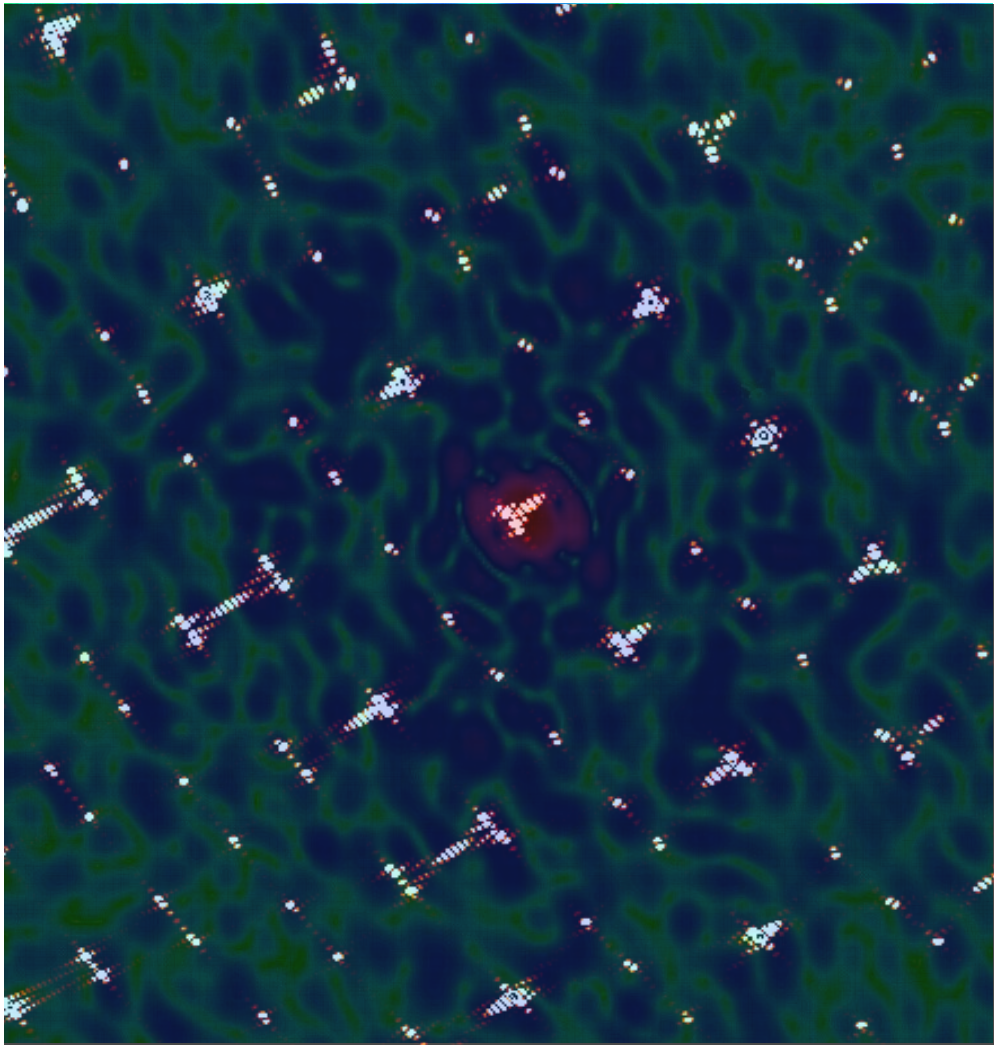




Space-grown Insulin crystals
NASA

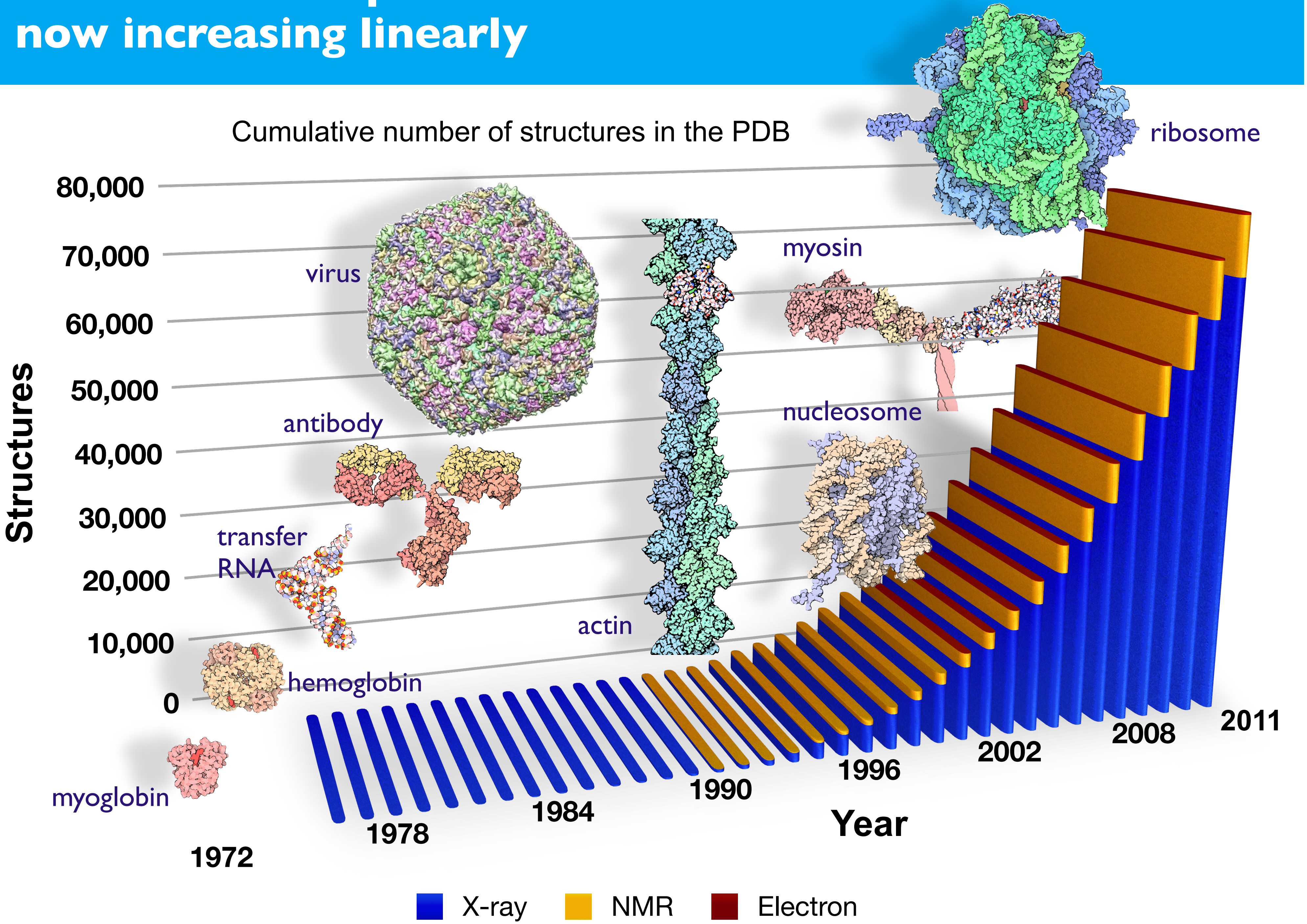
The weak X-ray scattering cross section requires amplification from the crystal





signal is proportional to the number of unit cells

The number of protein structures solved is now increasing linearly



High radiation dose causes changes in molecular structure

Elspeth Garman, U. Oxford
micrograph of crystal after exposing to x-rays and warming up

Tolerable dose in cryogenically-cooled crystals is 30 MGy

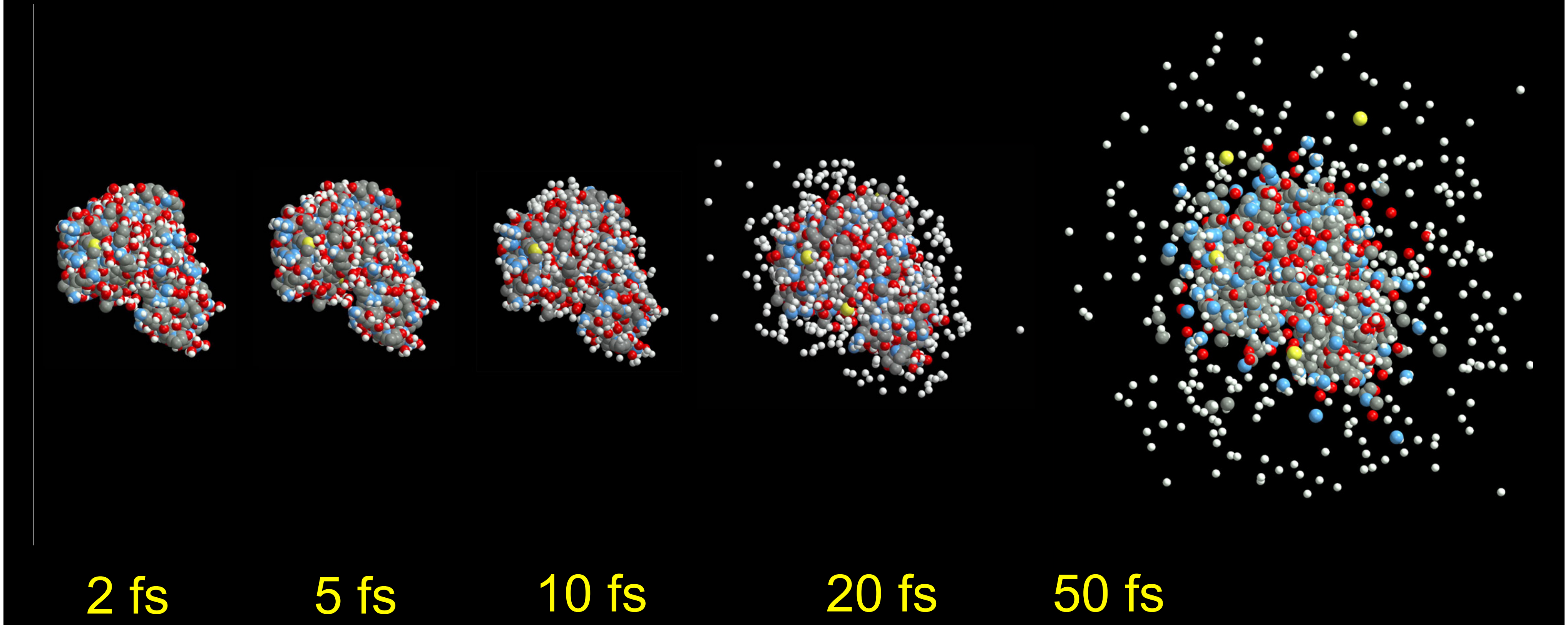
1 Gy = 1 J/kg

30 MGy ≈ 0.3 eV / Da
≈ 0.02 eV / atom

(about one ionization per 20 amino-acid residues)

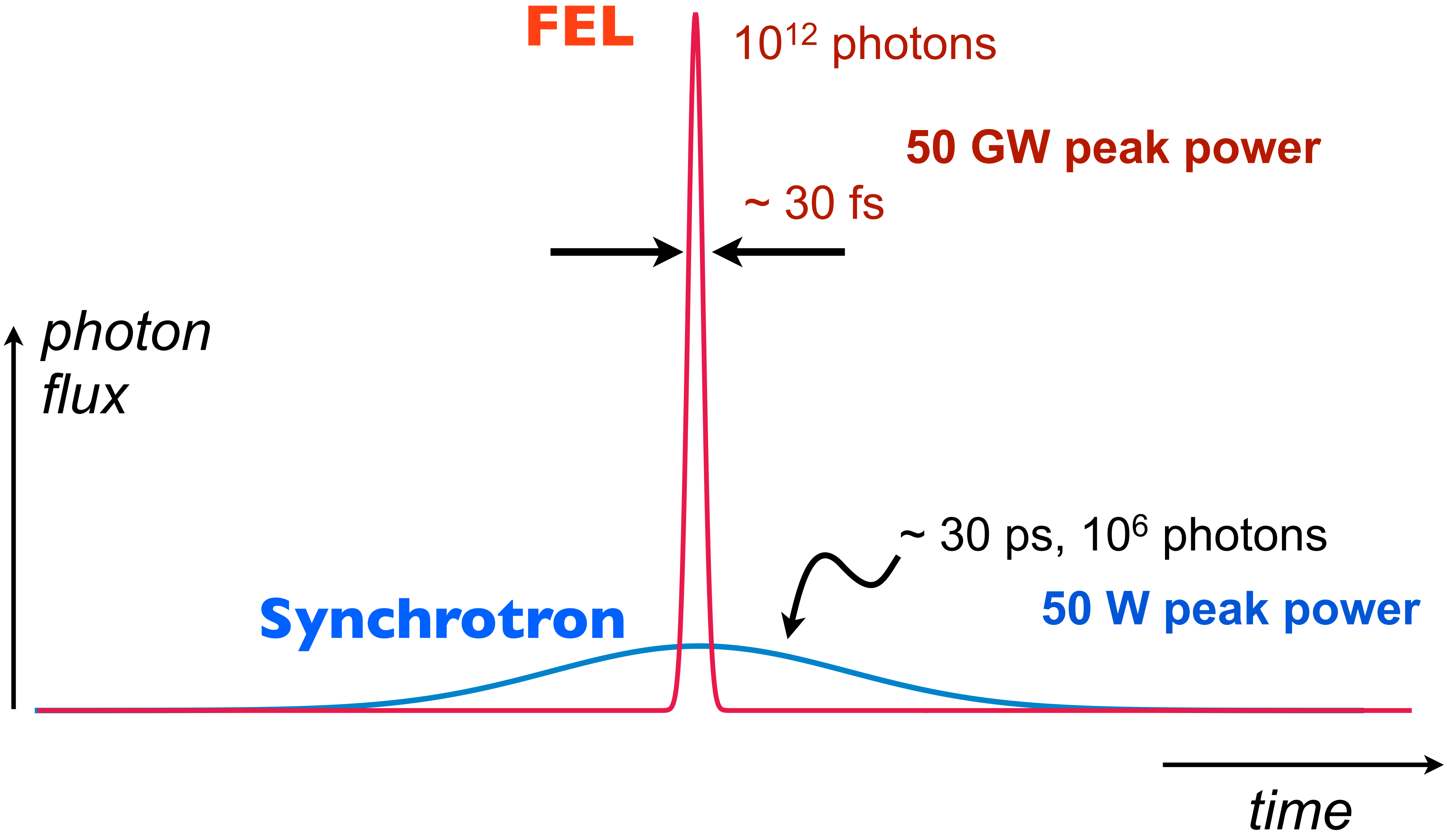
≈ 6×10^{10} ph/μm^2

X-ray free-electron lasers may enable atomic-resolution imaging of biological macromolecules

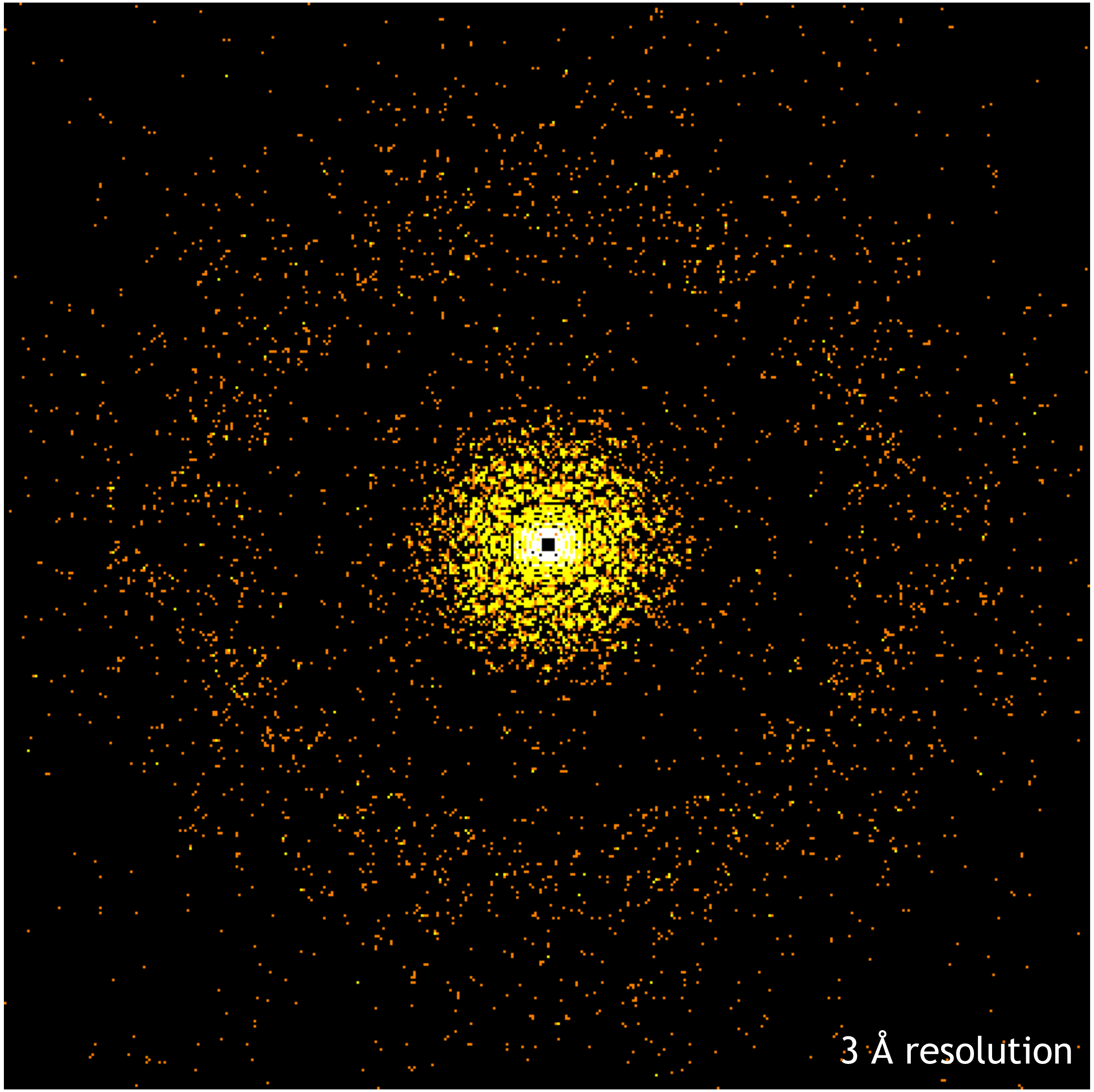


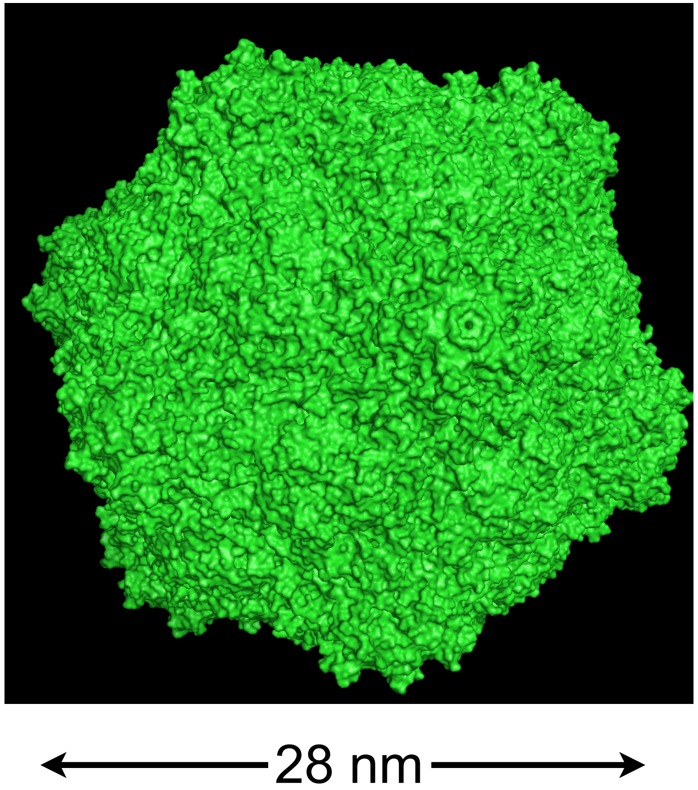
R. Neutze, R. Wouts, D. van der Spoel, E. Weckert, J. Hajdu, Nature **406** (2000)

X-ray FELs are a billion times brighter than synchrotrons



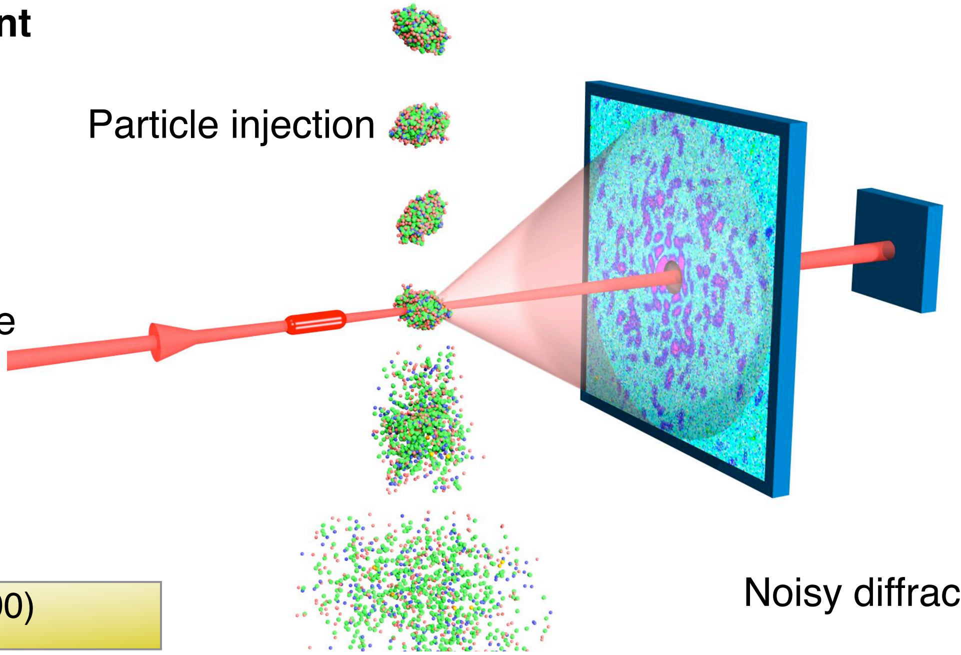
Atomic-resolution diffraction from single particles should be possible with 10^{14} ph/μm^2





X-ray free-electron lasers may enable atomic-resolution imaging of biological macromolecules

One pulse, one measurement



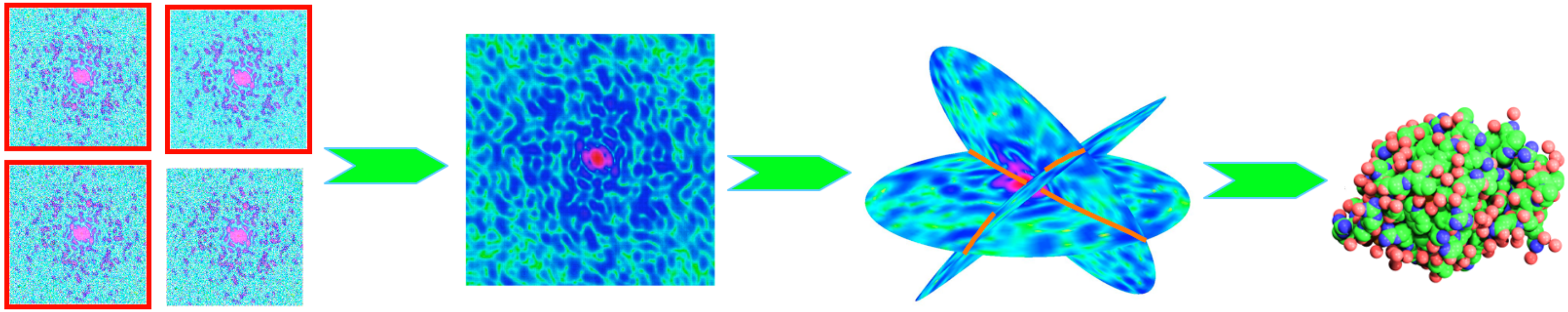
Particle injection

XFEL pulse

Noisy diffraction pattern

R. Neutze et al, Nature **406** (2000)

Combine 10^5-10^7 measurements



Classification

Averaging

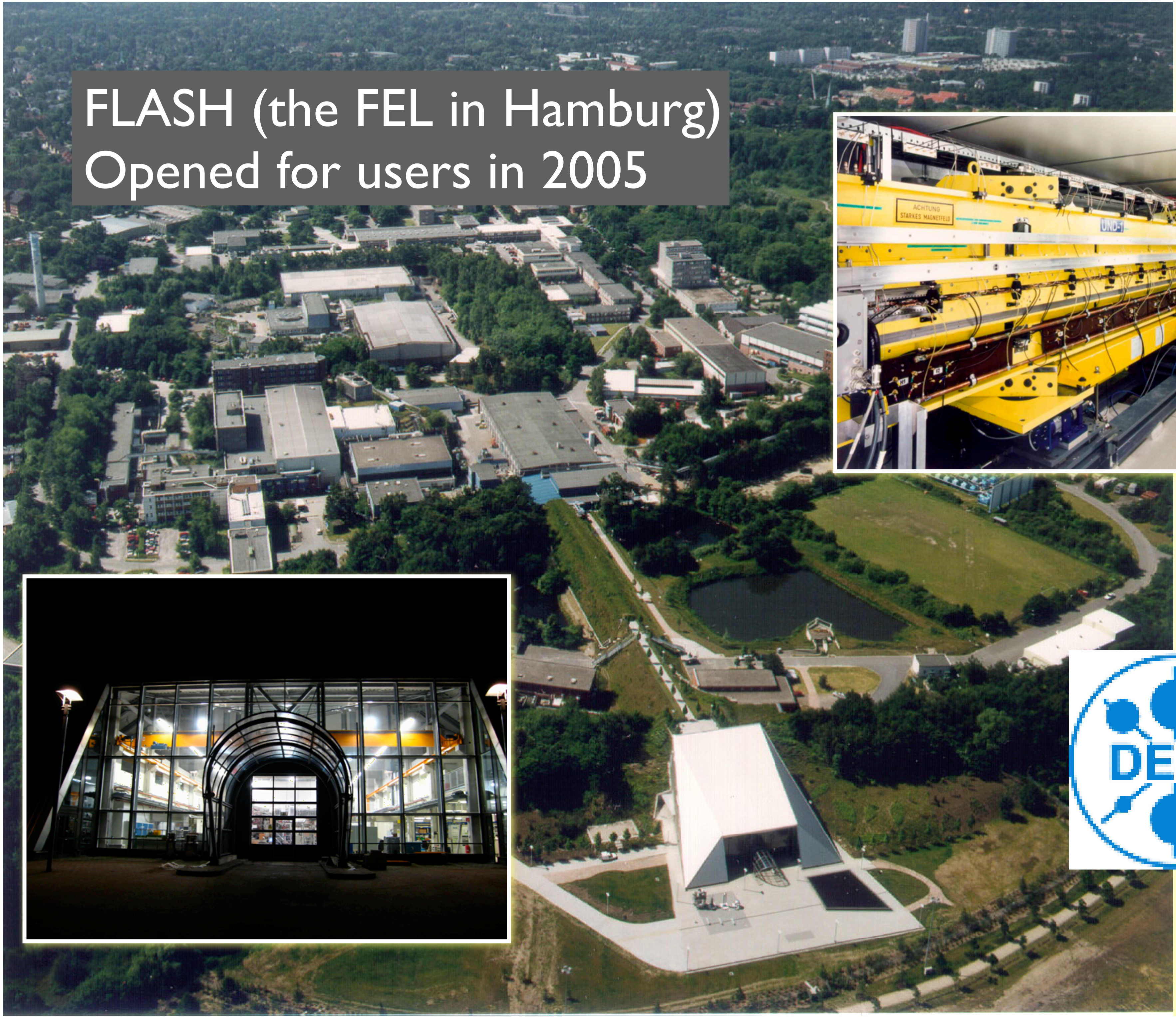
Orientation

Reconstruction

G. Huldt et al, J. Struct. Biol **144** (2003)

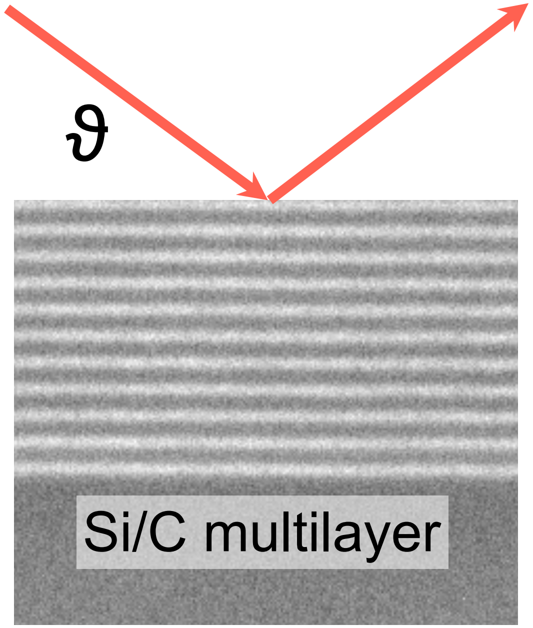
J. Miao, Hodgson, Sayre, PNAS **98** (2001)

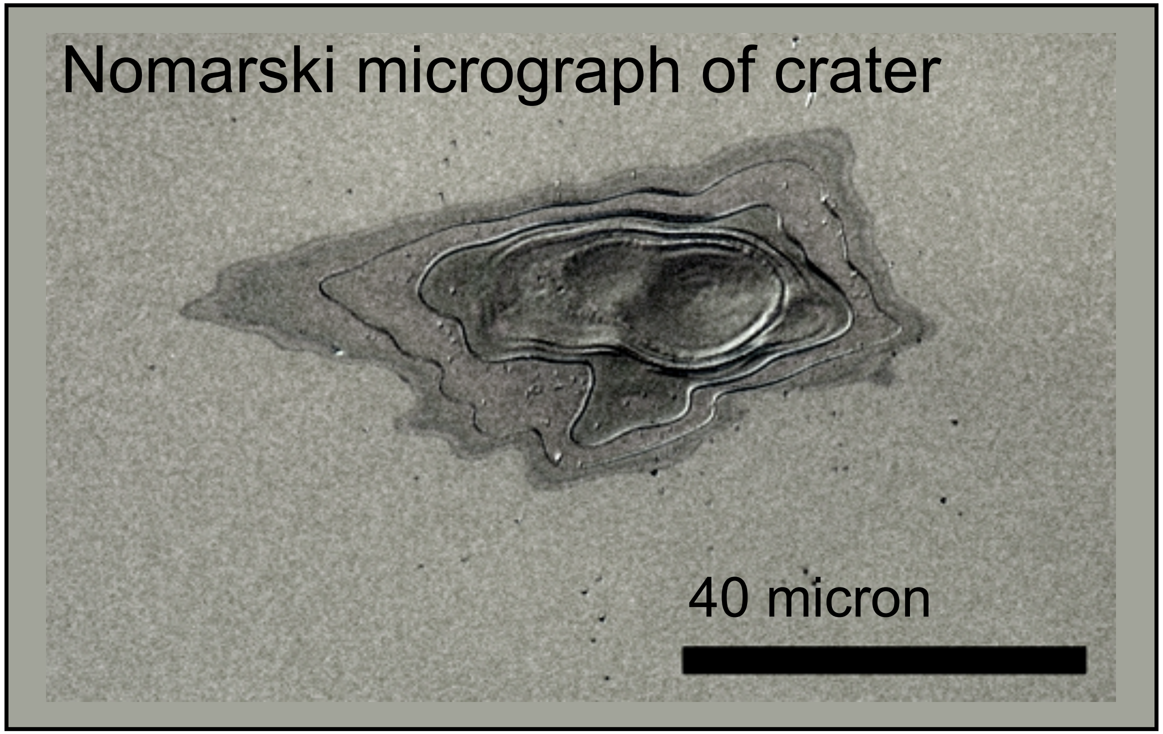
FLASH (the FEL in Hamburg)
Opened for users in 2005



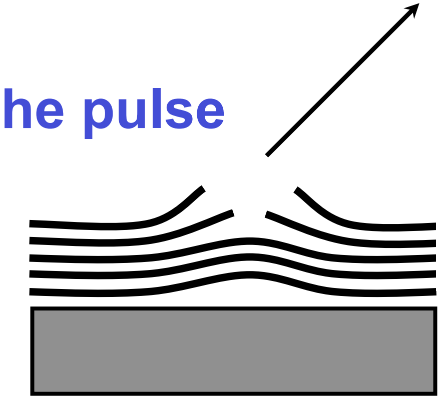
DESY

First EUV-FEL experiments show that pulses are indeed destructive





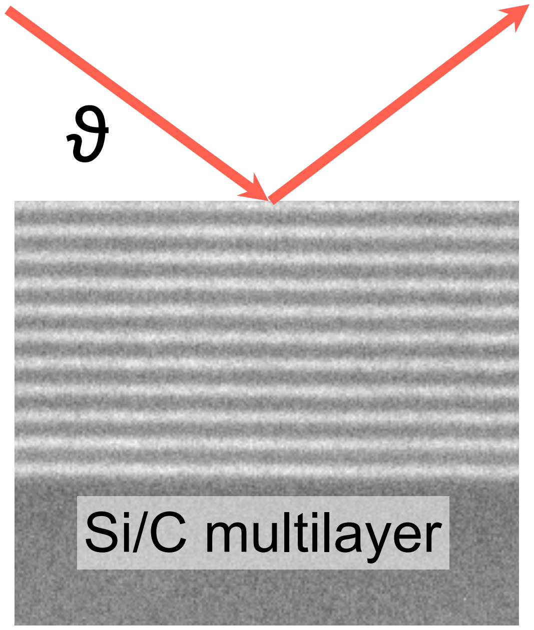
After the pulse

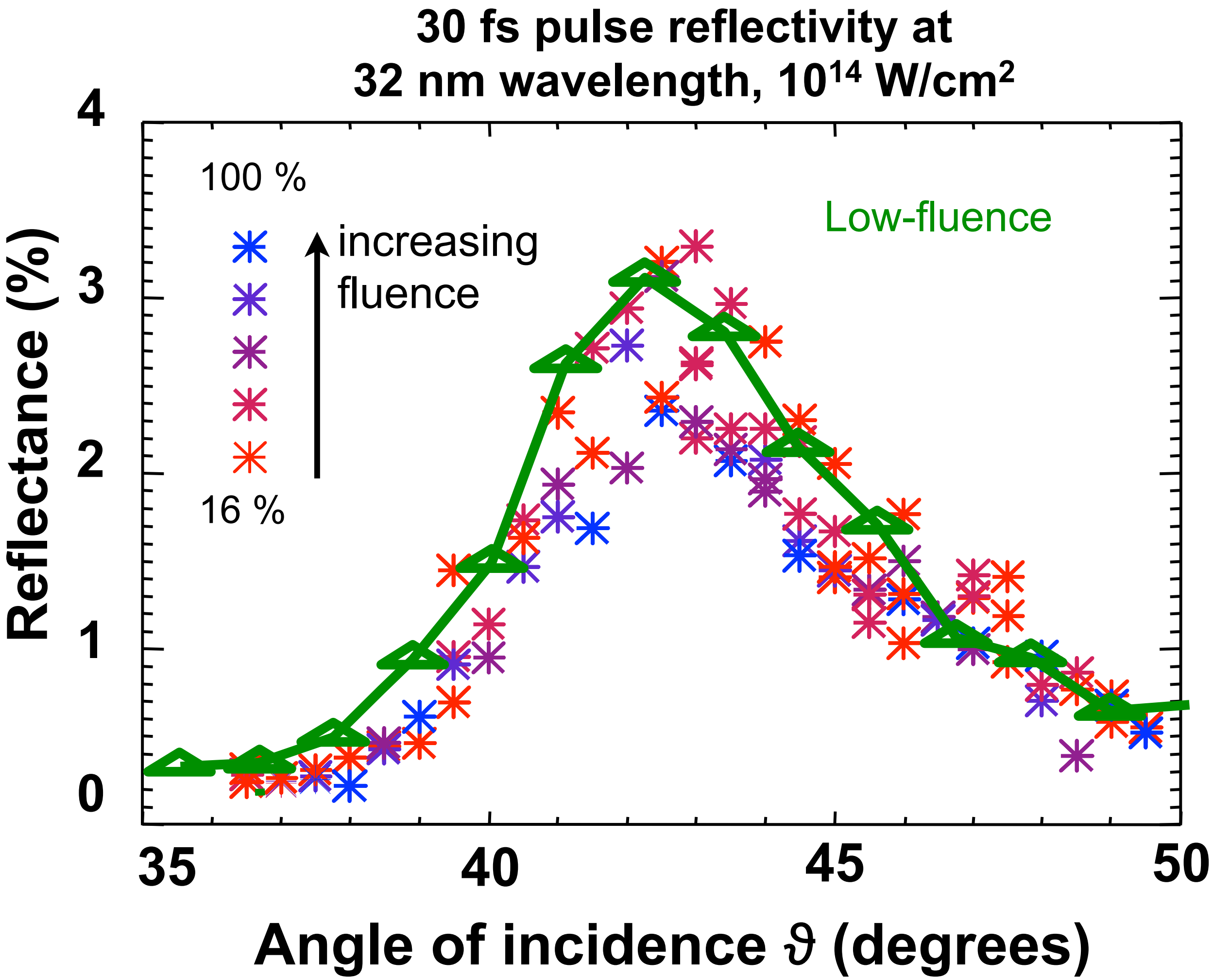


Plasma forms, layers ablate

Electron temperature reaches 28 eV (300,000 K)

First EUV-FEL experiments show that structural information can be obtained before destruction

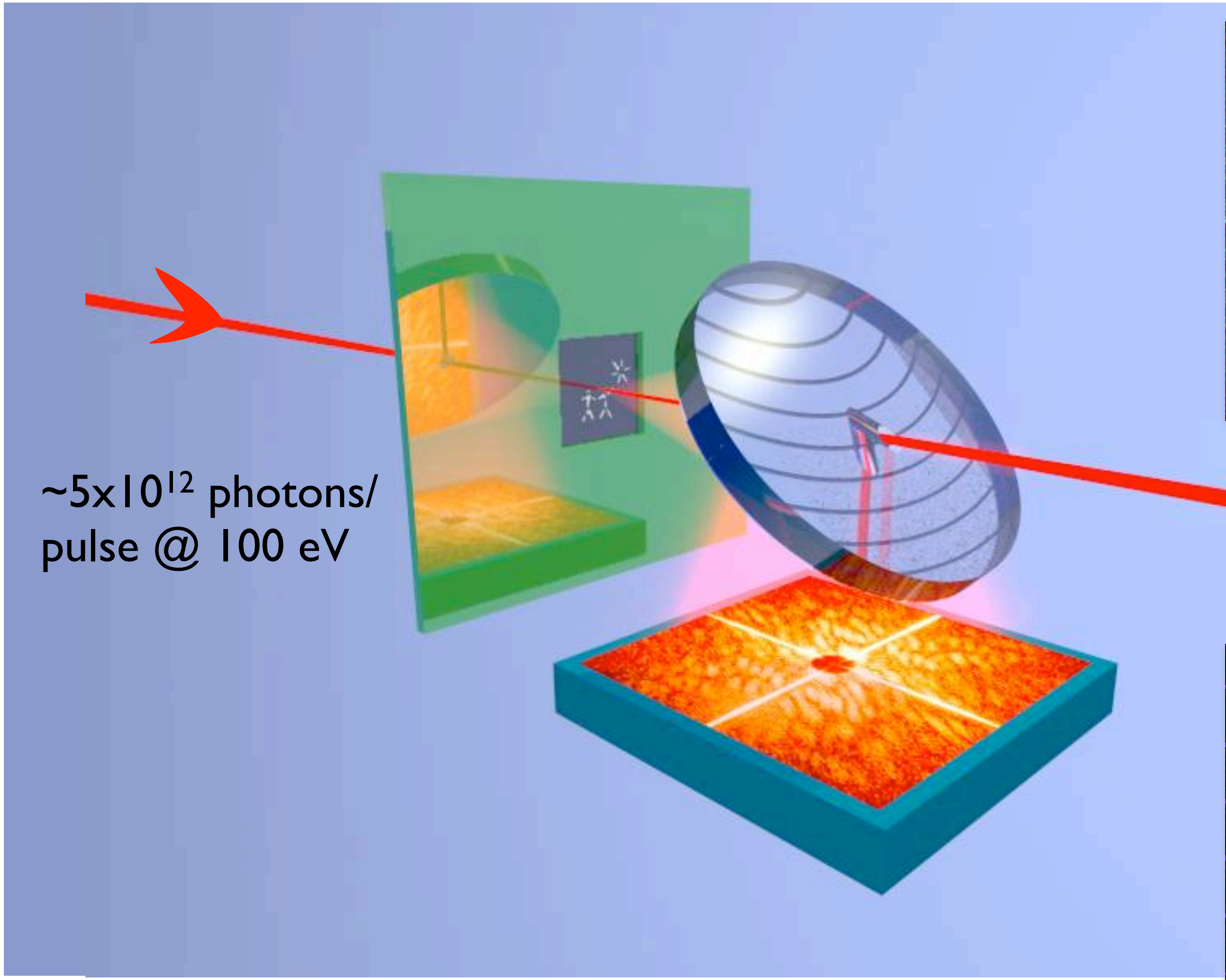




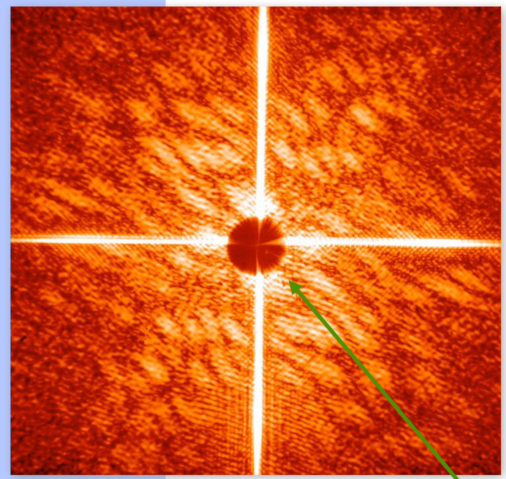
Reflectivity unchanged

Multilayer *d* spacing not changed by more than 0.3 nm

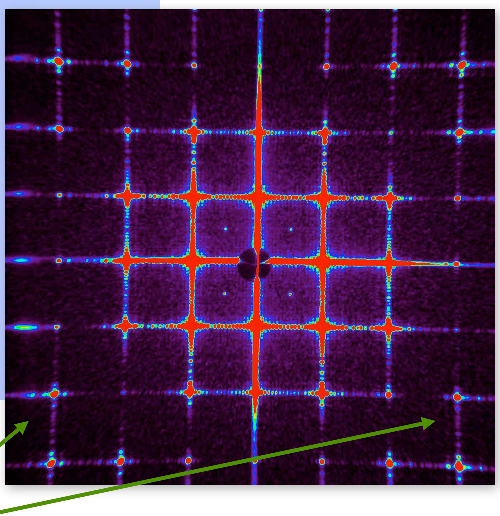
Our diffraction camera can measure forward scattering close to the direct soft-X-ray FEL



~5x10^{12} photons/ pulse @ 100 eV

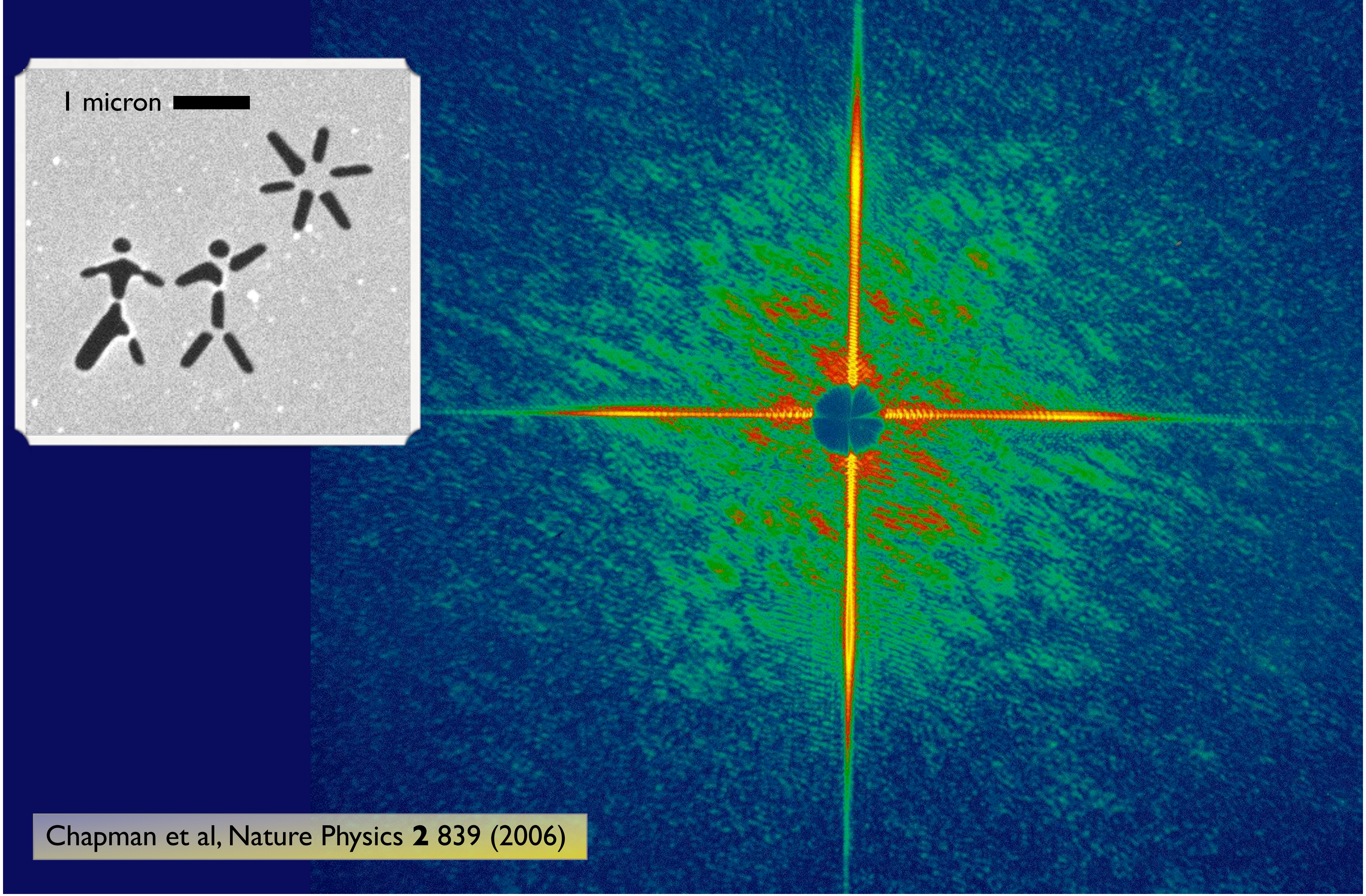


“Soft edge” prevents any scatter from the hole



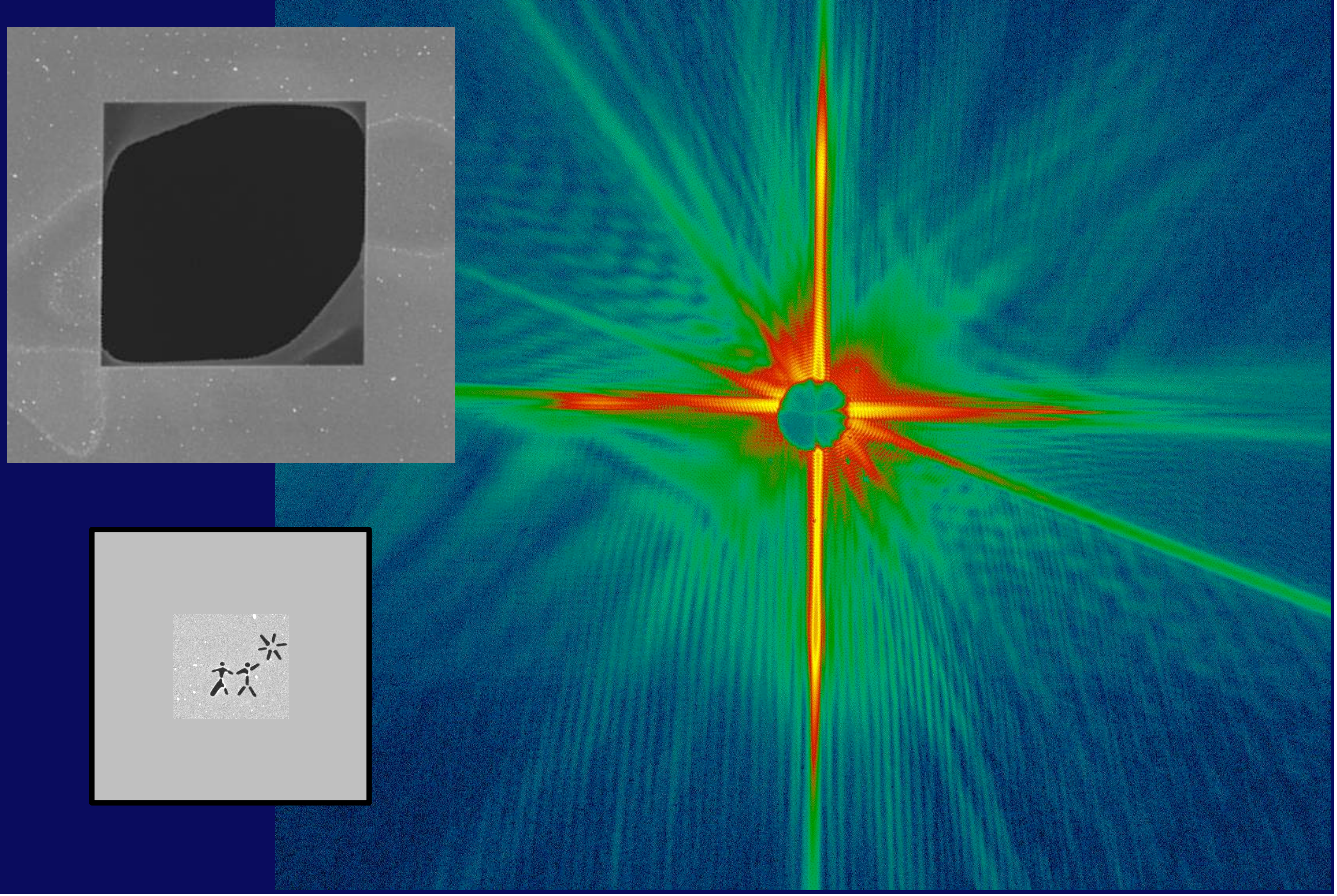
Multilayer reflectivity is uniform across the 30° to 60° gradient

“Diffraction before destruction” was demonstrated with soft X-rays at DESY’s FLASH FEL

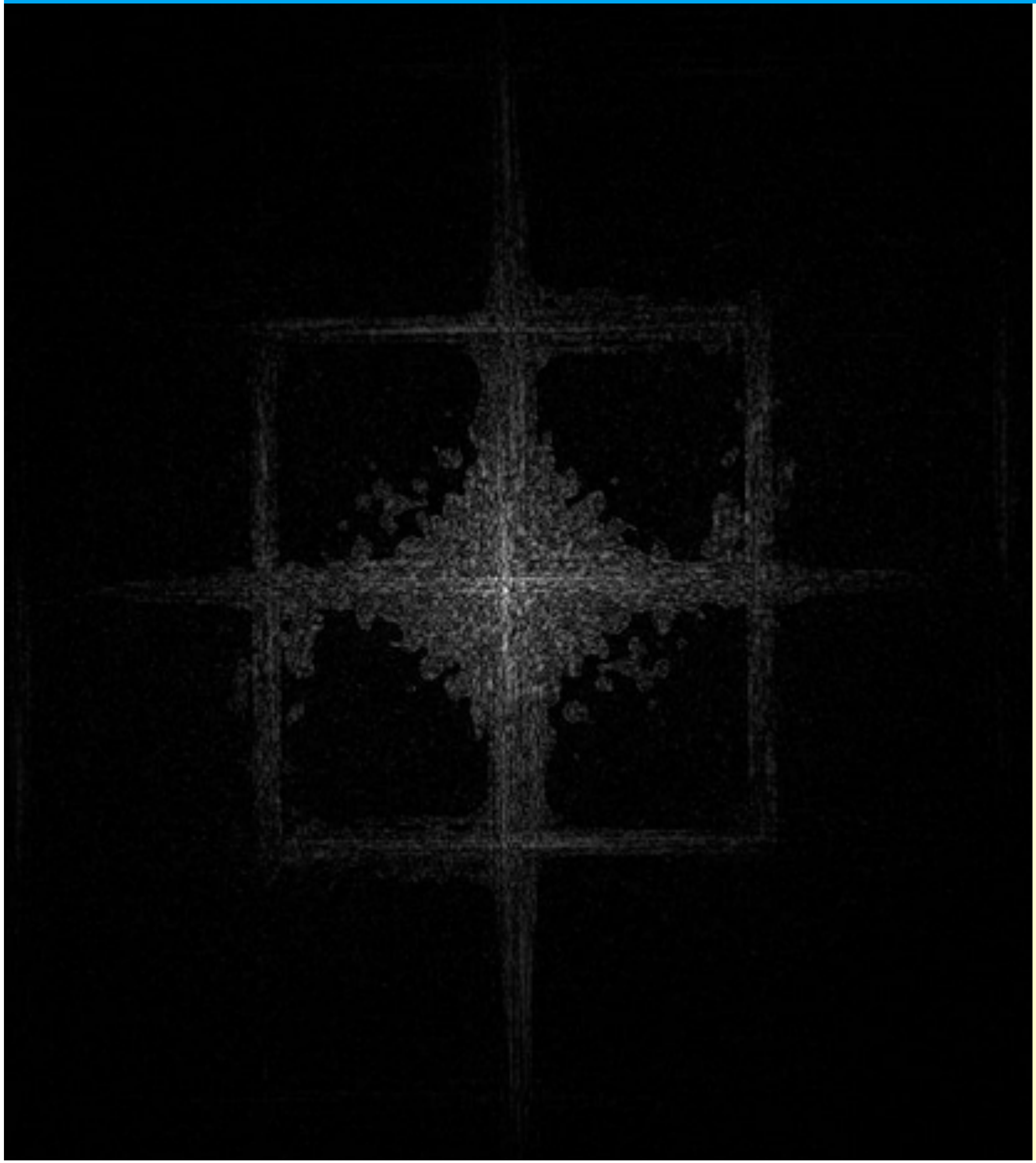


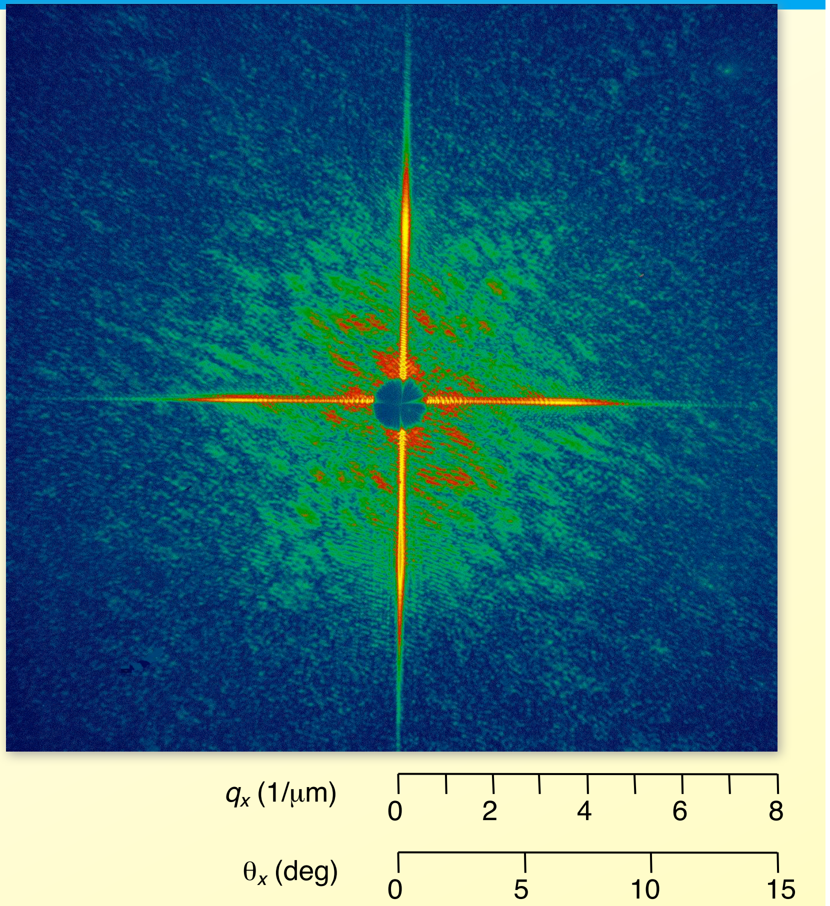
Chapman et al, Nature Physics **2** 839 (2006)

“Diffraction before destruction” was demonstrated with soft X-rays at DESY’s FLASH FEL



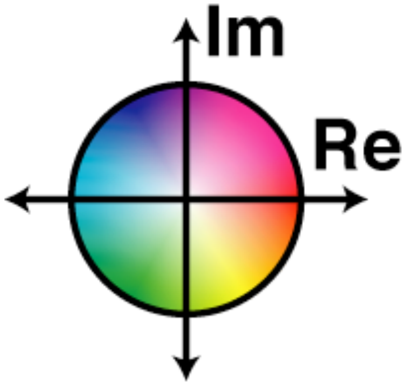
We perform ab initio image reconstruction with our "Shrinkwrap" algorithm



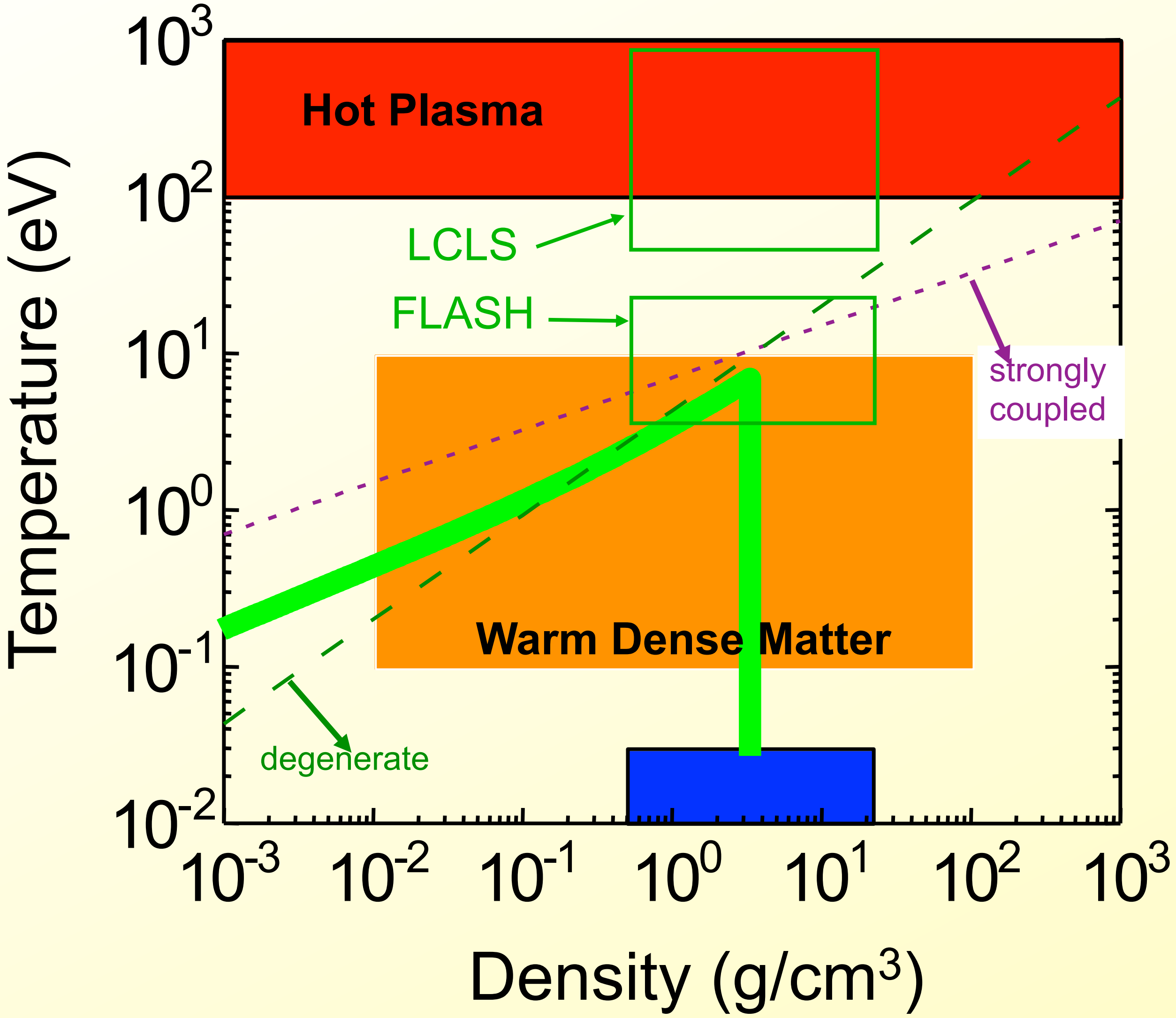


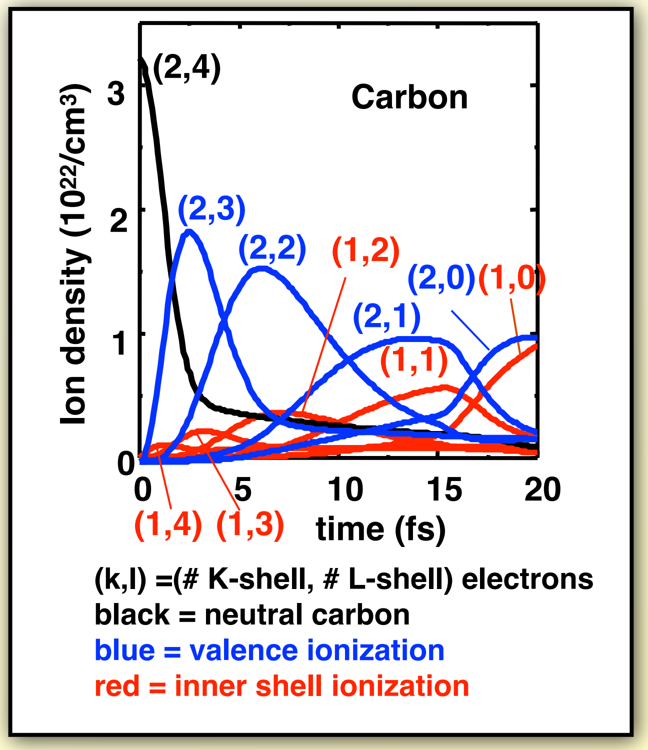
S. Marchesini et al. Phys Rev B **68** 140101 (2003)

2 micron



We model the response of matter illuminated by intense X-ray pulses as a hot plasma



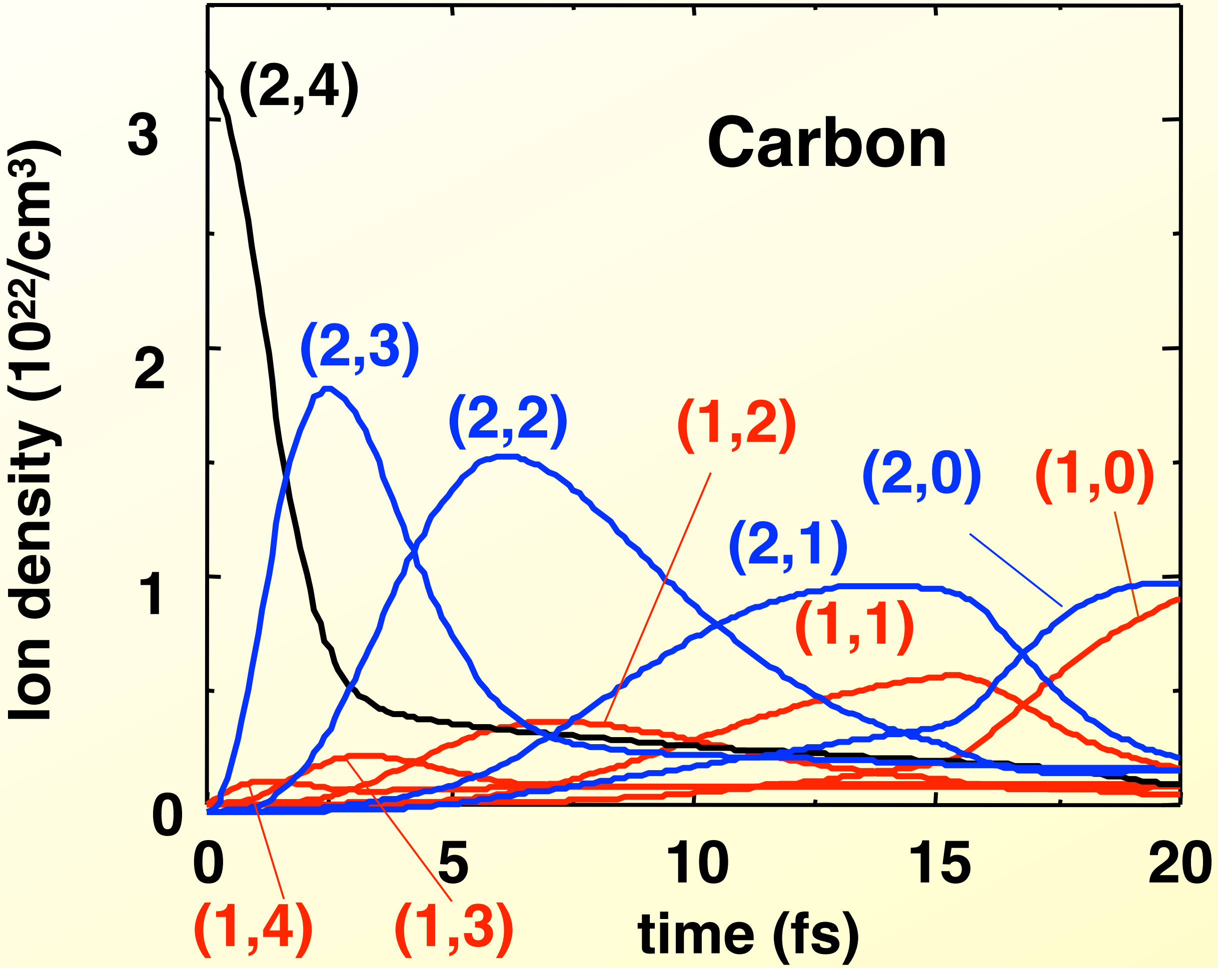


Hydrodynamic continuum model for the atomic motion and the ionization processes:

- Allows for trapping and secondary effects (such as inverse Bremsstralung, 3-body recombination)
- Damage is dominated by ionization at short times

S. Hau-Riege et al, Phys Rev E **69**, 051906 (2004)

We model the response of matter illuminated by intense X-ray pulses as a hot plasma



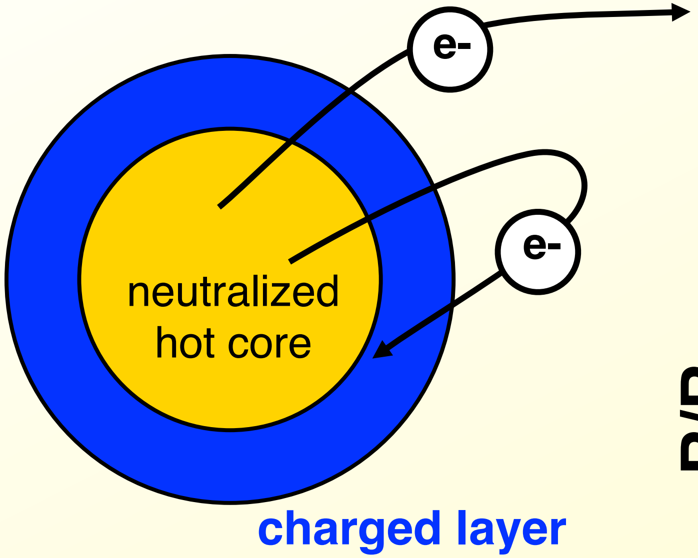
(k,l) =(# K-shell, # L-shell) electrons
black = neutral carbon
blue = valence ionization
red = inner shell ionization

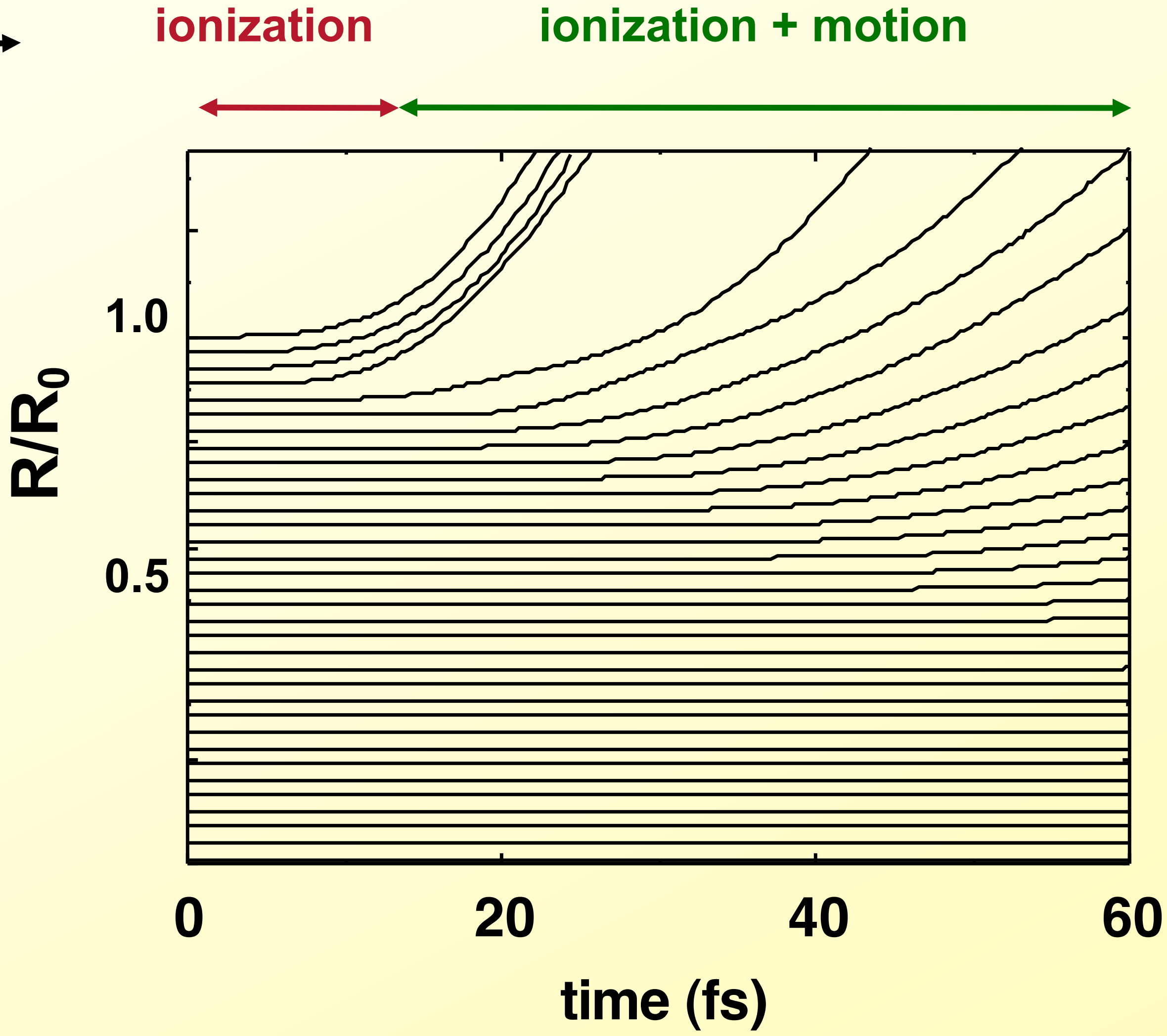
Hydrodynamic continuum model for the atomic motion and the ionization processes:

- Allows for trapping and secondary effects (such as inverse Bremsstralung, 3-body recombination)
- Damage is dominated by ionization at short times

S. Hau-Riege et al, Phys Rev E **69**, 051906 (2004)

XFEL diffraction of molecules and clusters is modified (damaged) by photoionization and motion of atoms

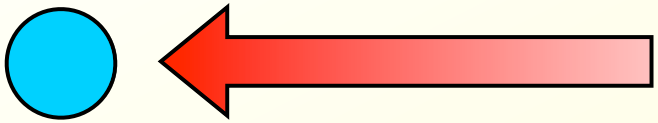




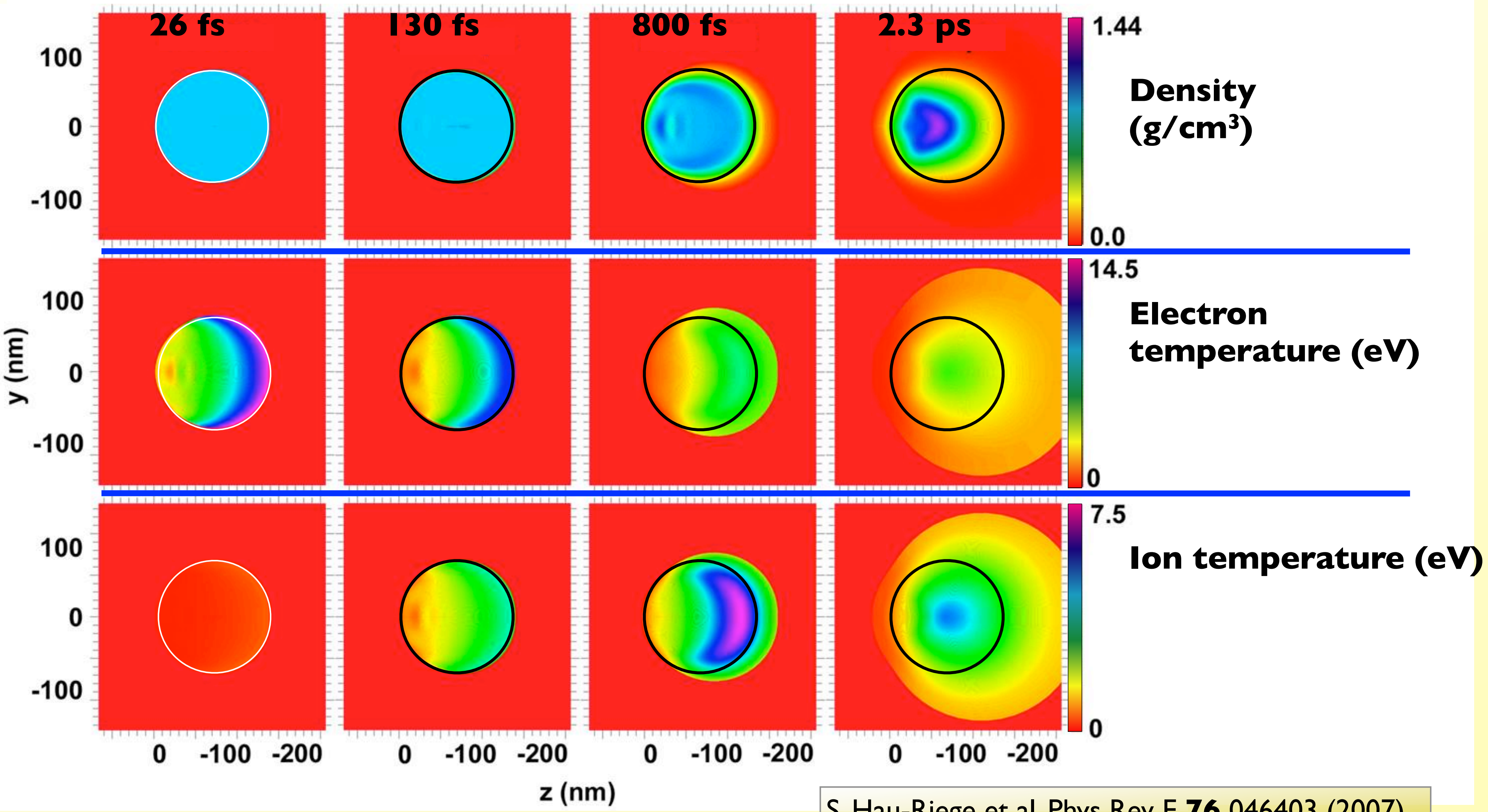
electron escapes if $E > \frac{3eQ}{2R}$

S. Hau-Riege et al, Phys Rev E **69**, 051906 (2004)

Our VUV hydrodynamic code shows that latex spheres start exploding in ~ 2 ps

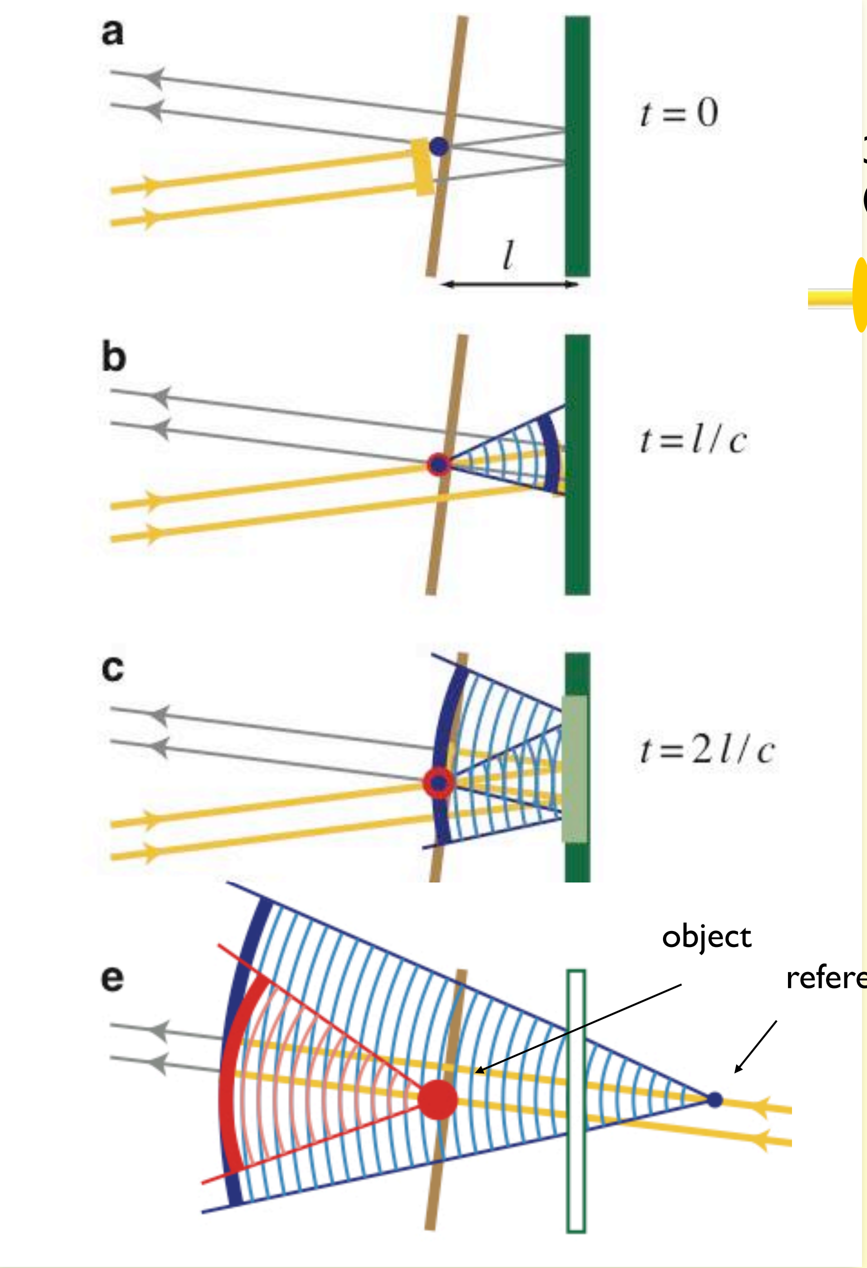


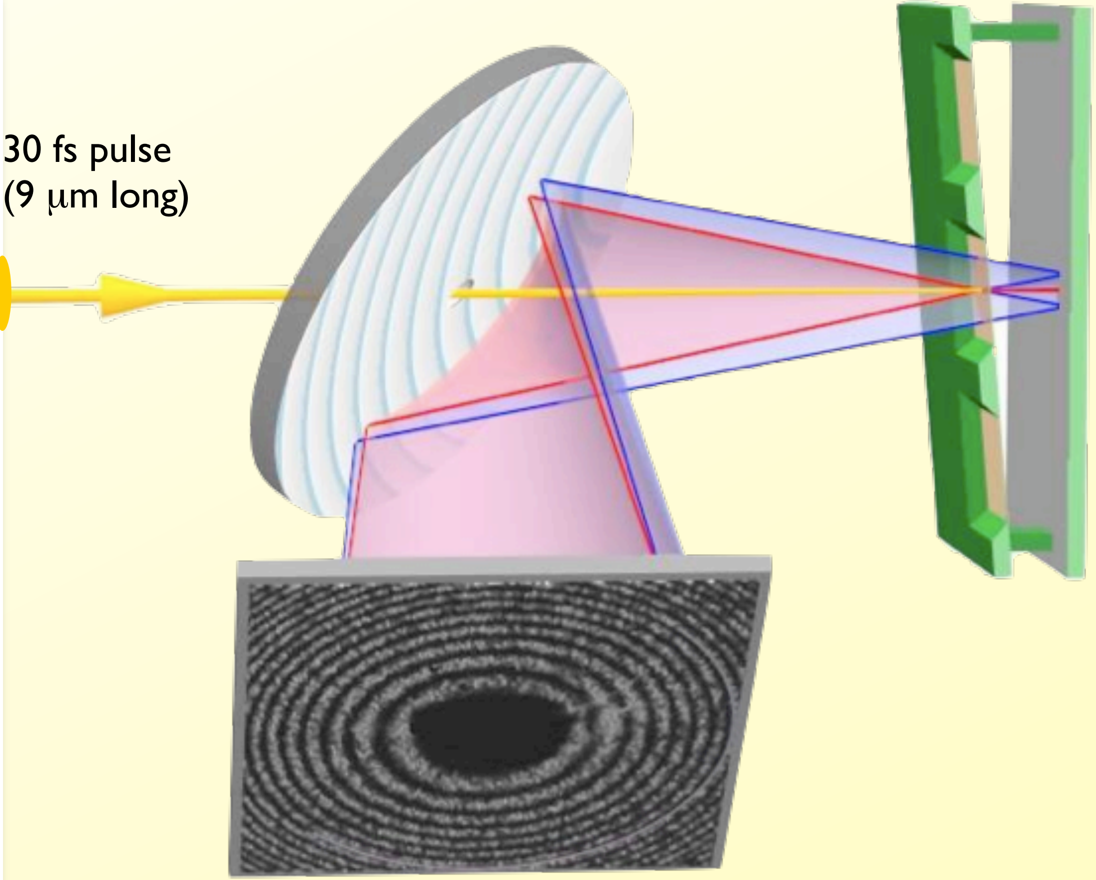
λ = 32 nm,
10^{14} J/cm^2



S. Hau-Riege et al, Phys Rev E **76** 046403 (2007)

We invented a new method called femtosecond time-delay holography





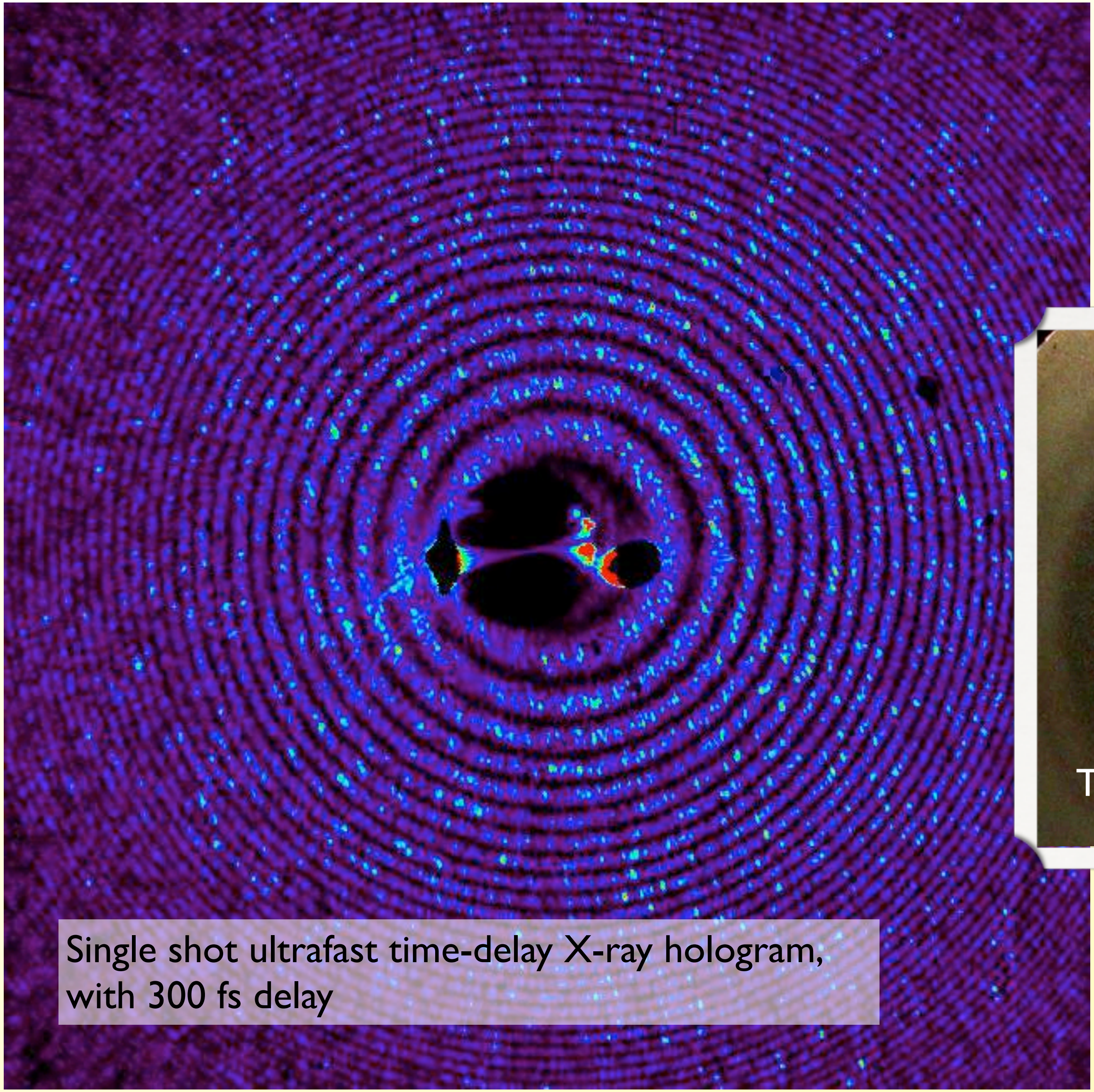
Prompt diffraction

Delayed diffraction

Time delay $2\,l\,/\,c$

H. Chapman et al., Nature **448** 676 (2007)

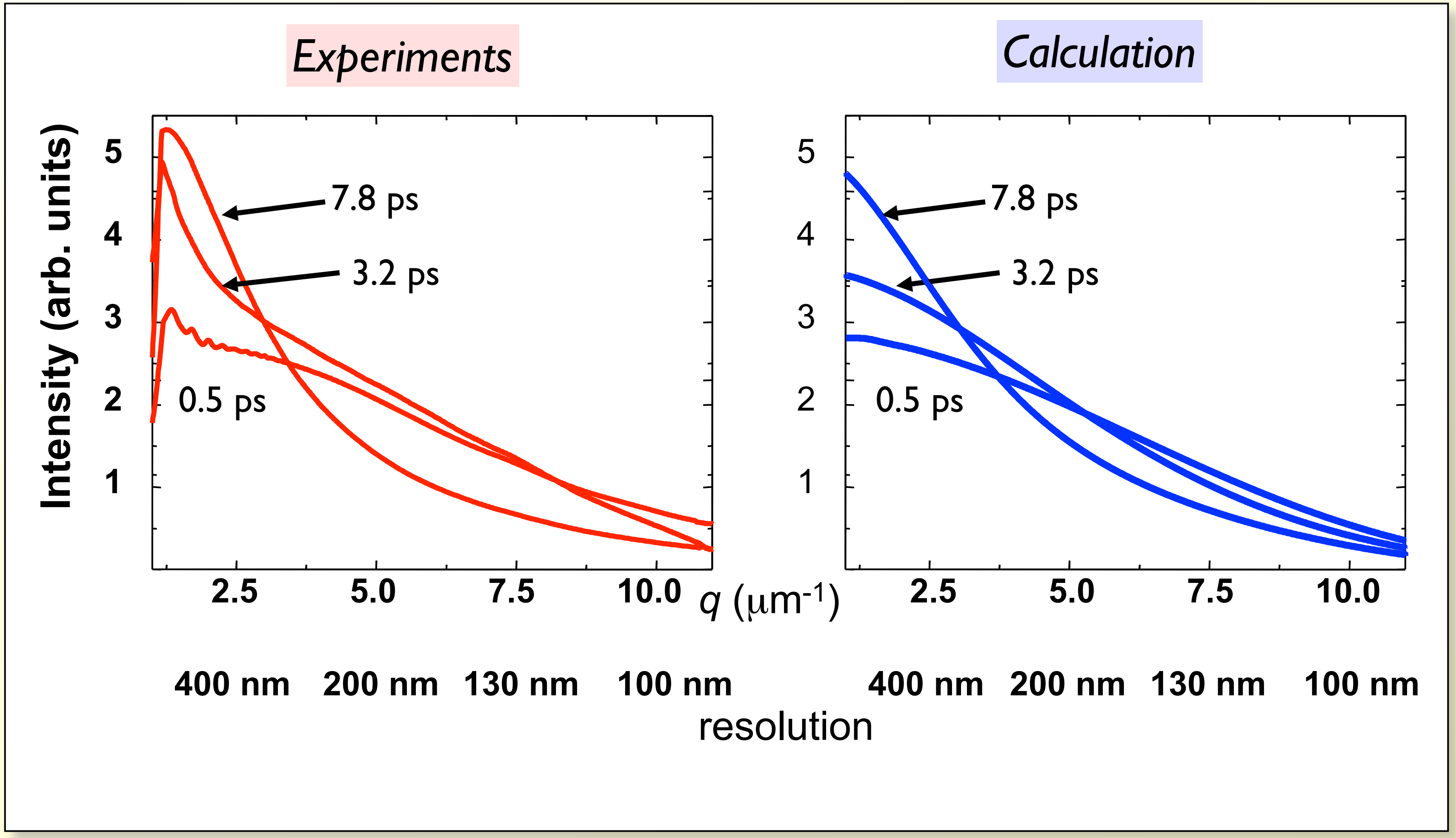
First demonstration of time-delay holography with 3 fs time resolution indicates the particle explosion



Single shot ultrafast time-delay X-ray hologram, with 300 fs delay

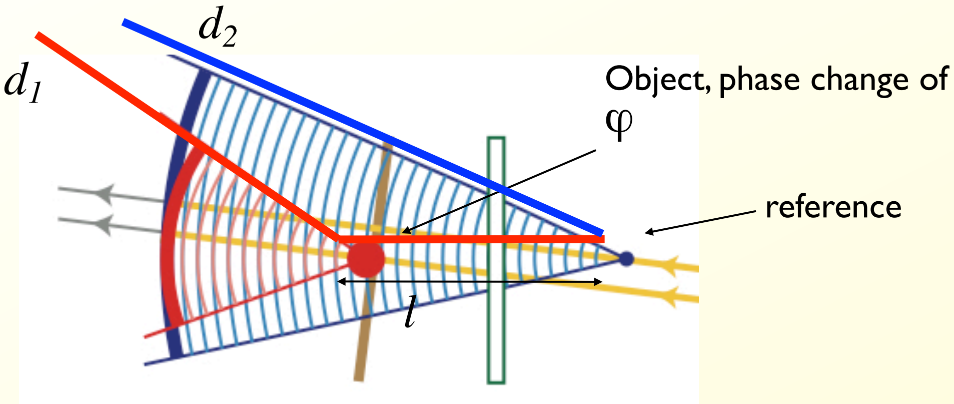
The “dusty mirror” experiment

The explosion is in good agreement with our hydrodynamic model



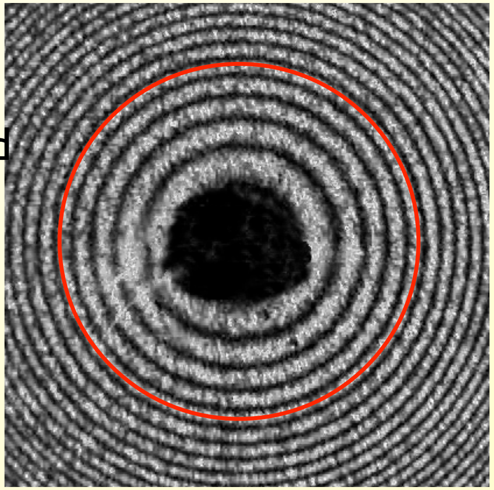
The structure factor narrows, showing the particle exploding

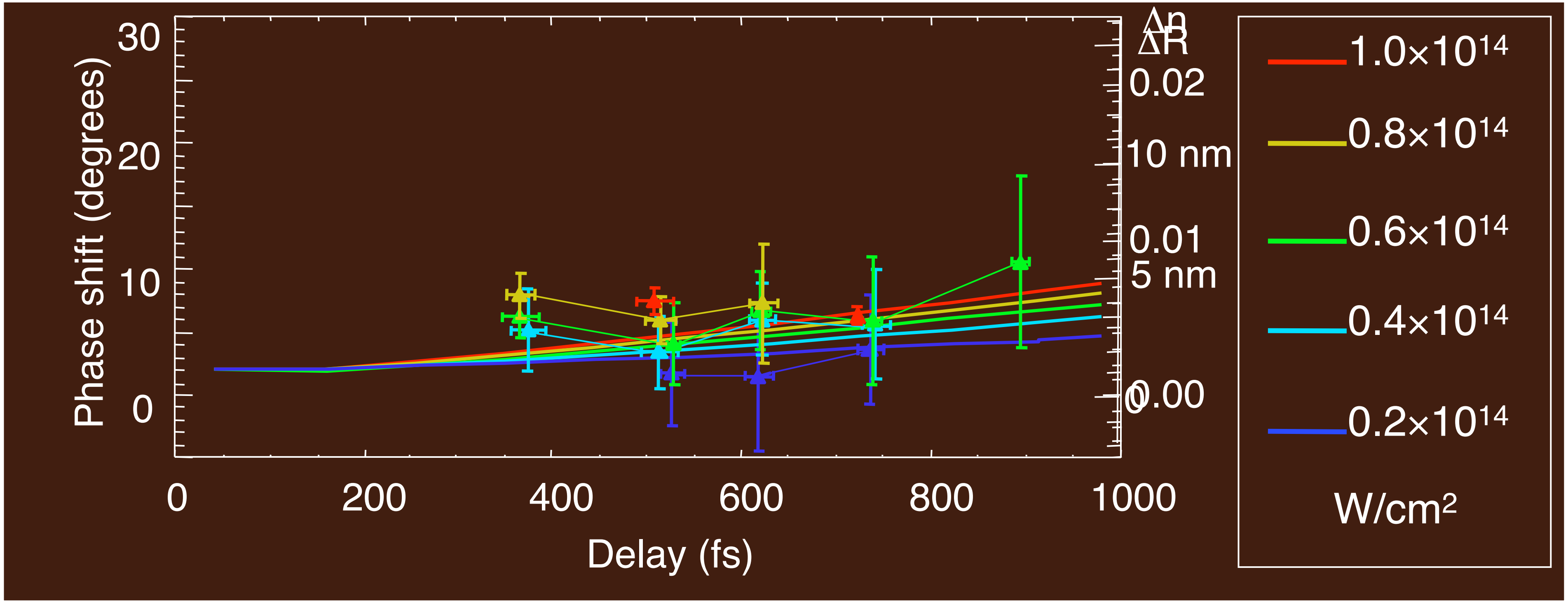
We interferometrically measure the change in optical density of the particle at short delays



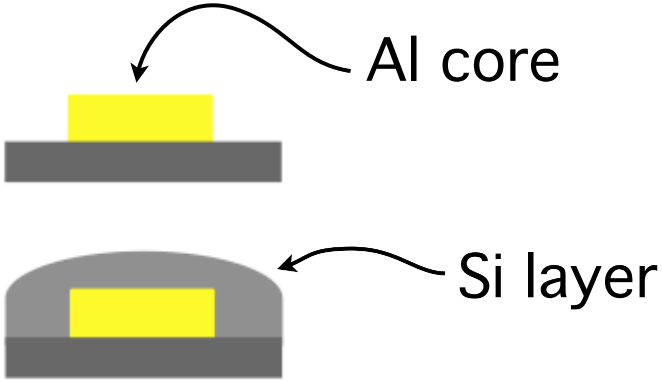
Rings occur when $l+\varphi+d_1=d_2+N\lambda$

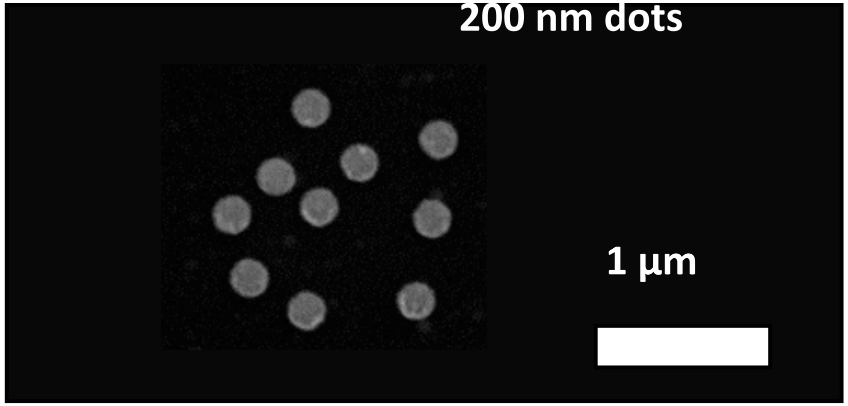
Fitting the ring radii gives l and φ

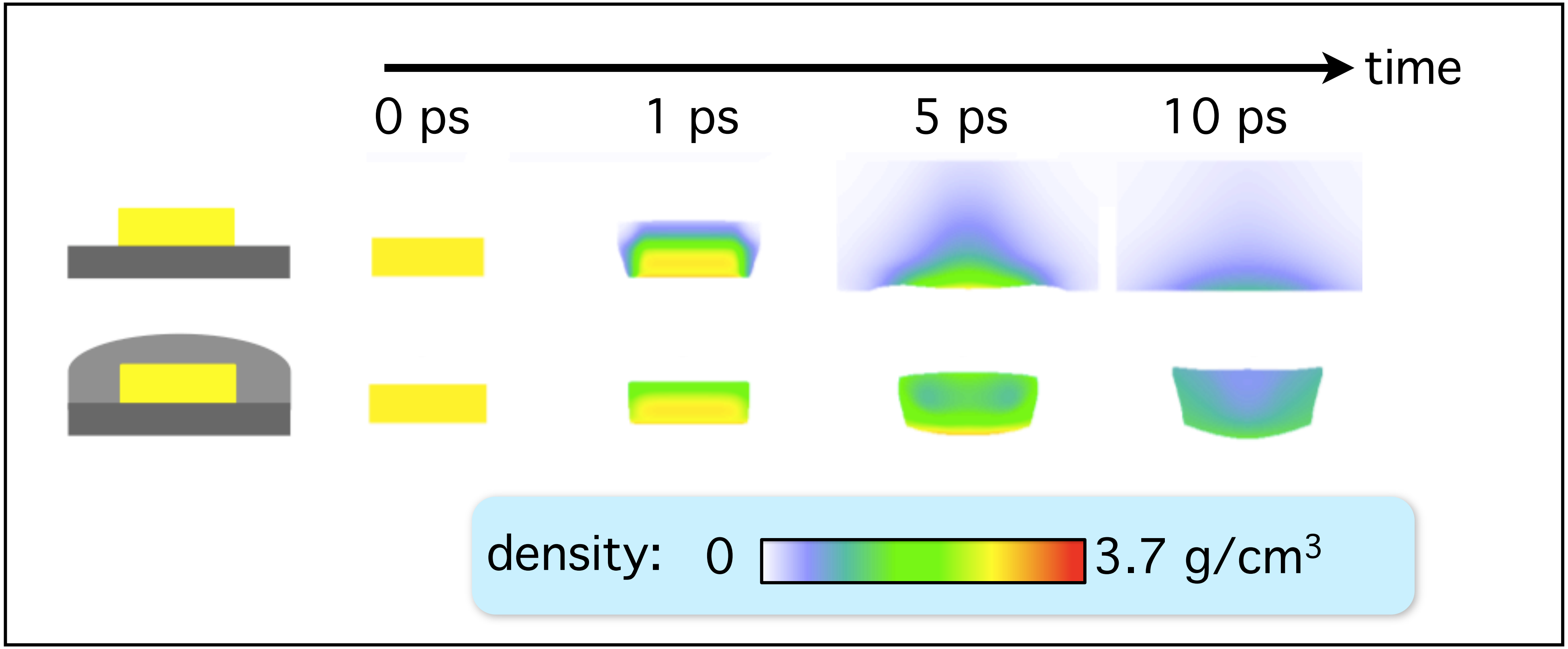




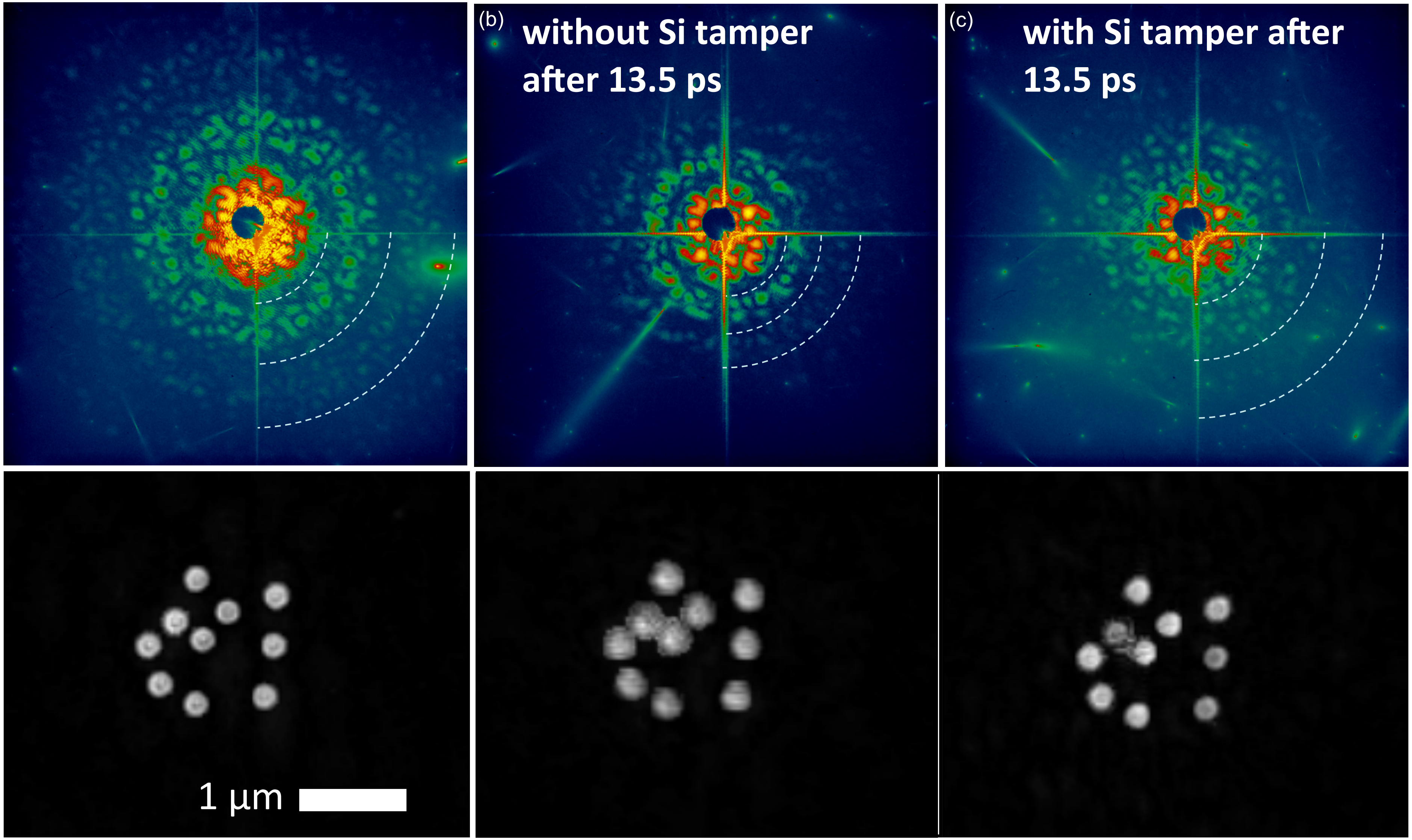
We expect that the tamper reduces the explosion of the particle





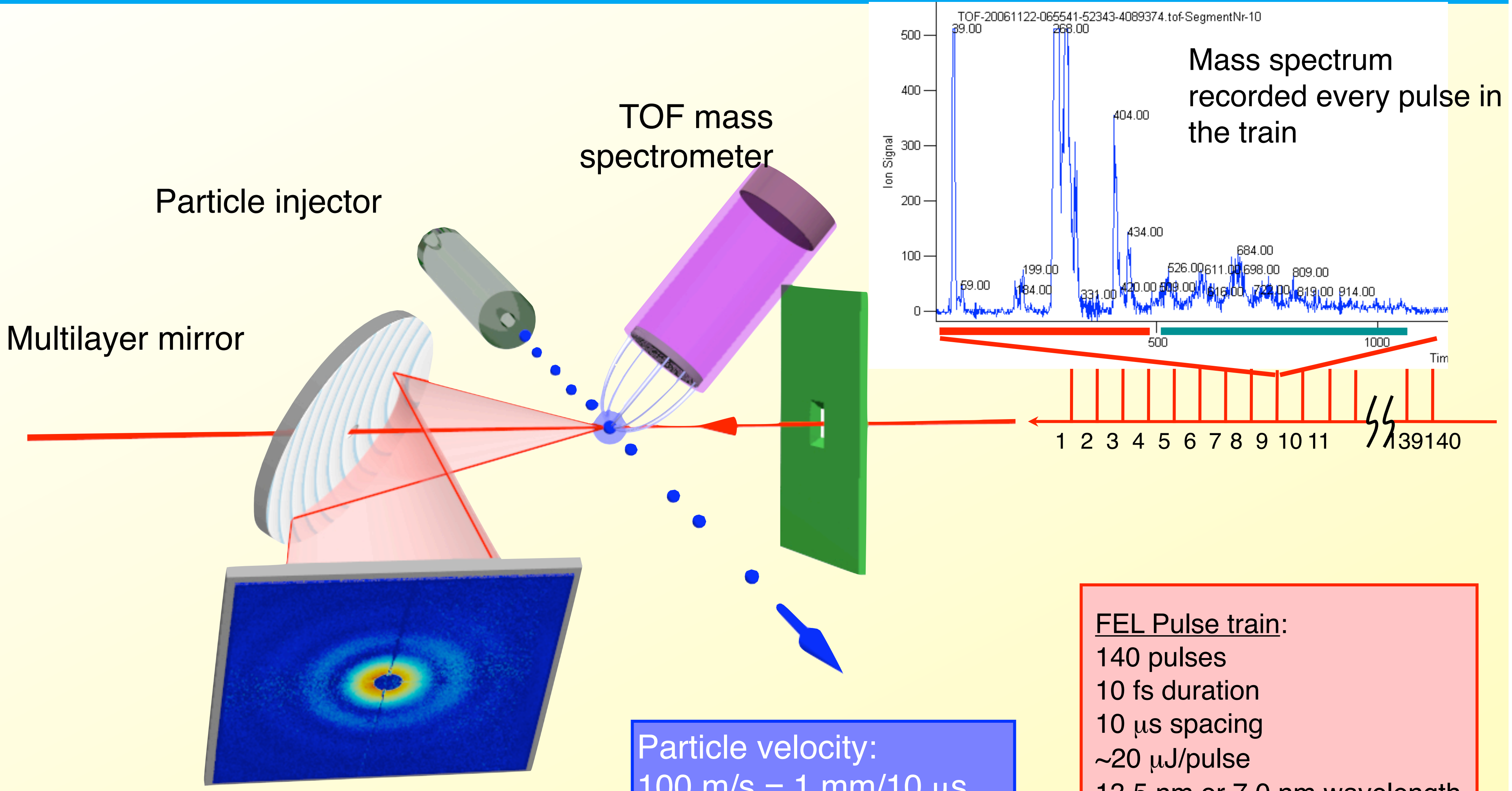


The tamper reduces the explosion



reconstructions: Sebastien Boutet

Single-particle FEL diffraction of “on-the-fly” particles has been demonstrated for the first



Mass spectrum recorded every pulse in the train

TOF mass spectrometer

Particle injector

Multilayer mirror

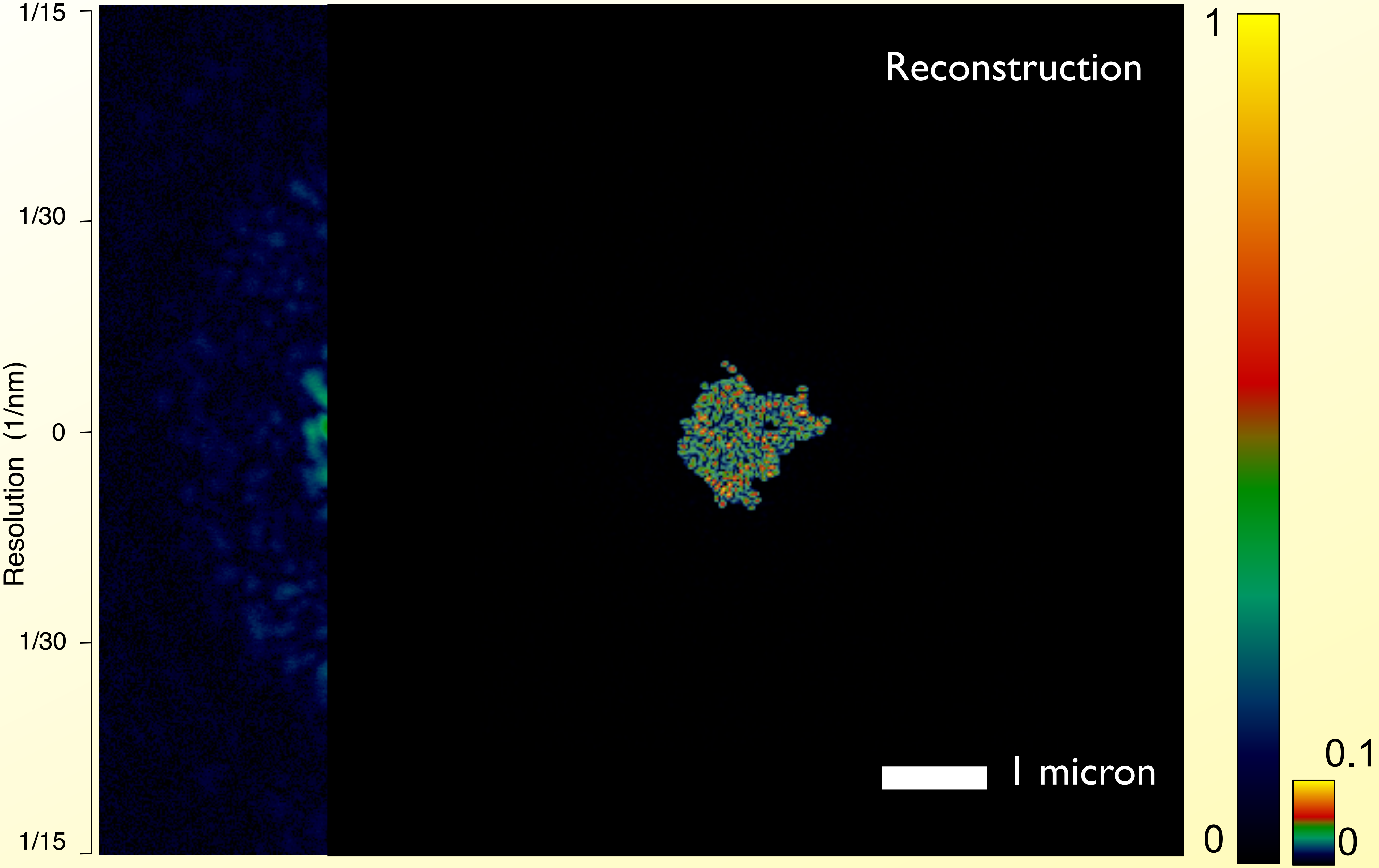
Single particle diffraction pattern (one hit + 699 no-hits)

Particle velocity:
100 m/s = 1 mm/10 μs
(c.f. 20 μm beam)

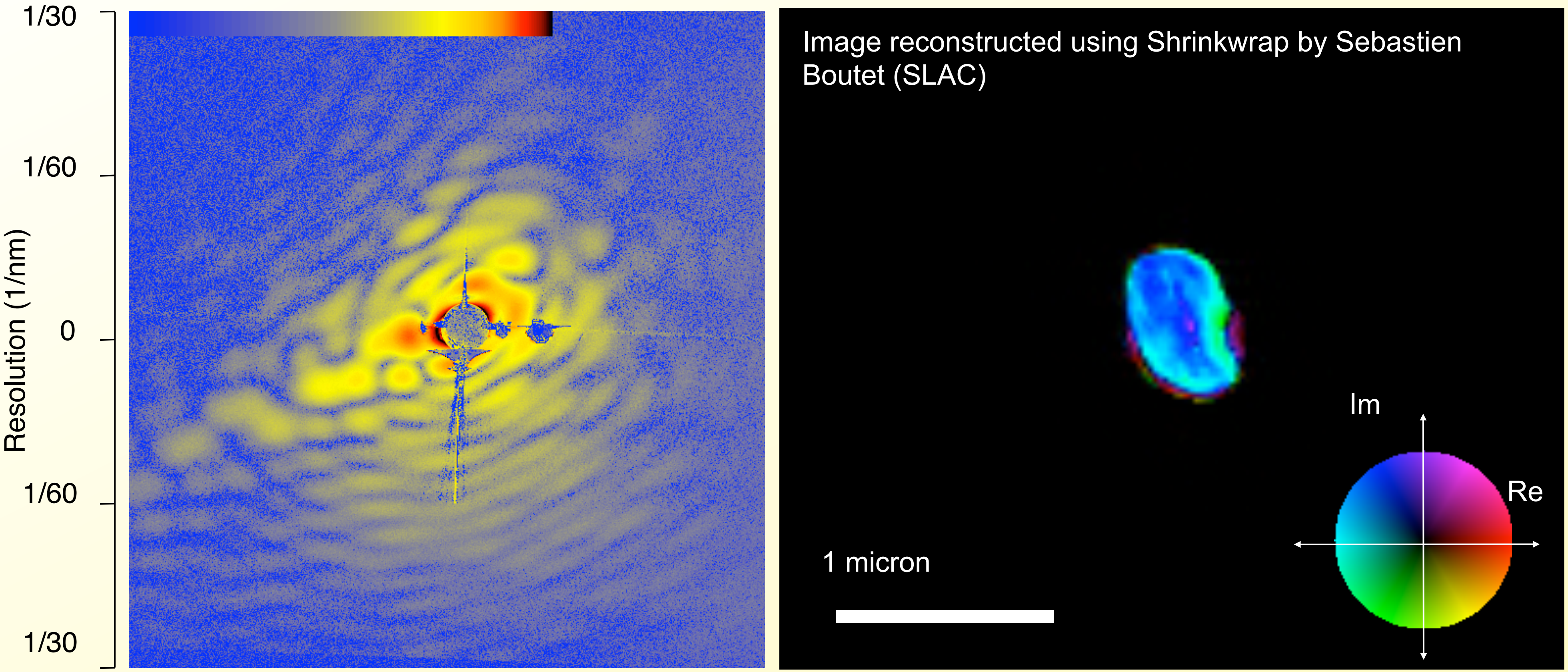
FEL Pulse train:
140 pulses
10 fs duration
10 μs spacing
~20 μJ/pulse
13.5 nm or 7.0 nm wavelength

M.J. Bogan et al., Nano Letters **8**, 310 (2008)

The absence of a substrate gives clean patterns free of aliased scattering sources and plasma radiation



We have performed the first X-ray imaging of free-falling unstained live biological cells

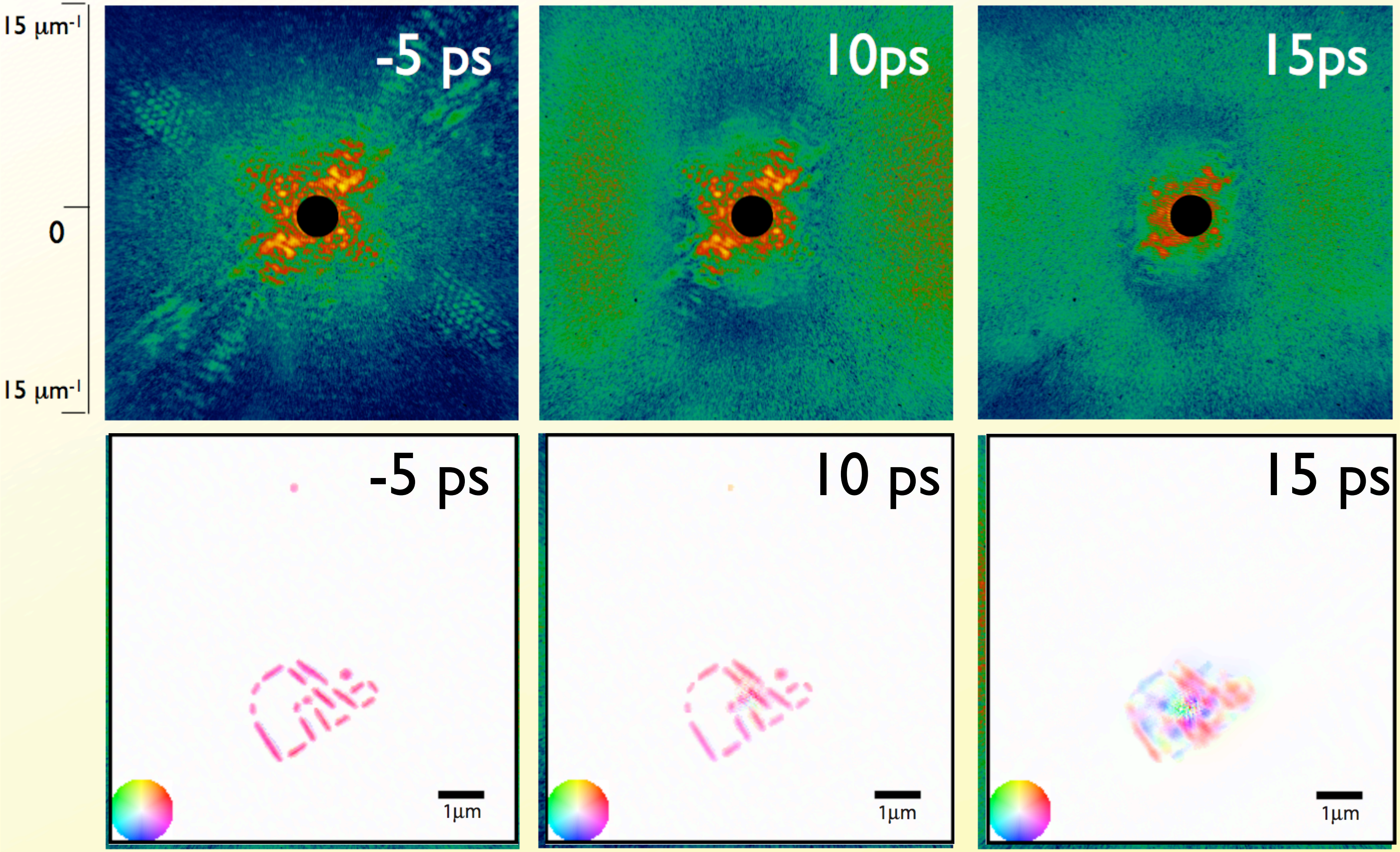


Single shot ~10 fs diffraction pattern of a picoplankton organism.
λ =13.5 nm

This cell was injected into vacuum from solution, and shot through the beam at 100 m/s

J. Hajdu, I. Andersson, M. Svenda, M. Seibert (Uppsala), S. Boutet (SLAC)
M. Bogan, H. Benner, U. Rohner, H. Chapman (LLNL)

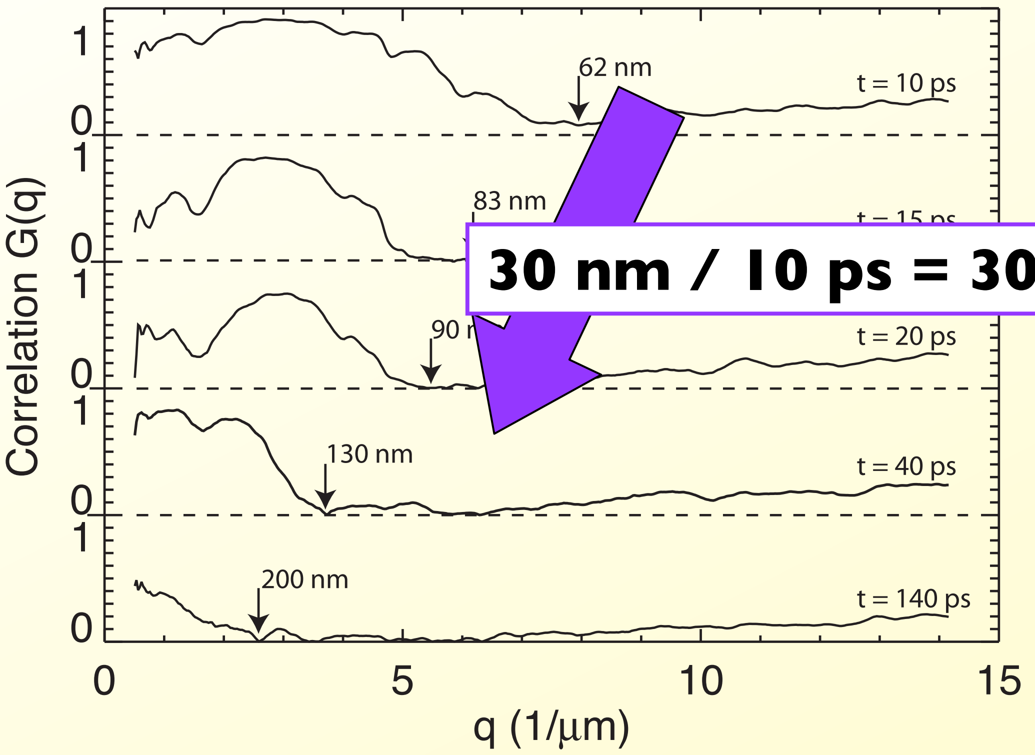
We performed ultrafast coherent X-ray diffraction to study ablation of materials



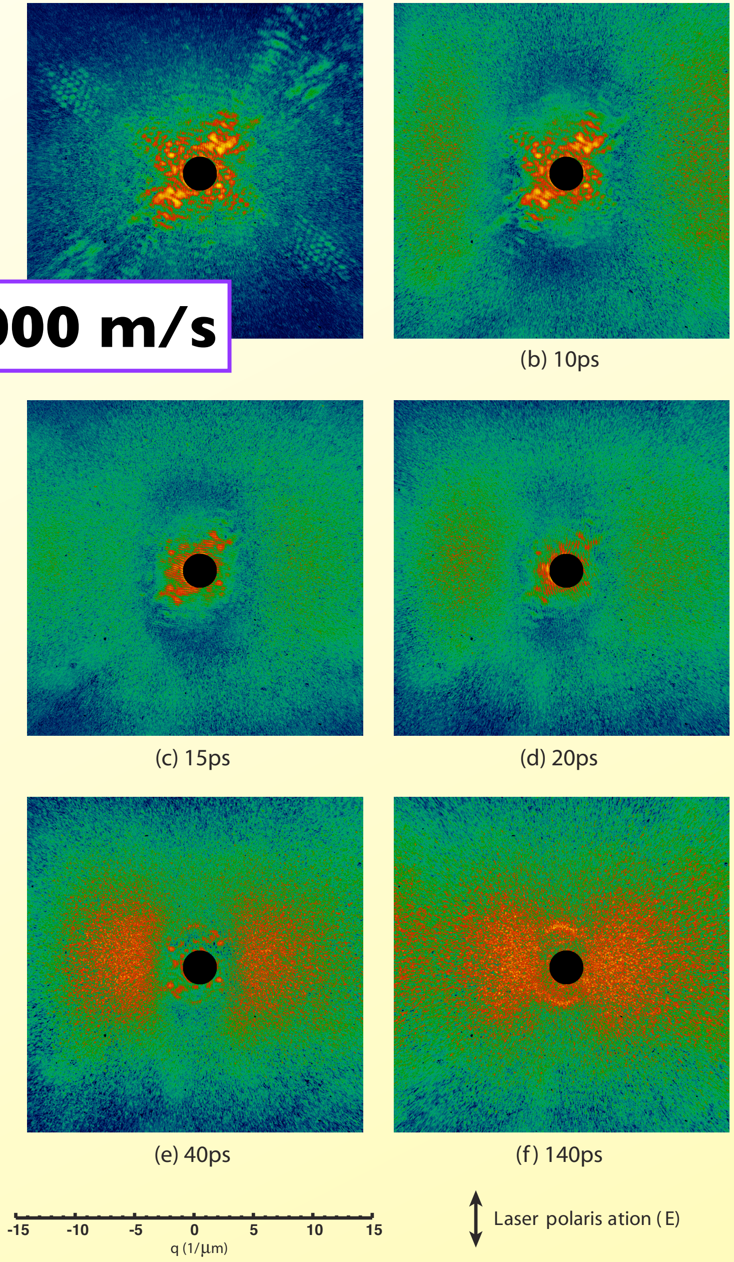
A. Barty et al., Nature Photonics **2** 415 (2008)

With Klaus Sokolowski-Tinten (Essen) and Andrea Cavalleri (Oxford)

Patterns can be cross-correlated to reveal the dynamics of the structure



30 nm / 10 ps = 3000 m/s



(b) 10ps

(c) 15ps

(d) 20ps

(e) 40ps

(f) 140ps

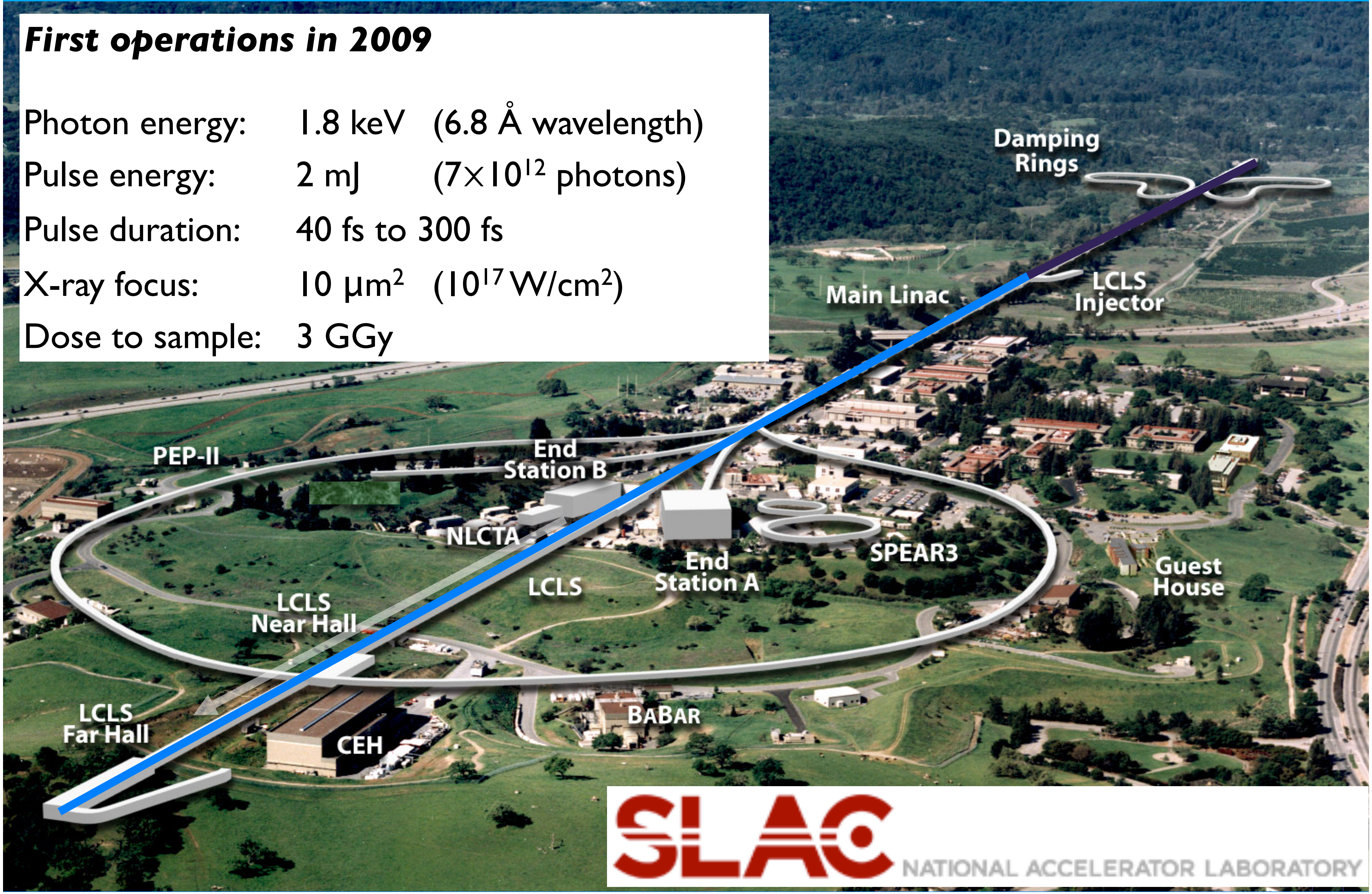
$$G(q) = \frac{I'_1(q) \cdot I'_2(q)}{|I'_1(q)|\,|I'_2(q)|}$$

$$I'(q) = I(q) - \langle I(q) \rangle$$

LCLS is the world's first hard X-ray FEL

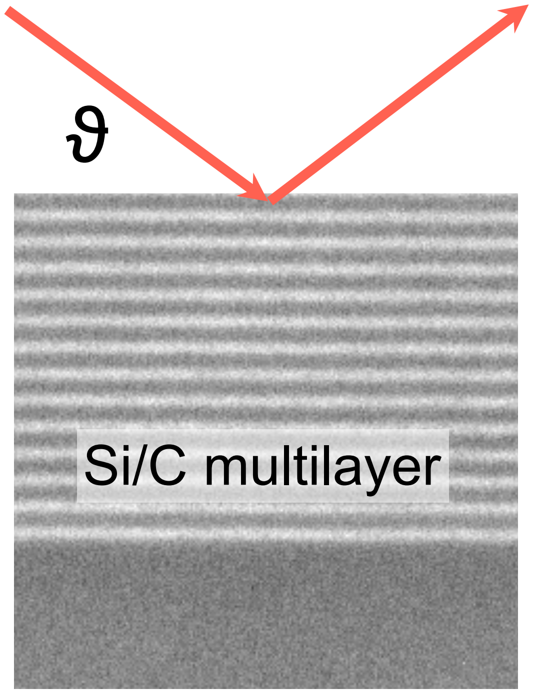
First operations in 2009

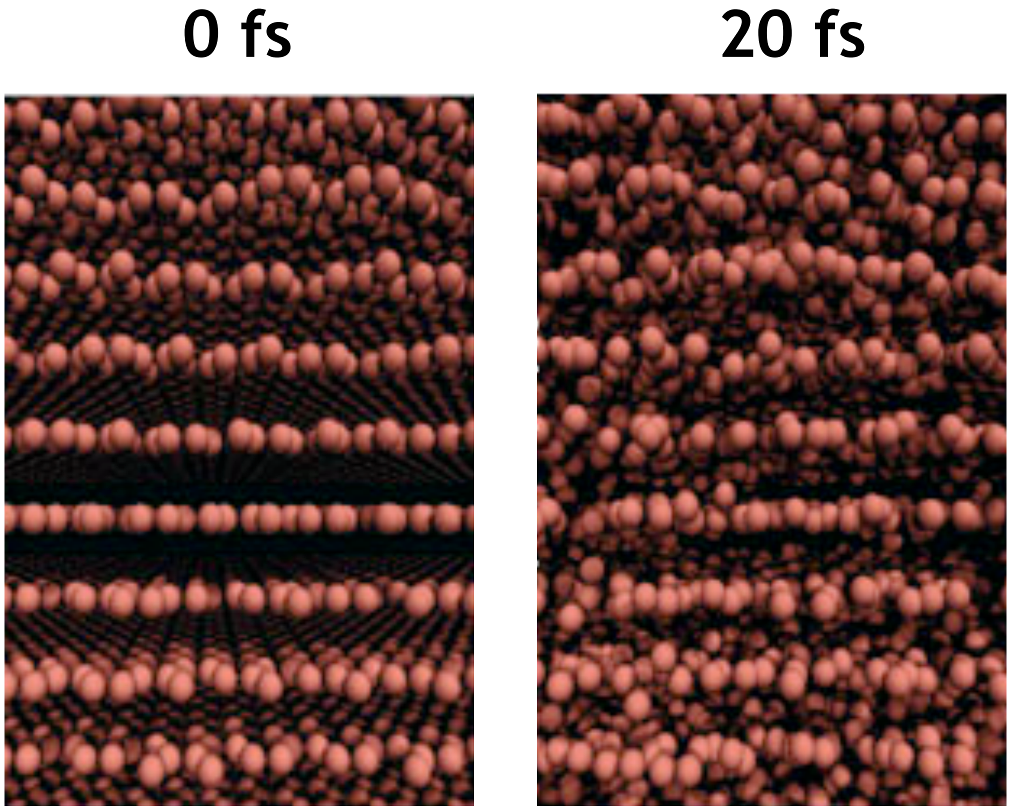
Photon energy:	1.8 keV	(6.8 Å wavelength)
Pulse energy:	2 mJ	(7×10^{12} photons)
Pulse duration:	40 fs to 300 fs	
X-ray focus:	10 μm^2	(10^{17} W/cm^2)
Dose to sample:	3 GGy	



SLAC NATIONAL ACCELERATOR LABORATORY

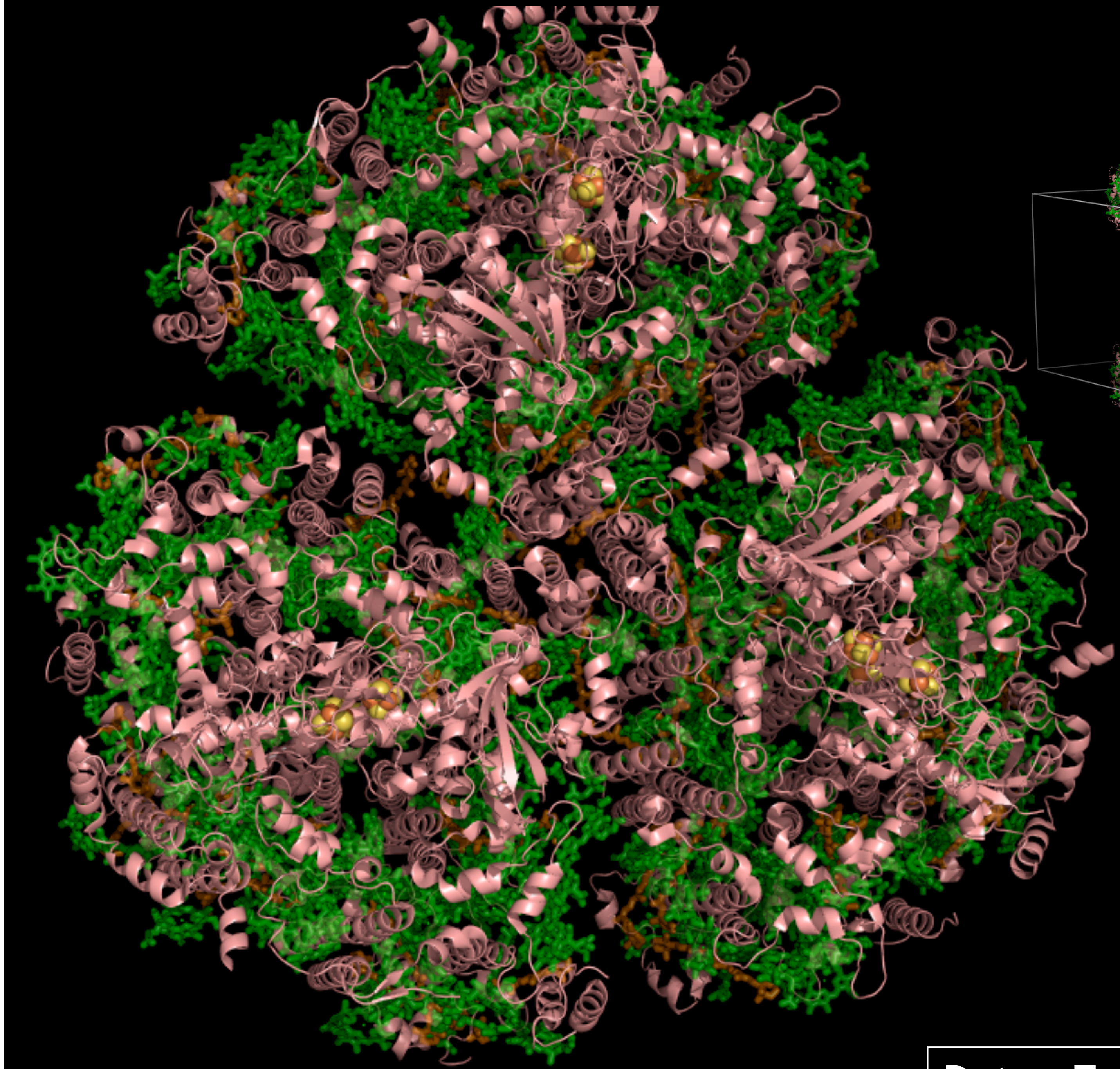
We used the same strategy as at FLASH to monitor sample destruction during the pulse

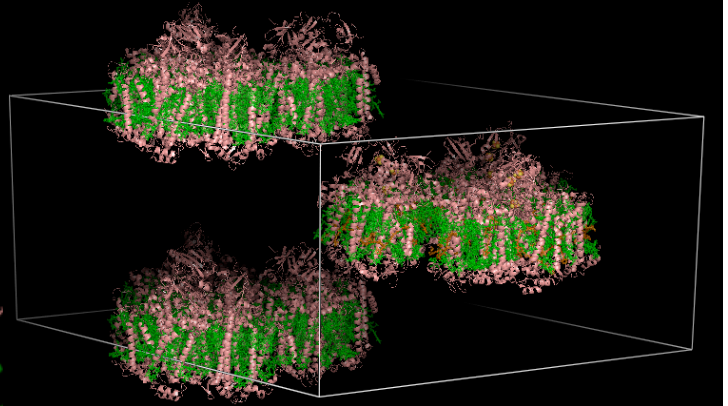




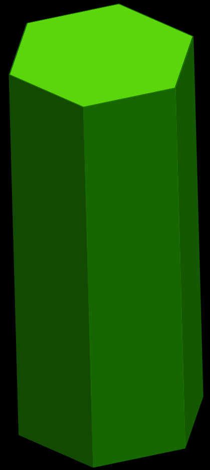
FLASH: Wavelength 100 Å
Structures: 100 Å to microns

LCLS: Wavelength 6.8 Å
Structures: 6 Å to microns





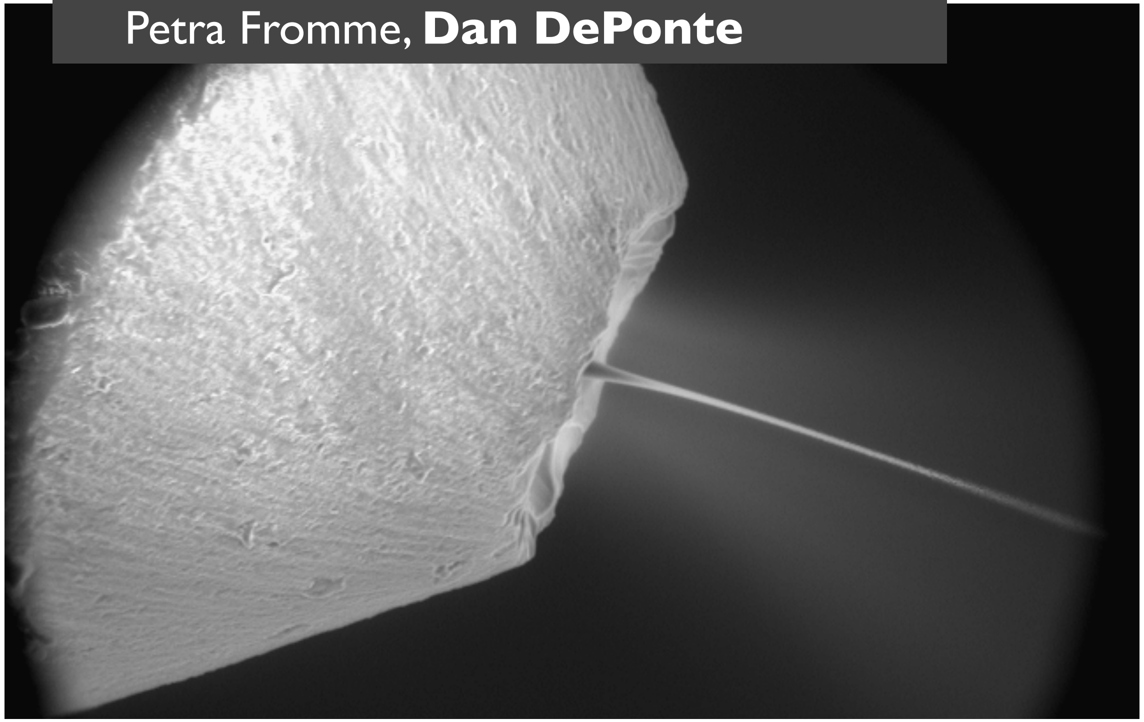
a = *b* = 288 Å
c = 167 Å

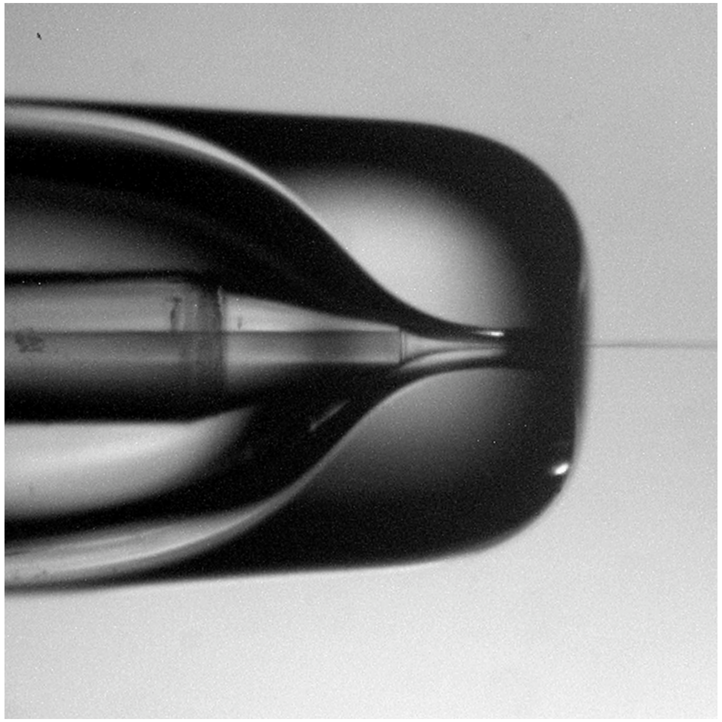


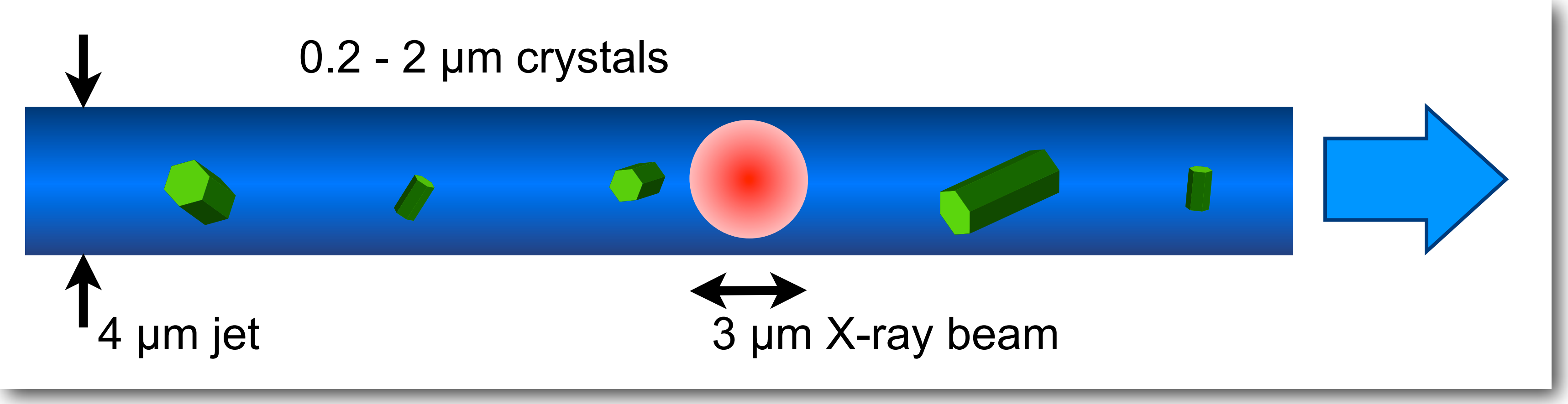
Petra Fromme, ASU

Submicron droplet sources and liquid jet sources have been developed for LCLS and FLASH

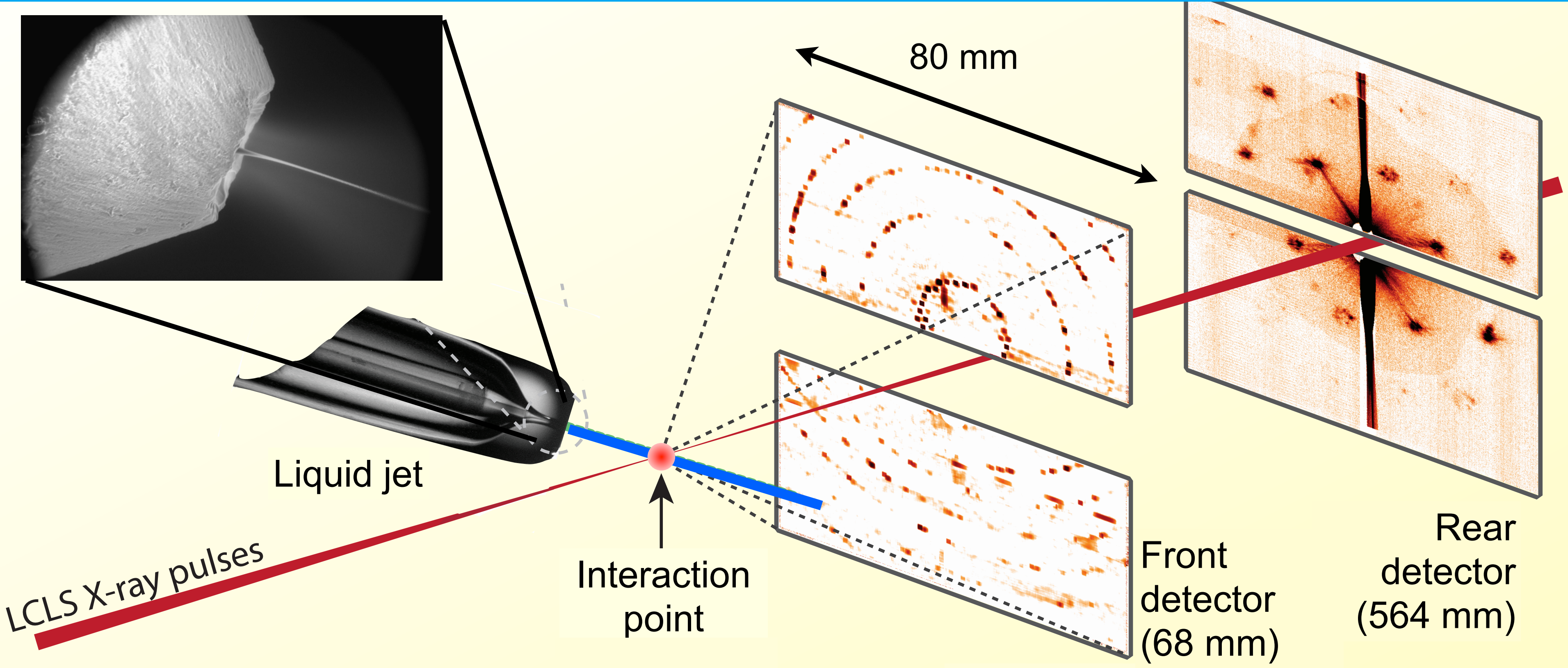
John Spence, Uwe Weierstall, Bruce Doak,
Petra Fromme, **Dan DePonte**



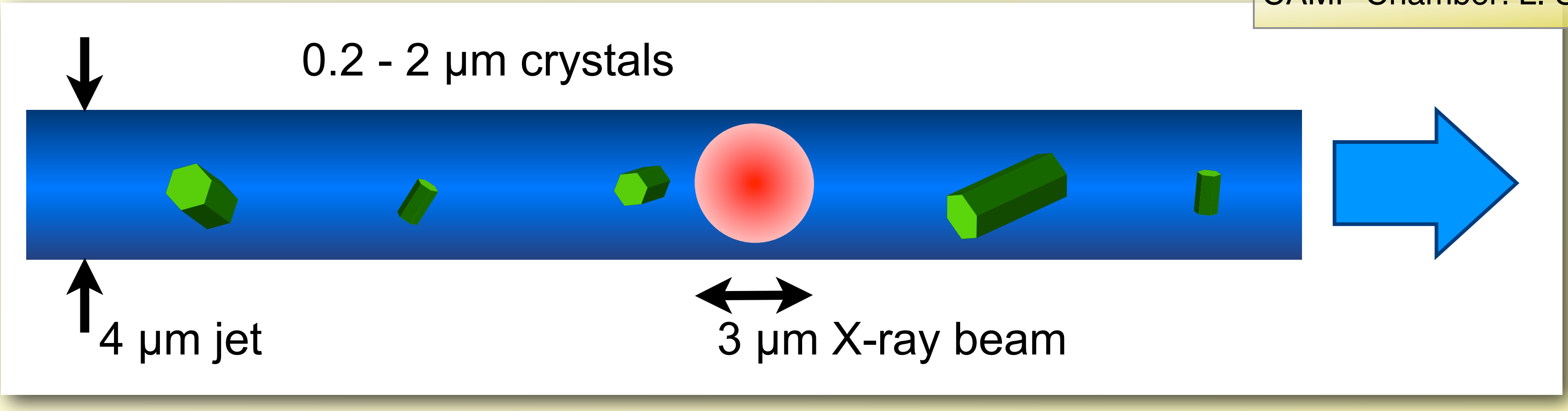




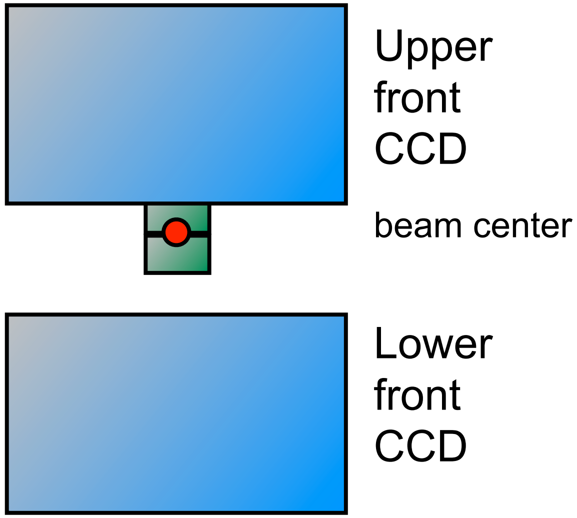
Nanocrystallography is carried out in a flowing water microjet



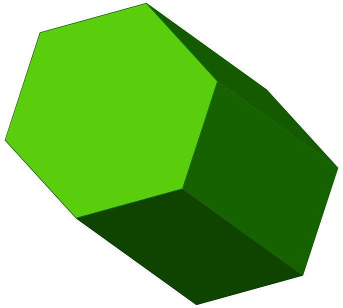
CAMP Chamber: L. Struder *et al.*



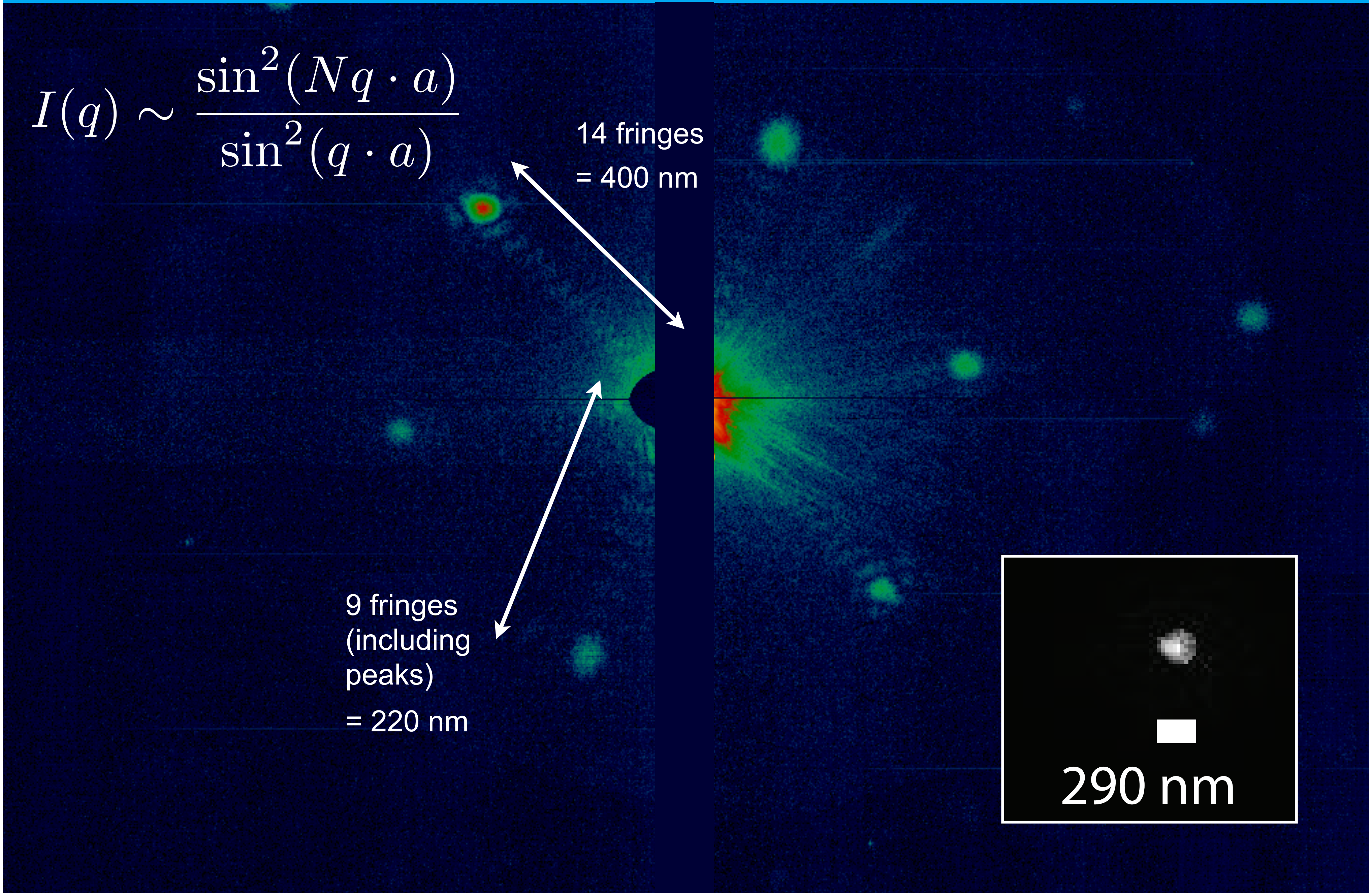
Single pulse diffraction from Photosystem I nanocrystals at LCLS



Resolution at corner = 8.9Å



The crystals are sub-micron size



$$I(q) \sim \frac{\sin^2(Nq \cdot a)}{\sin^2(q \cdot a)}$$

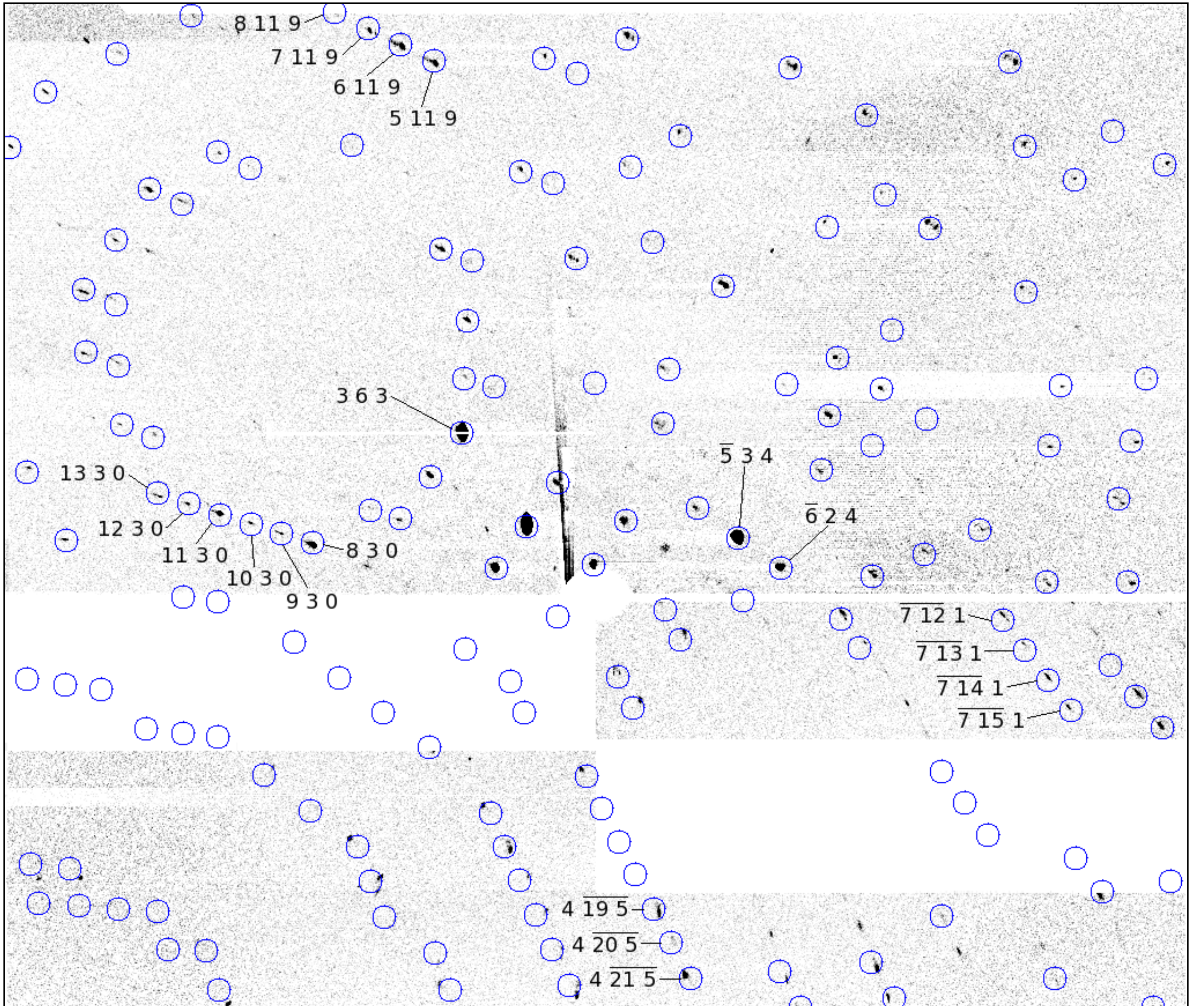
14 fringes
= 400 nm

9 fringes
(including
peaks)
= 220 nm

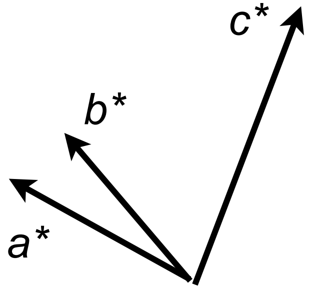
We can sum patterns to create a virtual powder pattern

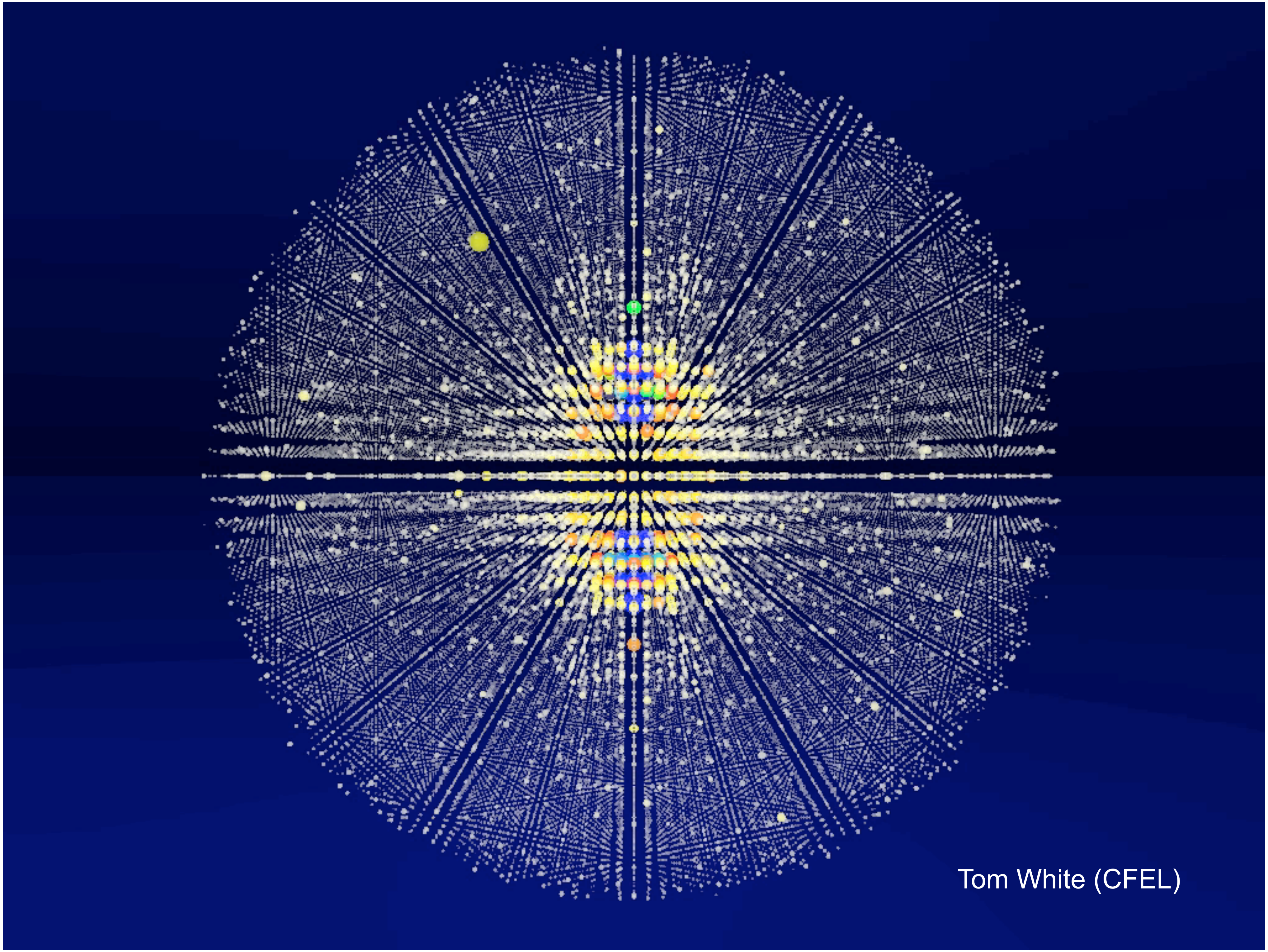
Lysozyme nano-crystals
2 keV

We have indexed the patterns



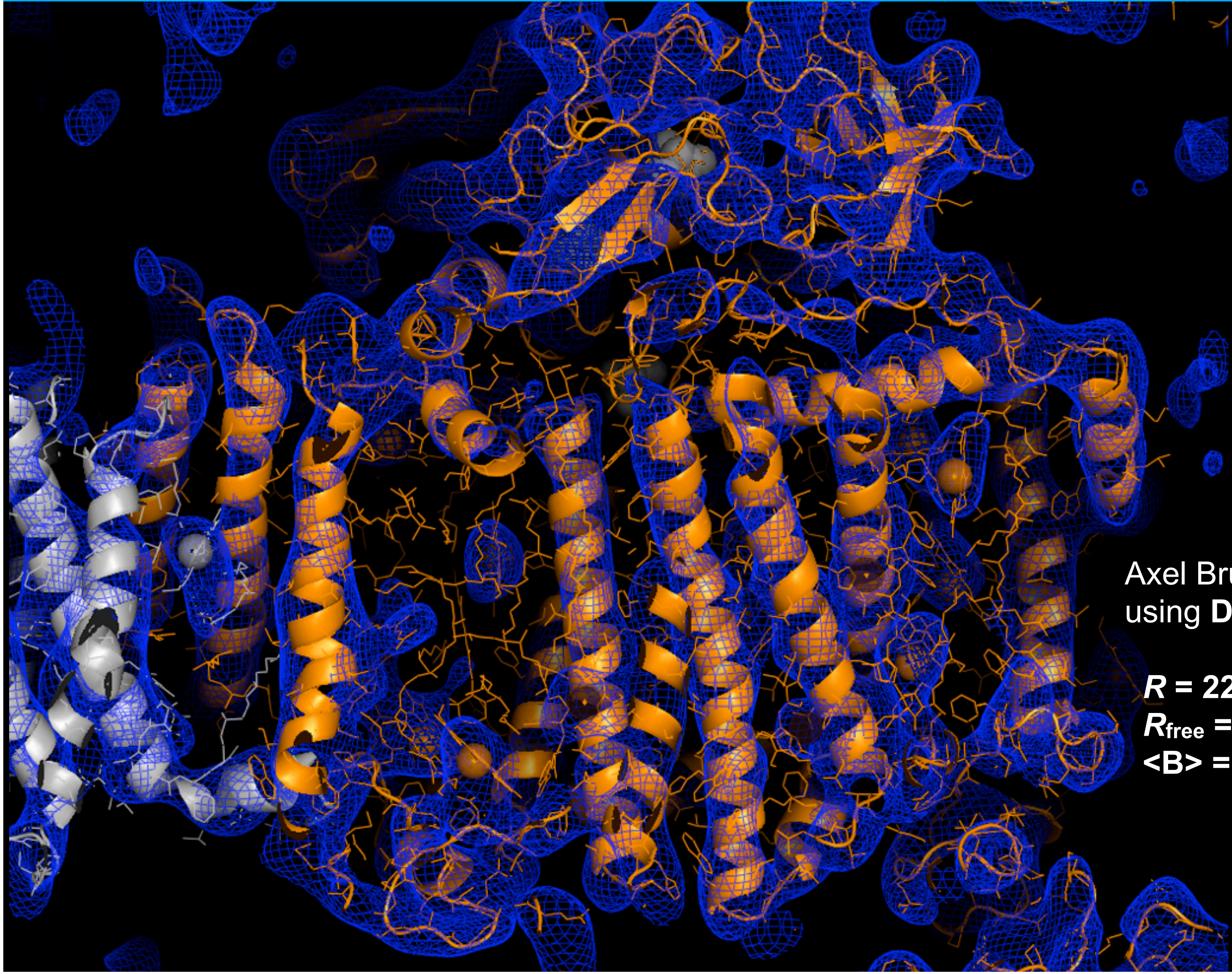
Tom White (CFEL)
Rick Kirian (ASU)





Tom White (CFEL)

Molecular replacement reconstructs the 7.4Å structure at 2 keV photon energy



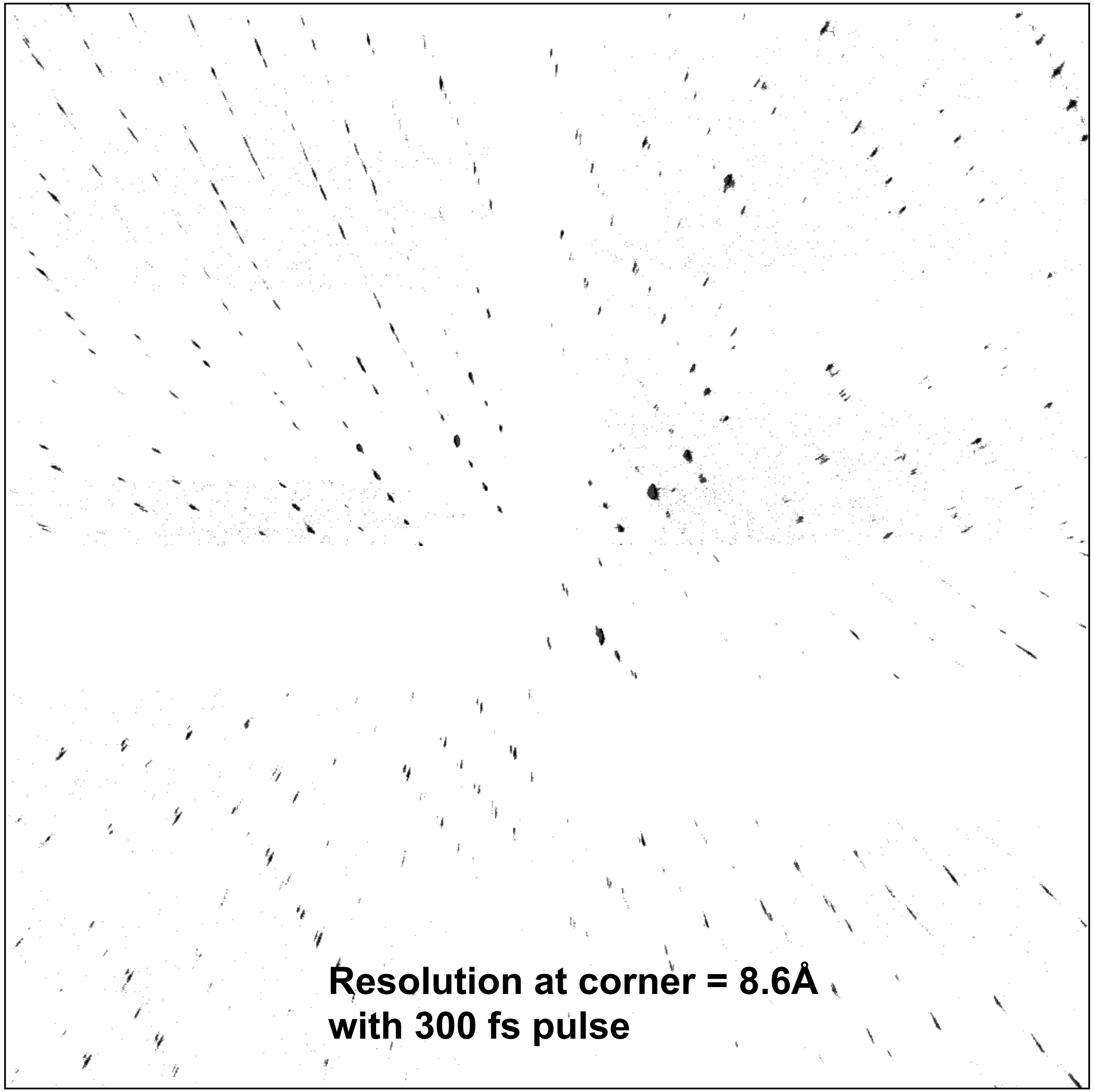
Axel Brunger (Stanford) using **DEN**

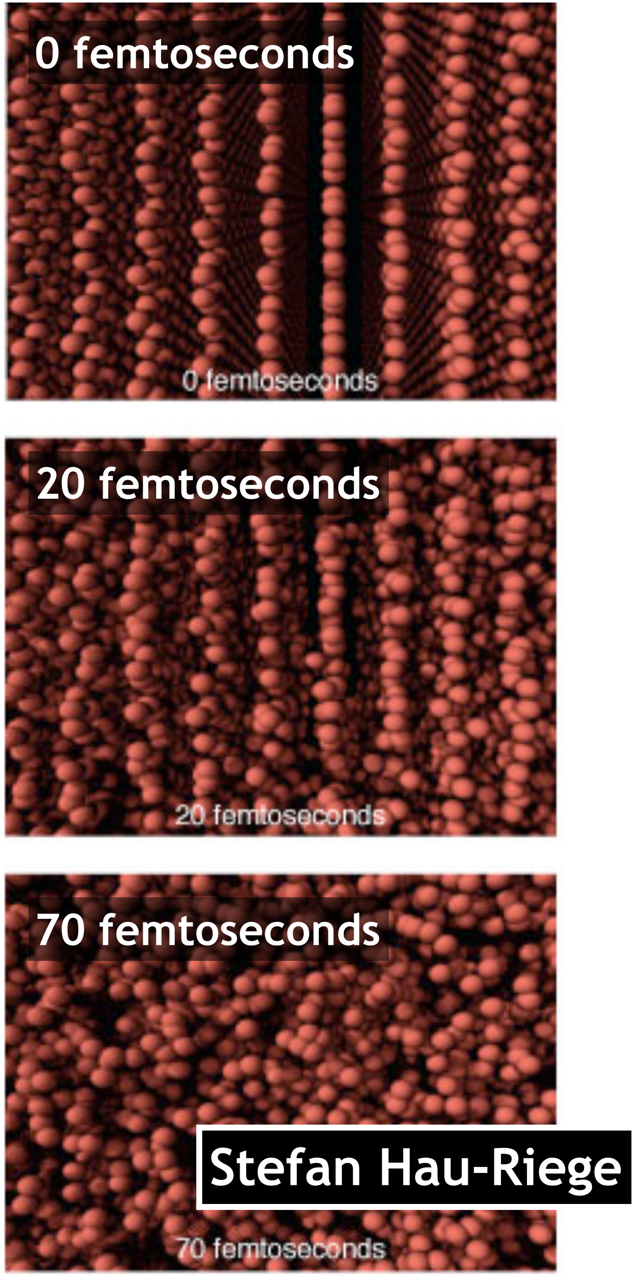
R **= 22.2%**

R_{free} = 25.7%

<B> = 10.3Å^2

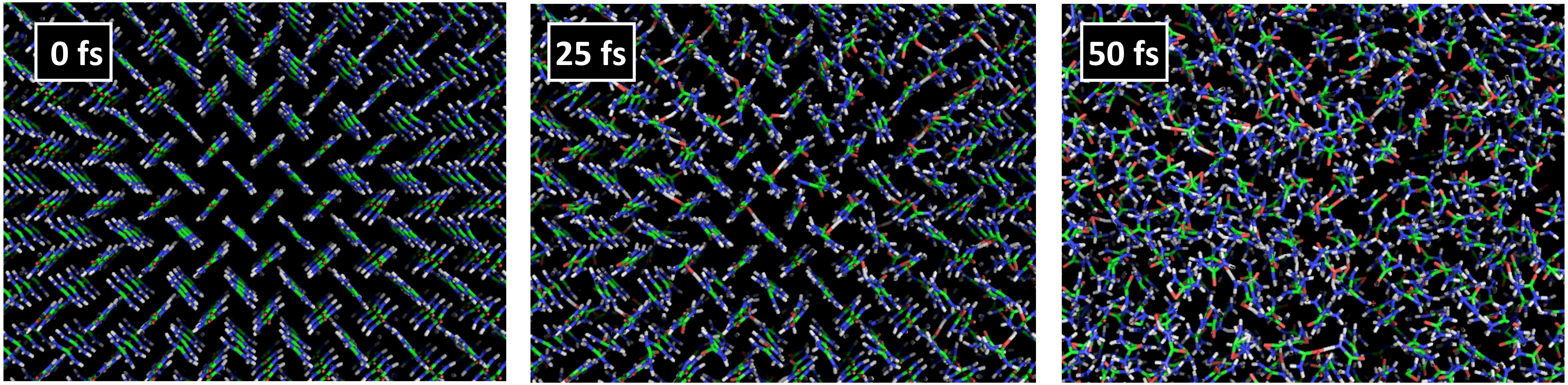
Bragg peaks are observed even with 300 fs pulses

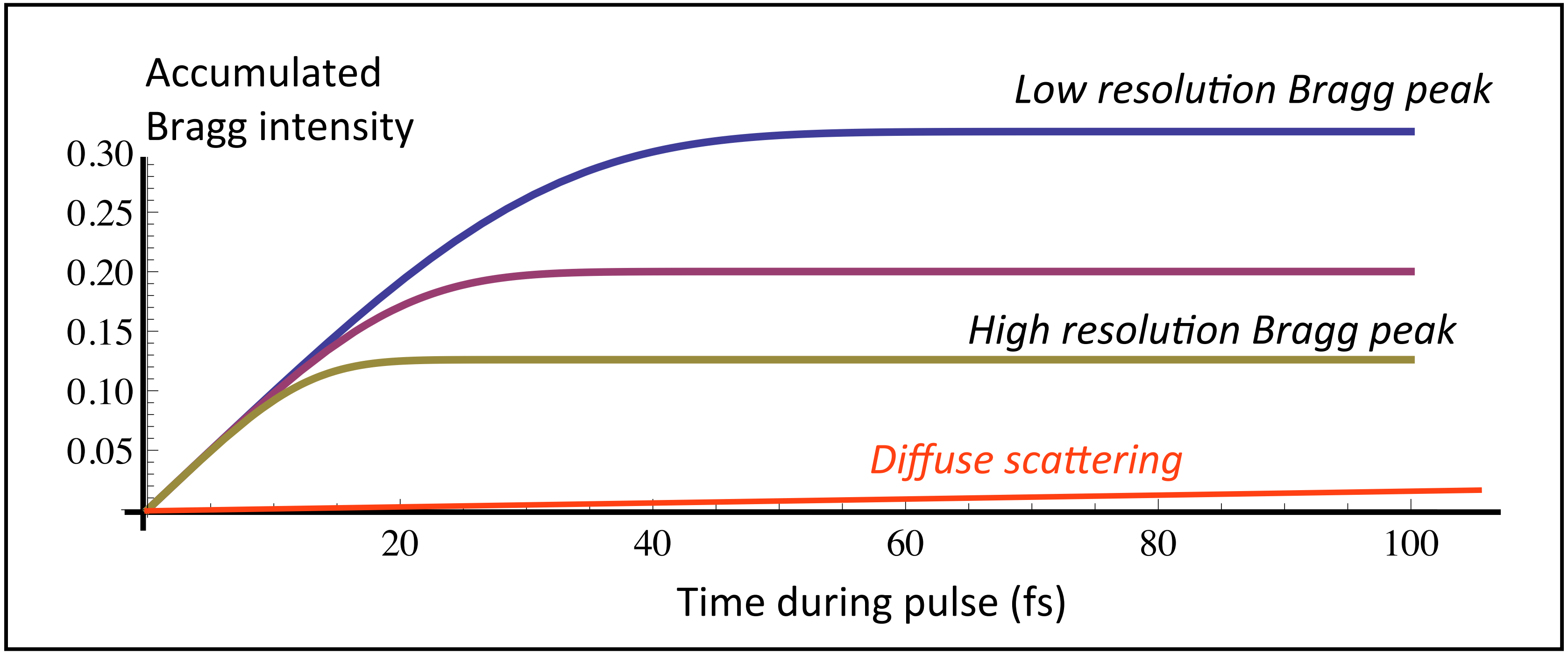

Resolution at corner = 8.6Å
with 300 fs pulse



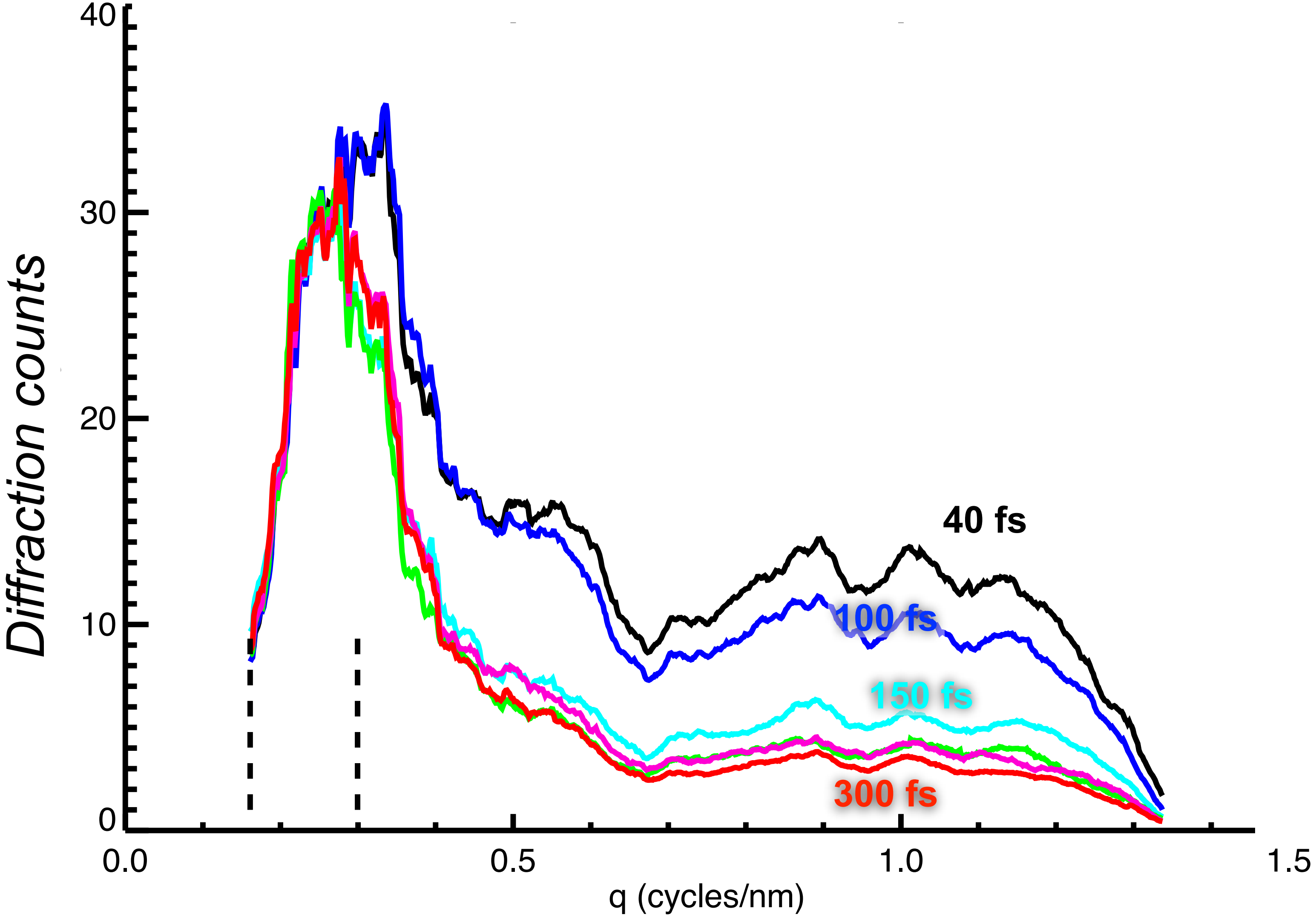
Stefan Hau-Riege

A crystal only gives Bragg diffraction when it is a crystal!





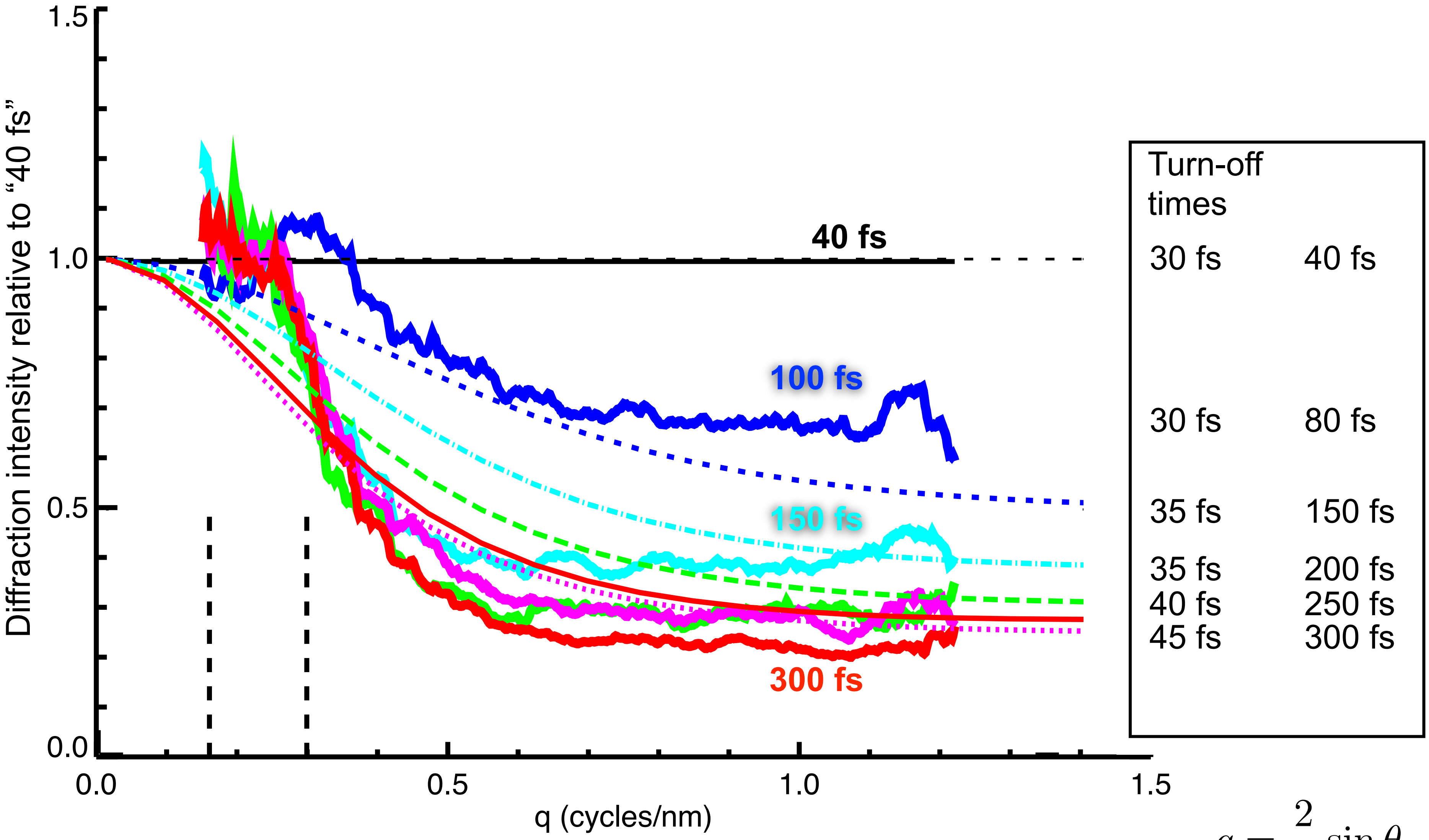
We see a degradation of the sample at longer pulse durations



$$q = \frac{2}{\lambda}\sin\theta$$

Barty et al, Nature Physics **6,** 35 (2012)

Only the first 30 fs contributes to the diffraction

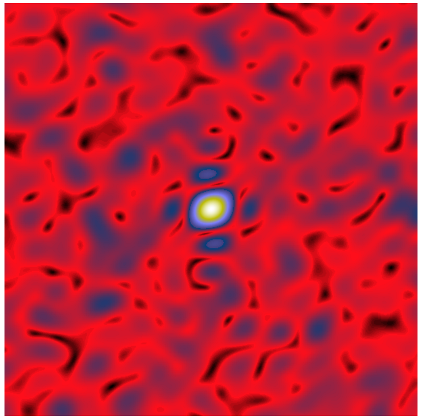


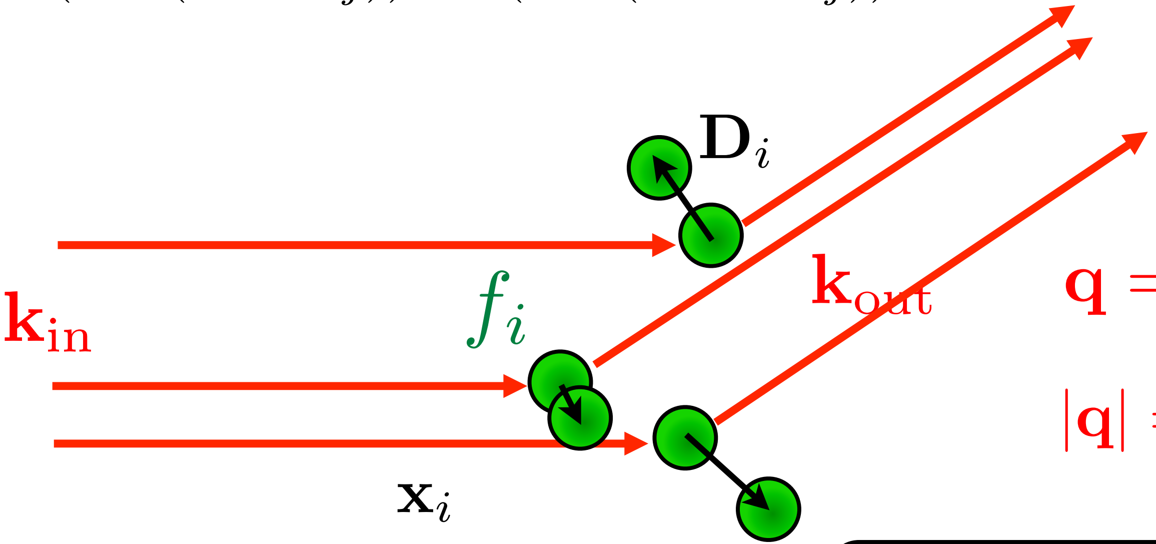
$$q = \frac{2}{\lambda} \sin \theta$$

In our experiments we average over many different but almost-identical objects

$$I(\mathbf{q}) = |f(\mathbf{q})|^2 = \sum_{i,j} f_i f_j \exp(i\mathbf{q}\cdot(\mathbf{x}_i - \mathbf{x}_j))$$

$$= \sum_{i,j} f_i f_j \exp(i\mathbf{q}\cdot(\bar{\mathbf{x}}_i - \bar{\mathbf{x}}_j)) \exp(i\mathbf{q}\cdot(\mathbf{D}_i - \mathbf{D}_j))$$





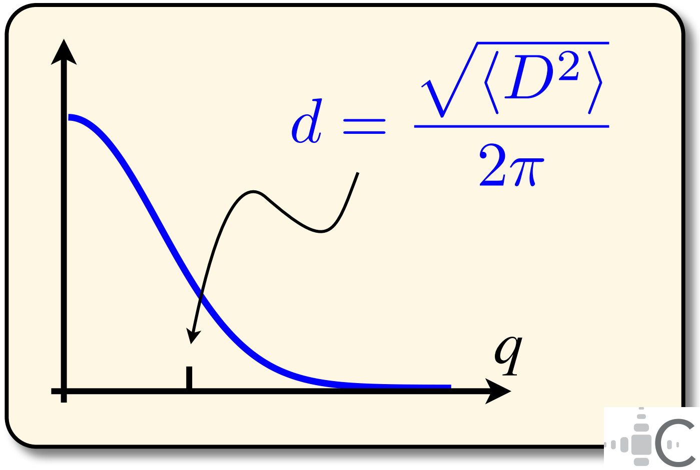
$$\mathbf{q} = \mathbf{k}_{\text{out}} - \mathbf{k}_{\text{in}}$$

$$|\mathbf{q}| = \frac{2\pi}{d}$$

$$\langle I(\mathbf{q})\rangle = I_0(\mathbf{q}) \left\langle \exp(i\mathbf{q}\cdot(\mathbf{D}_i - \mathbf{D}_j))\right\rangle$$

$$+\nu \sum_i f_i^2$$

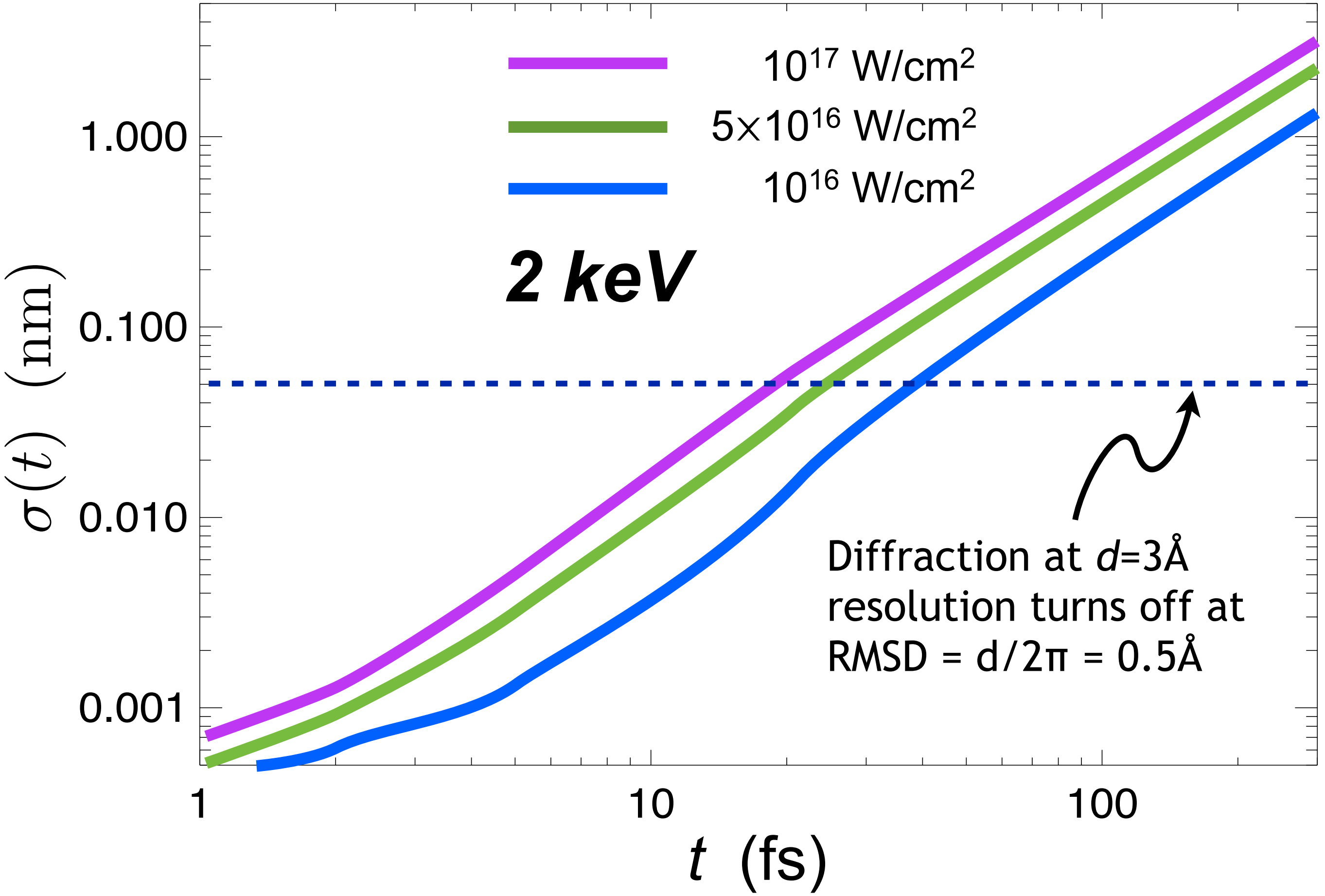
$$= I_0(\mathbf{q}) \exp\left(-q^2 \left\langle D^2\right\rangle\right) + \nu \sum_i f_i^2$$



$$d = \frac{\sqrt{\langle D^2\rangle}}{2\pi}$$

The diffusion of ions in a plasma is calculated using a hydrodynamic plasma code

$$I(q) = I_0\, r_e^2\, \Delta\Omega\, |F_0(q)|^2 \int_0^T e^{-q^2\sigma^2(t)}\, dt$$



Diffraction at d=3Å resolution turns off at RMSD = d/2π = 0.5Å

Ion diffusion:

temperature

$$D_i(t) = \frac{k_b T_i(t)}{m_i v_i(t)}$$

collision frequency

RMS displacement:

$$\sigma(t) = \sqrt{2ND_i t}$$

$$\propto t^{3/2}$$

$$\propto I_0^{1/2}$$

Barty *et al*. Nature Photon **6**, 35-40 (2012)

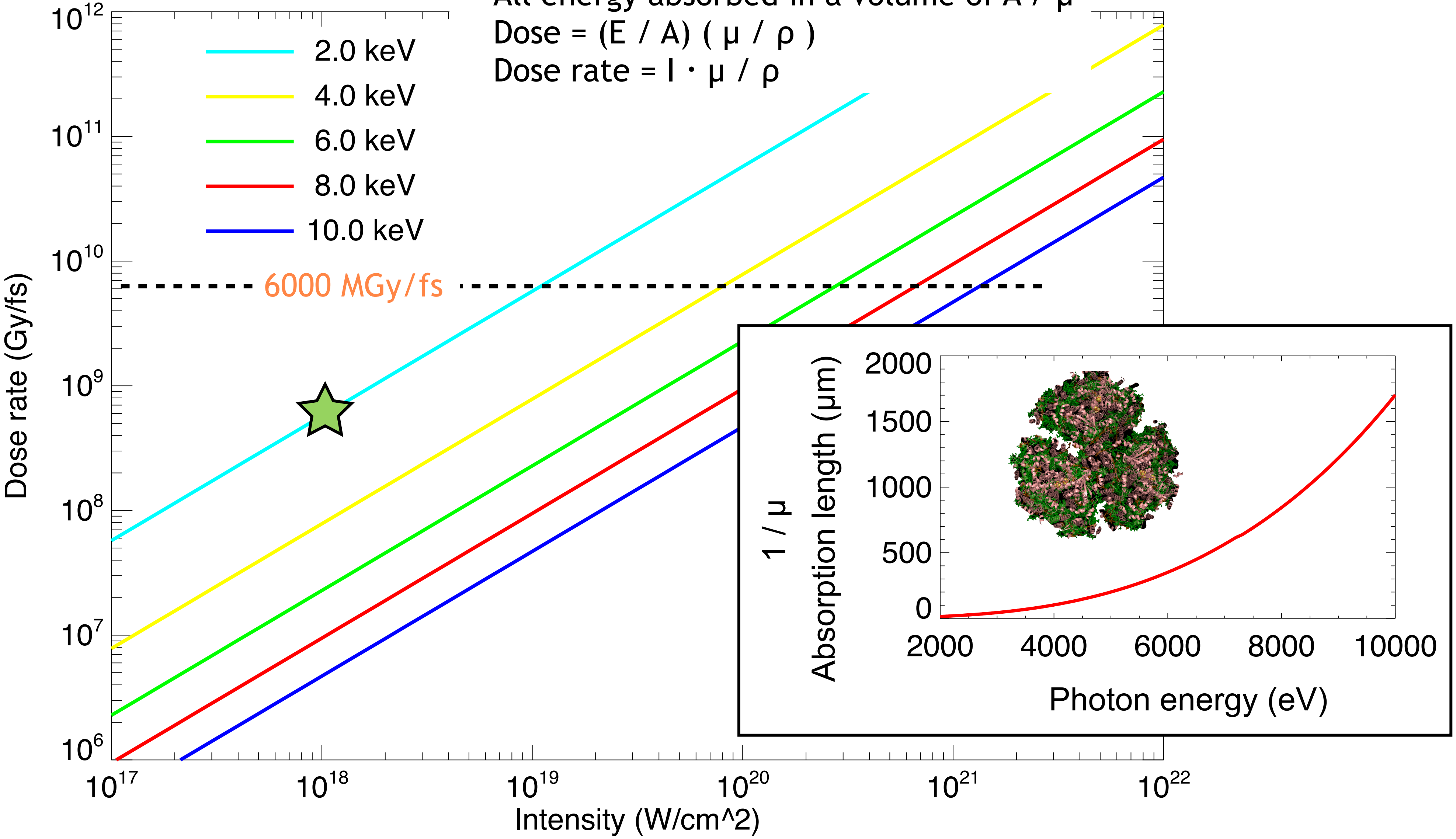
We have explored the explosion dynamics up to almost 1 GGy/fs

Dose = (Energy absorbed) / mass

All energy absorbed in a volume of A / μ

Dose = $(E / A)\ (\mu / \rho)$

Dose rate = $I \cdot \mu / \rho$



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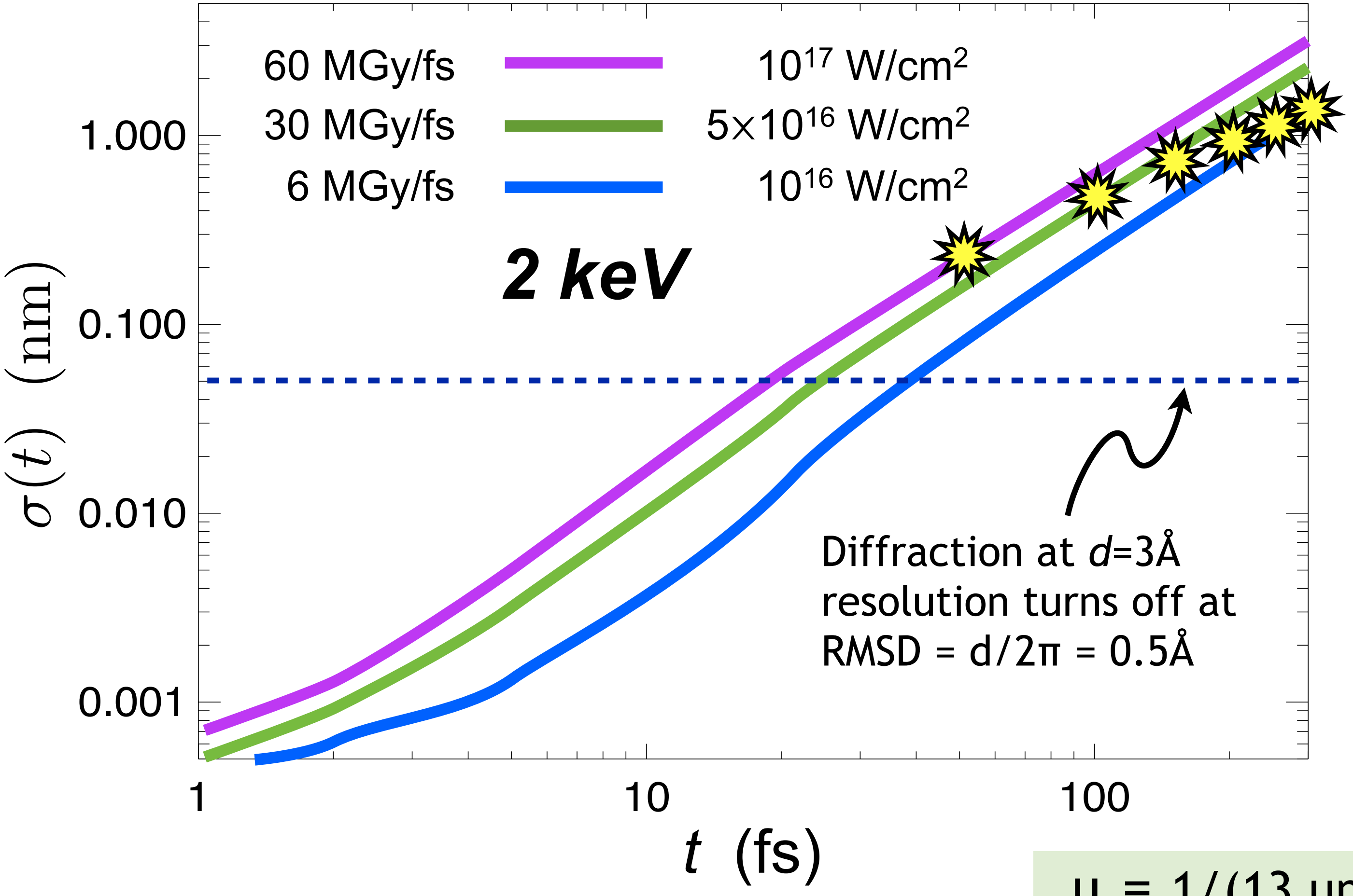


Diffraction at *d*=3Å resolution turns off at RMSD = d/2π = 0.5Å

Ion diffusion:

temperature

$$D_i(t) = \frac{k_b T_i(t)}{m_i v_i(t)}$$

collision frequency

RMS displacement:

$$\sigma(t) = \sqrt{2ND_it}$$

$$\propto t^{3/2}$$

$$\propto I_0^{1/2}$$

Dose rate

rate of energy absorbed / mass

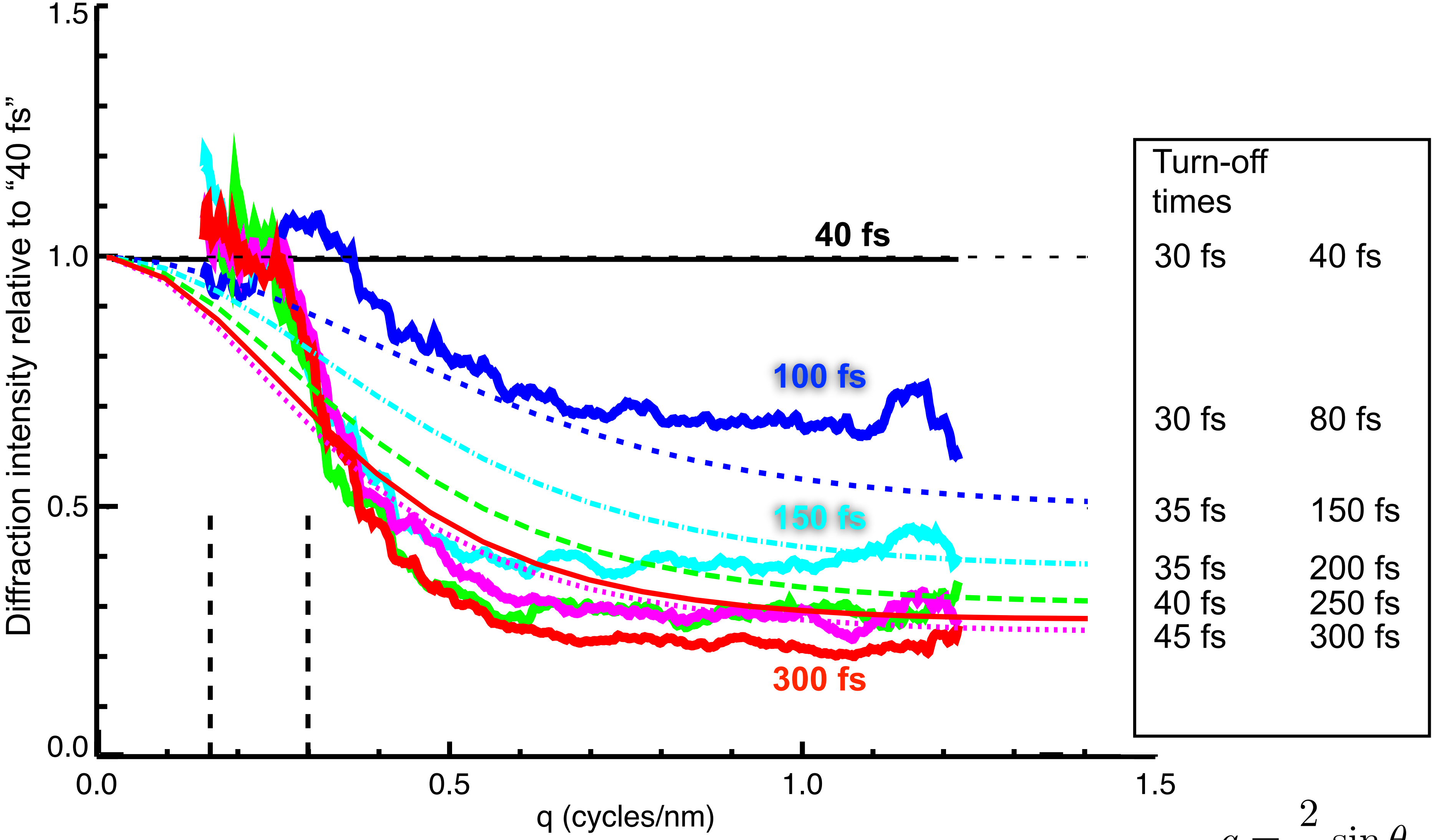
= I_0 • μ / ρ

μ = 1/(13 μm) at 2 keV

μ = 1/(850 μm) at 8 keV

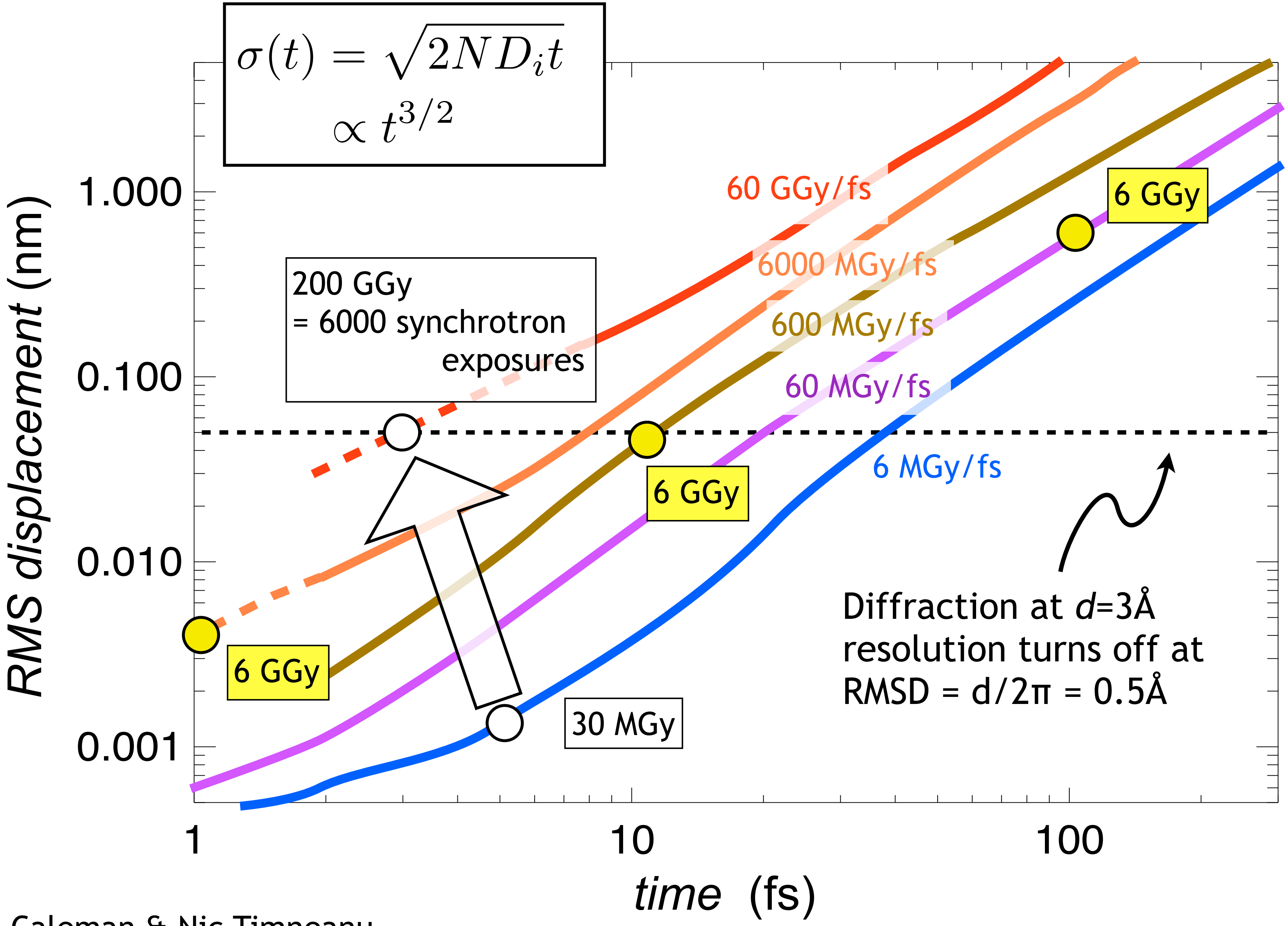
Barty *et al*. Nature Photon **6**, 35-40 (2012)

Only the first 30 fs contributes to the diffraction



$$q = \frac{2}{\lambda} \sin \theta$$

The explosion accelerates during the pulse



$$\sigma(t) = \sqrt{2ND_i t}$$
$$\propto t^{3/2}$$

200 GGy
= 6000 synchrotron exposures

Diffraction at *d*=3Å resolution turns off at RMSD = d/2π = 0.5Å

Carl Caleman & Nic Timneanu

Our method follows "best practices" to minimise the effects of radiation damage

- ☆ Don't waste dose on pre-alignment
- ☆ Use the very first photons hitting the sample, when the sample is still pristine
- ☆ Combine lots of independent measurements. We work at minimal dose per crystal (by relinquishing the goal of efficient peak integration and scaling)
- ☆ Software now available to crunch through hundreds of Terabytes of data: http://www.desy.de/~twhite/crystfel/index.html

Summary

- ☆ "Diffraction before destruction" holds to 1.8 Å resolution
- ☆ No effect of radiation damage is yet observed in refined protein structures
- ☆ Isotropic atomic displacements terminate the diffraction
- ☆ Specific damage could manifest as an expansion around heavy atoms, which are local centers of high charge. This may be gated by isotropic motion.
- ☆ Ionization should enhance anomalous signals, giving a route to phasing
- ☆ The key metric for this mode of imaging is X-ray *intensity* (photons per unit area per unit time). The optimal X-ray FEL source is that of highest pulse power