

Imaging Molecules with X-ray Free-Electron Lasers

Henry Chapman

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

Bad Honnef, April 2012

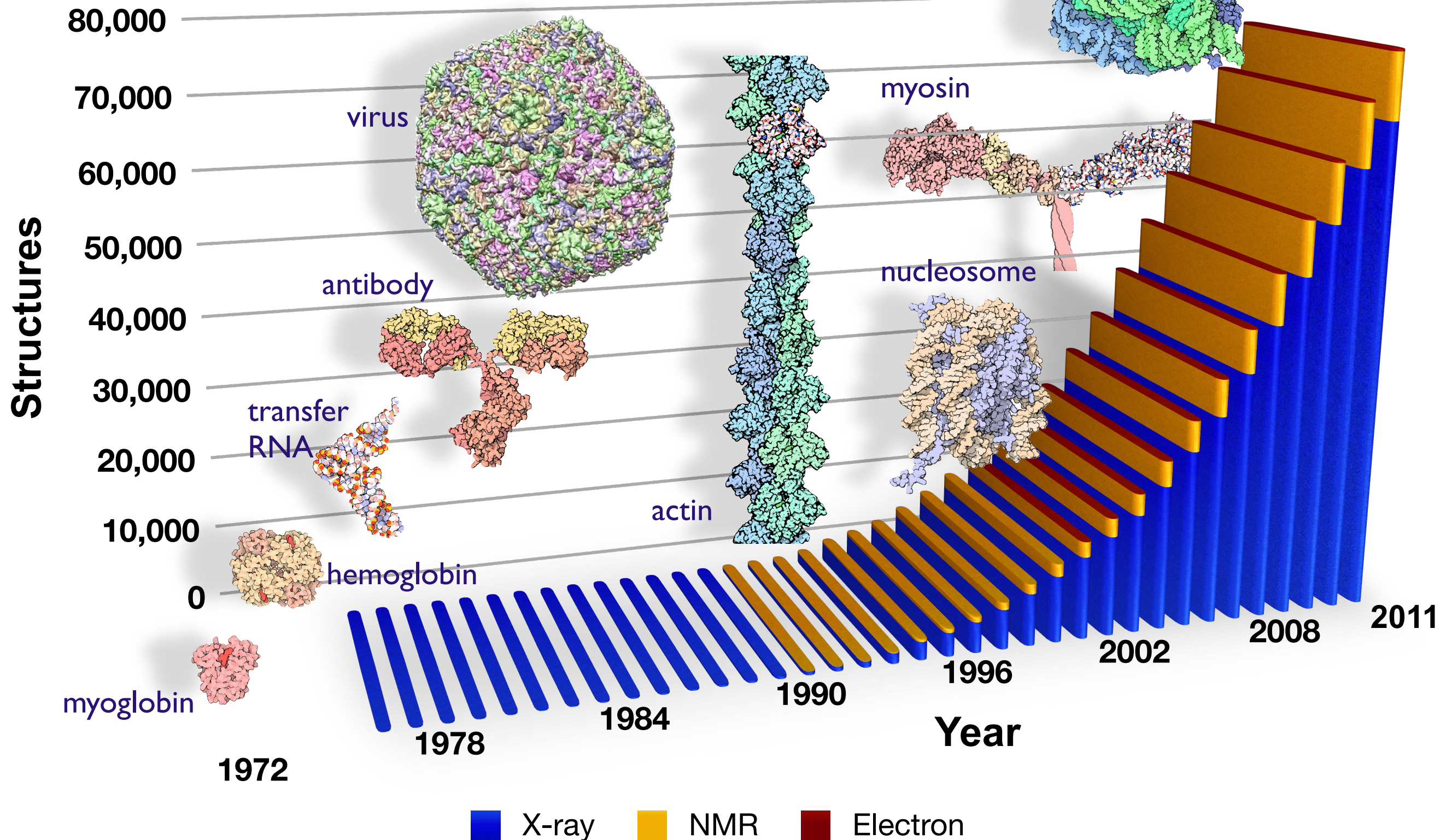


Experiments and analyses are carried out as a large collaboration

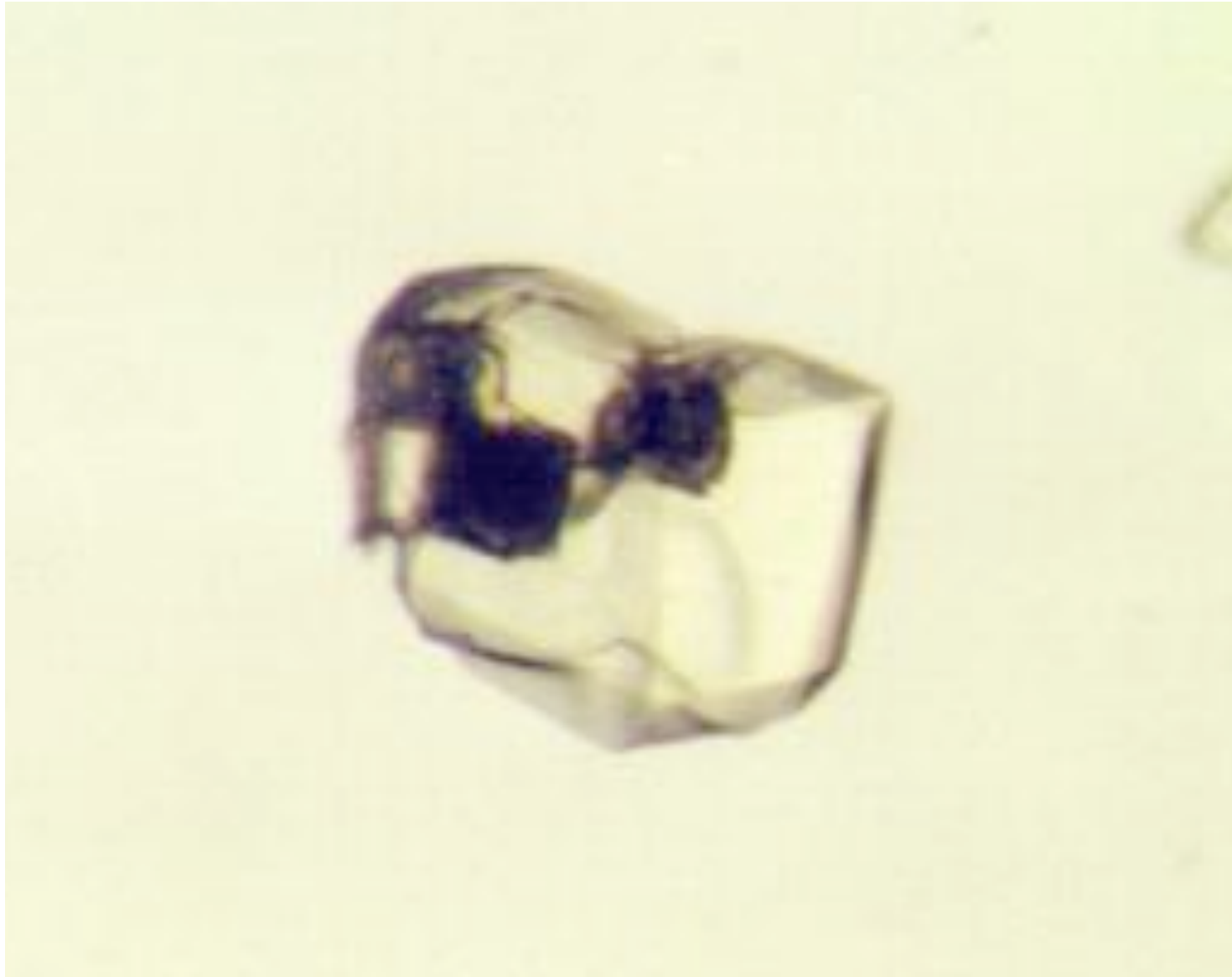
CFEL-DESY	A. Barty, M. Liang, T. White, D. Deponete, S. Stern, A. Martin, C. Caleman, K. Beyerlein, R. Kirian, K. Nass, F. Stellato, F. Wang, H. Fleckenstein, L. Gumprecht, L. Galli, S. Bajt, M. Barthelmess
ASU	J. Spence, P. Fromme, U. Weierstall, B. Doak, R. Kirian, X. Wang, I. Grotjohann, R. Fromme
MPG CFEL ASG	I. Schlichting, R. Shoeman, L. Lomb, S. Kassemeyer, S. Bari, T. Barends, J. Steinbrener, D. Rolles, S. Epp, A. Rudenko, L. Strüder, R. Hartmann, L. Foucar, N. Kimmel, P. Holl, J. Ullrich
SLAC-PULSE	M. Bogan, D. Starodub, R. Sierra, C. Hampton, D. Loh
SLAC-LCLS	S. Boutet, G. Williams, M. Seibert, J. Kryzwiniski, C. Bostedt, M. Messerschmidt, J. Bozek, W. White, R. Coffee, C. Kenney, R. Herbst, J. Pines, P. Hart, J. Morse, P. Emma, J. Frisch, J. Galayda <i>and many others</i>
Uppsala	J. Hajdu, Nic Timneanu, J. Andreasson, M. Seibert, F. Maia, M. Svenda, T. Ekeberg, J. Andreasson, A. Rucker, O. Jonsson, D. Westphal
Euro XFEL	J. Schulz, N. Coppola, A. Aquila
LLNL	S. Hau-Riege, M. Frank, M. Hunter
LBNL	S. Marchesini, J. Holton
Gothenburg	R. Neutze, L. Johansson, D. Arnlund
U. Hamburg	L. Redecke, C. Betzel
U. Tübingen	M. Duszynko, R. Koopman, K. Cupelli
CAMP Team	<i>Led by Joachim Ullrich and Ilme Schlichting</i>

The number of protein structures solved is now increasing linearly

Cumulative number of structures in the PDB



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

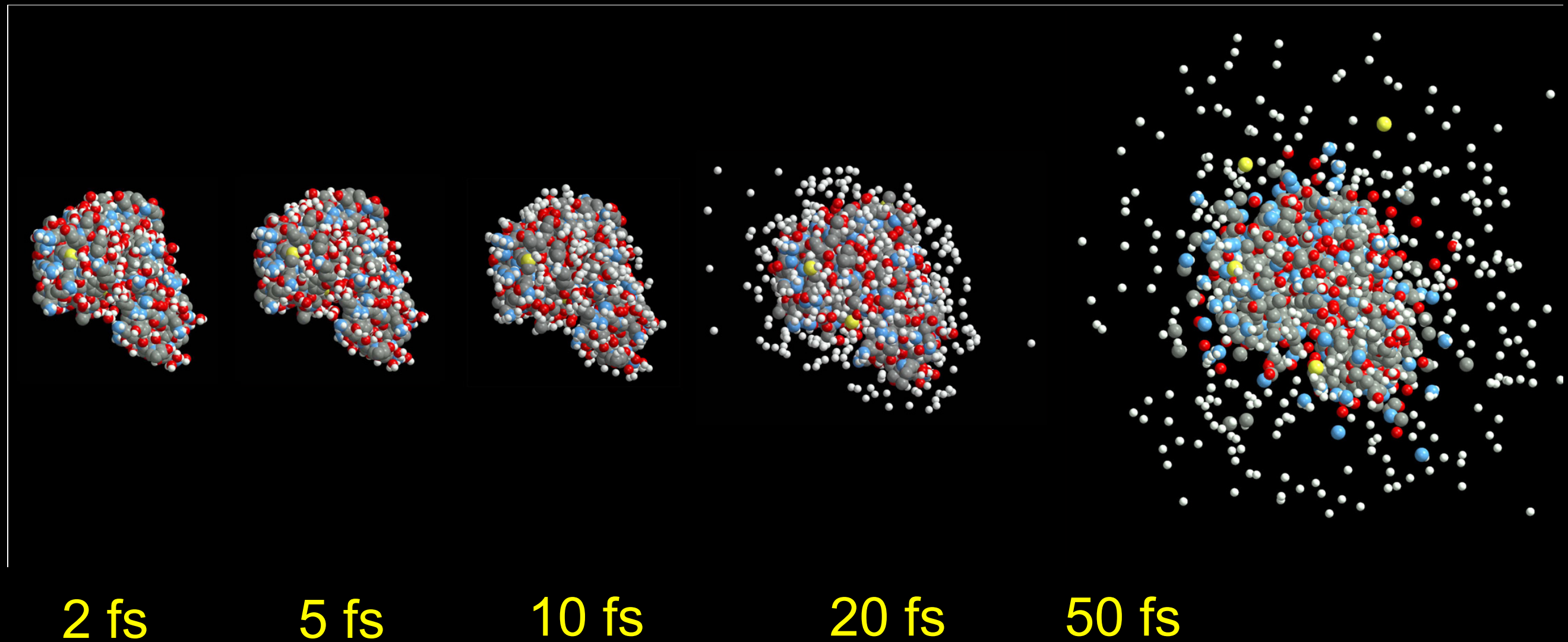
$$1 \text{ Gy} = 1 \text{ J/kg}$$

$$30 \text{ MGy} \approx 0.3 \text{ eV / Da} \\ \approx 0.02 \text{ eV / atom}$$

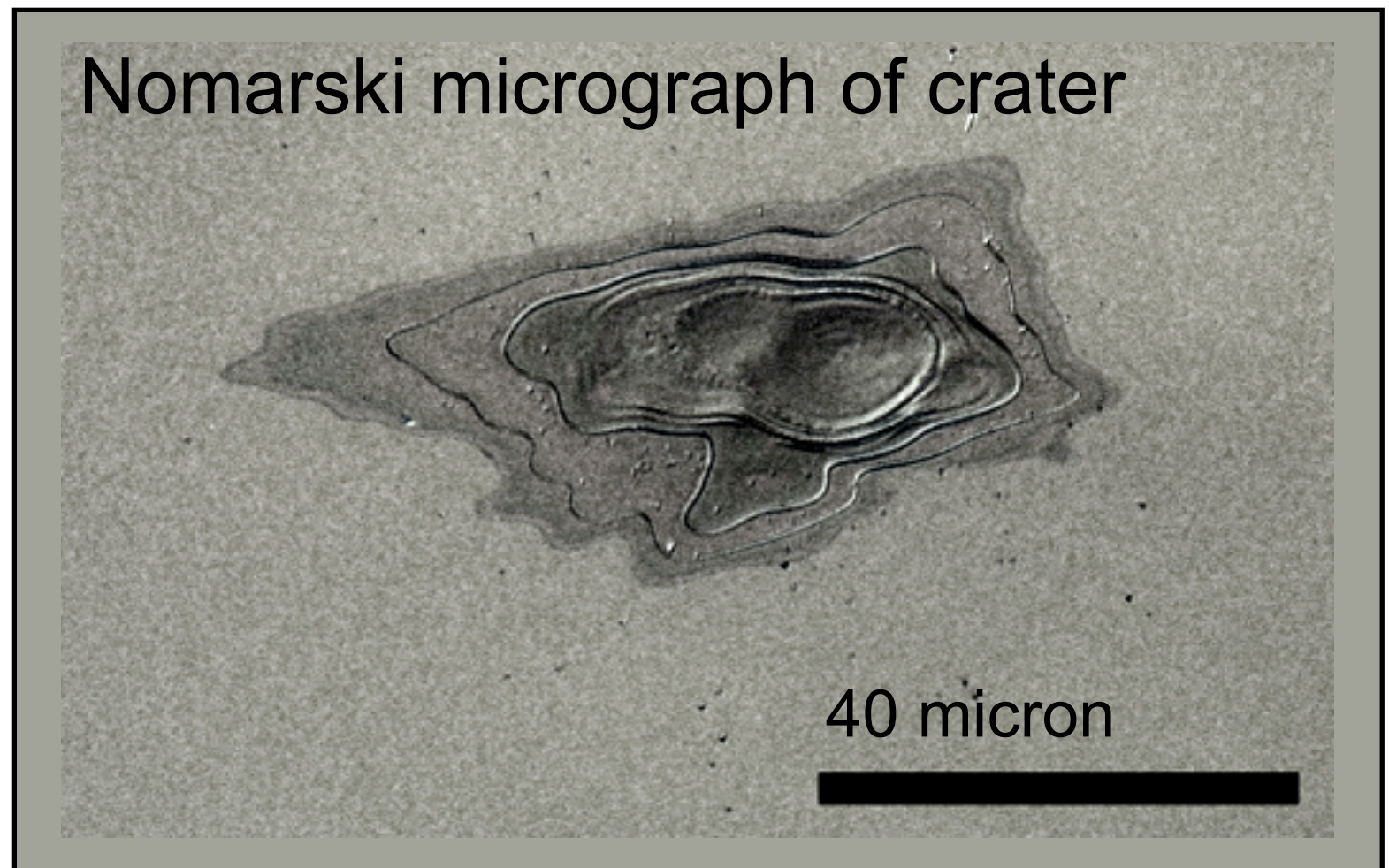
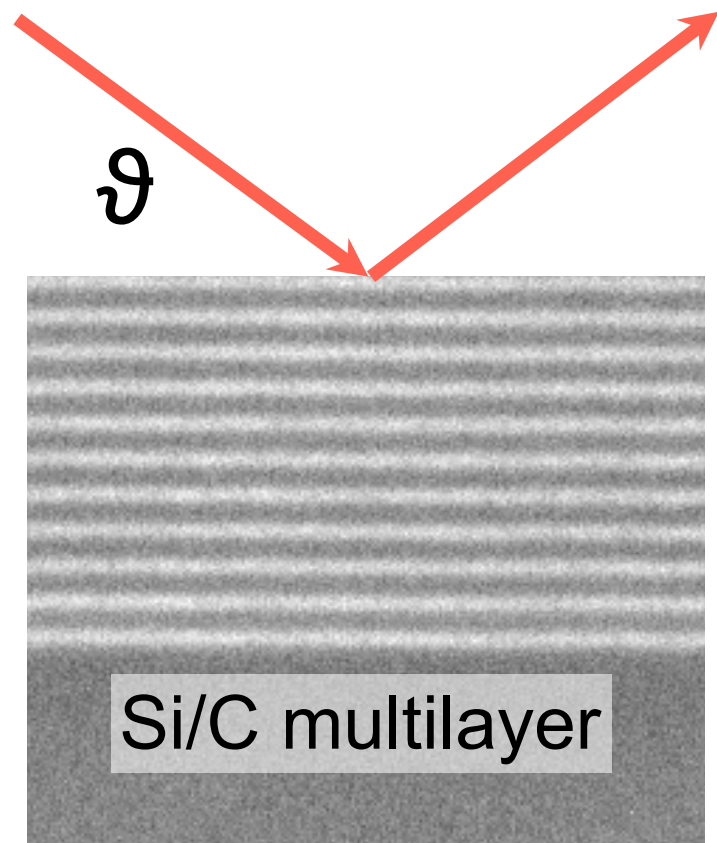
(about one ionization per
20 amino-acid residues)

$$\approx 6 \times 10^{10} \text{ ph}/\mu\text{m}^2$$

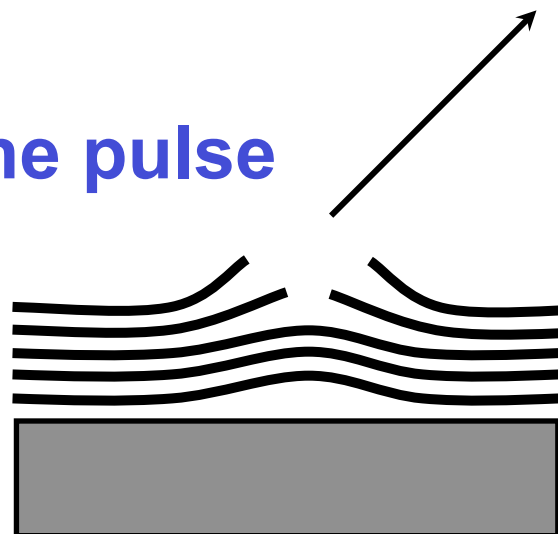
X-ray free-electron lasers may enable atomic-resolution imaging of biological macromolecules



First EUV-FEL experiments show that pulses are indeed destructive



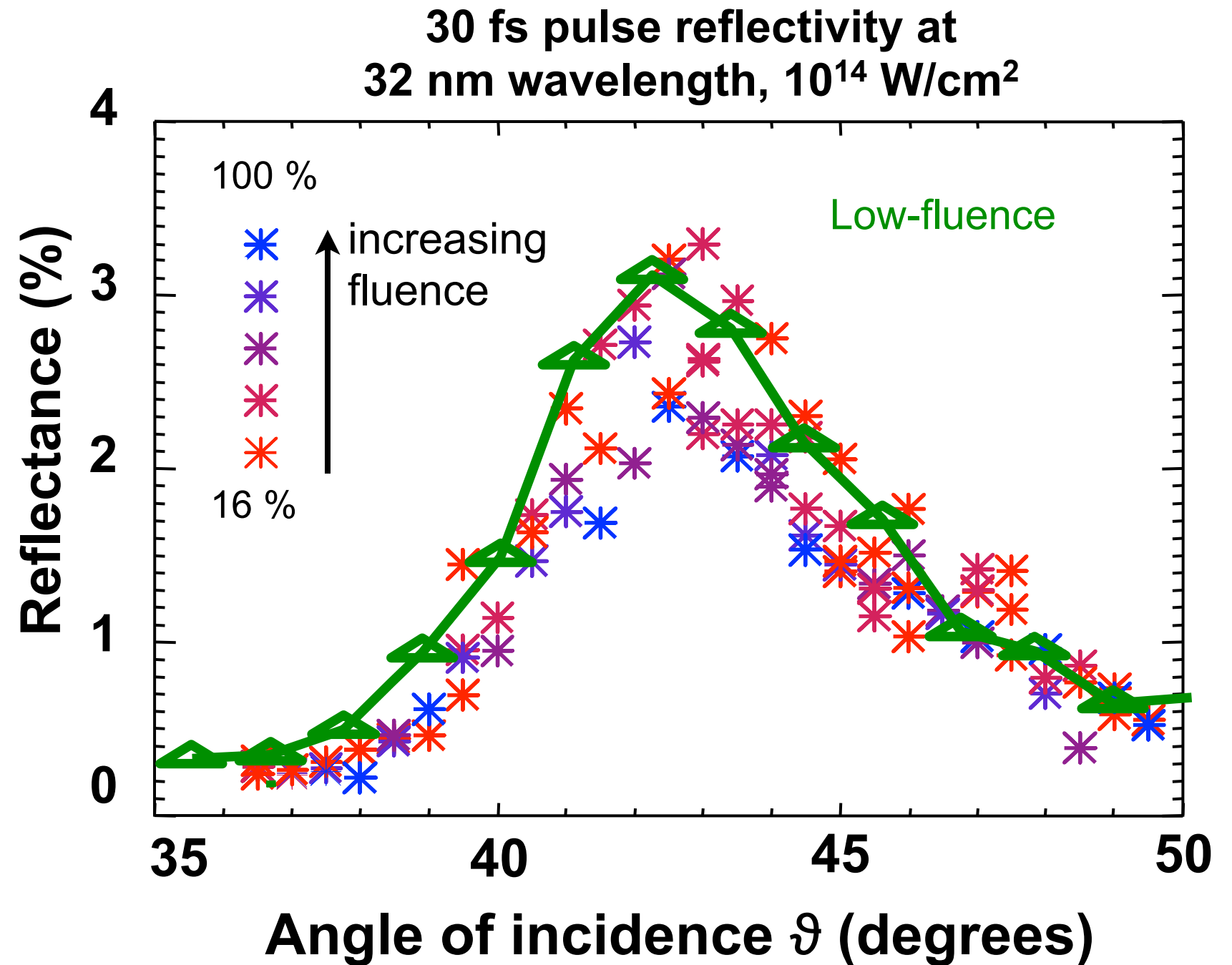
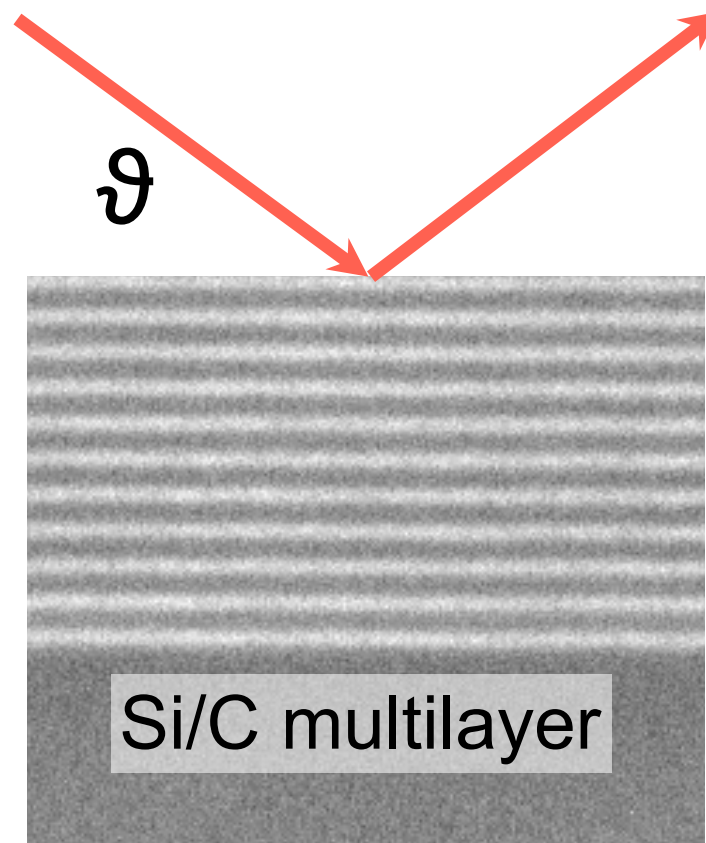
After the pulse



Plasma forms,
layers ablate

Electron temperature
reaches 28 eV
(300,000 K)

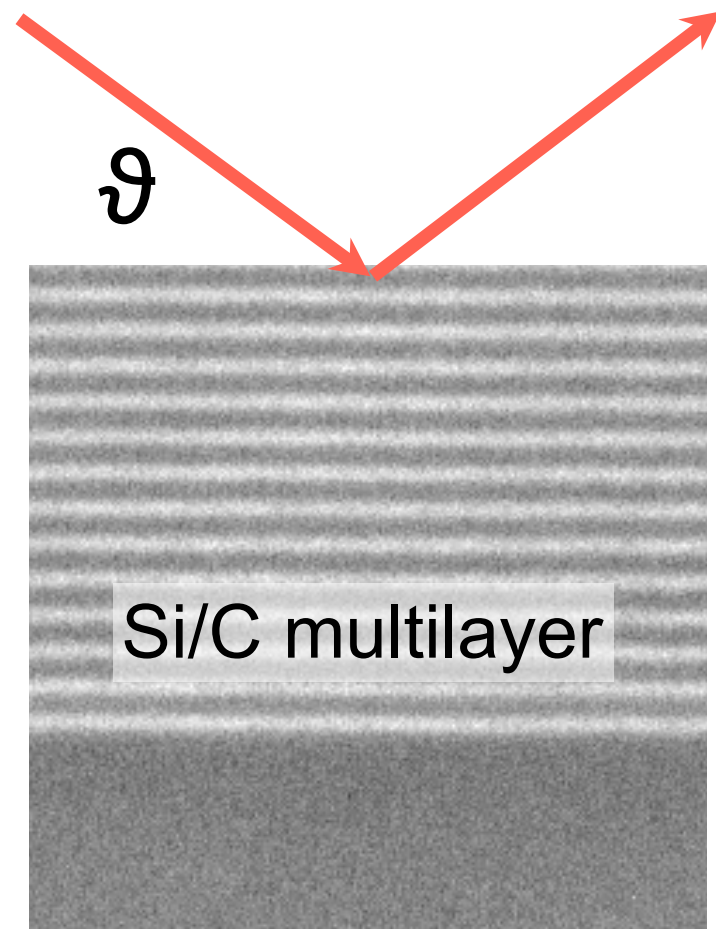
First EUV-FEL experiments show that structural information can be obtained before destruction



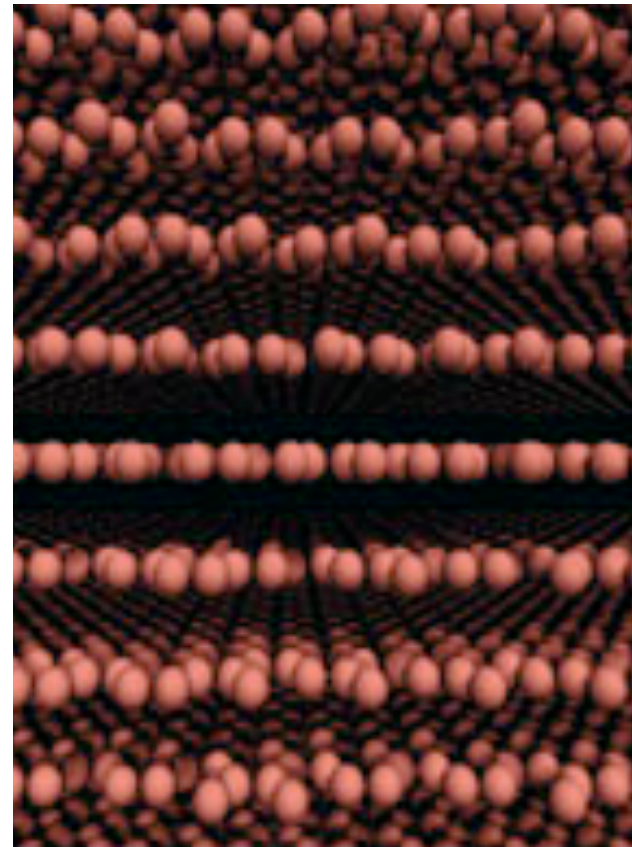
Reflectivity unchanged
Multilayer d spacing not changed by more than 0.3 nm

S. Hau-Riege *et al.* PRL 98, 145502 (2007)

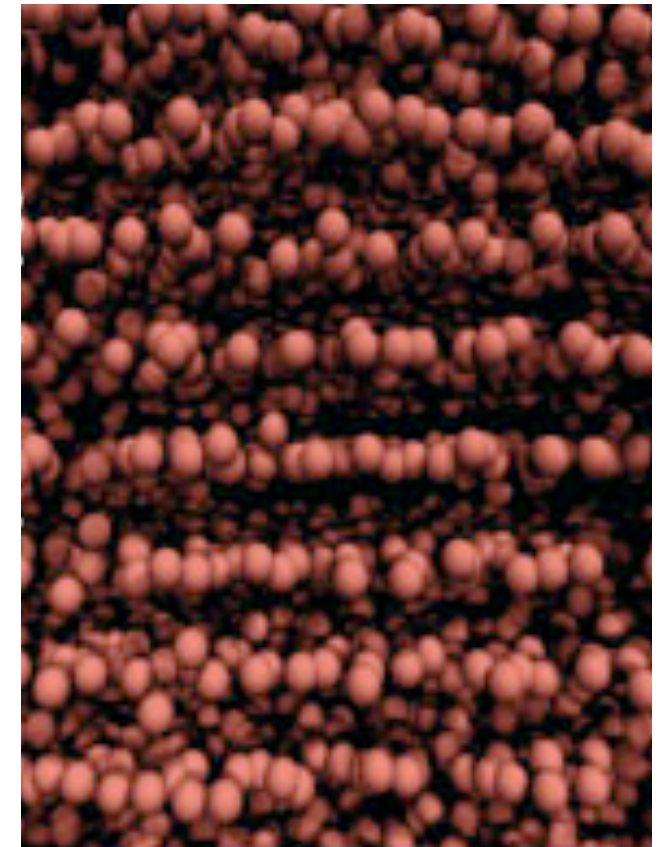
We used the same strategy as at FLASH to monitor sample destruction during the pulse



0 fs



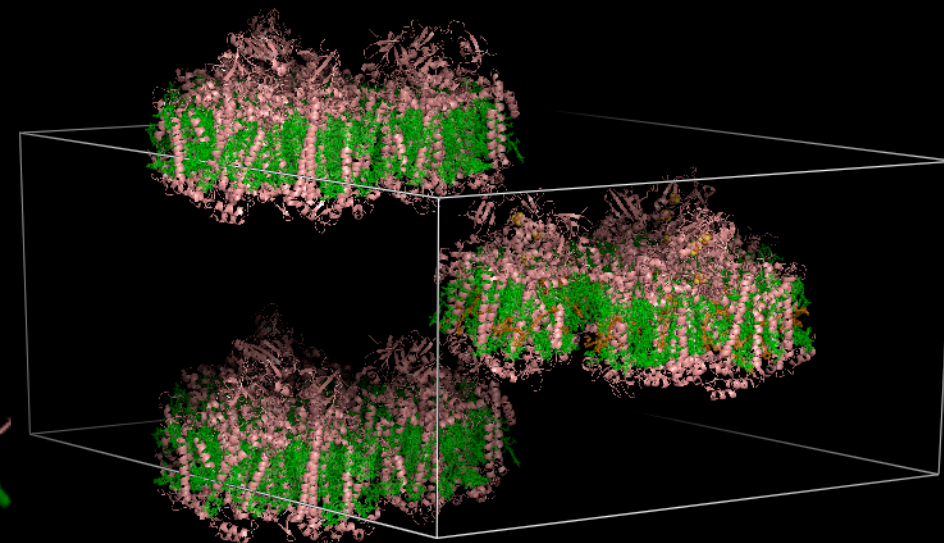
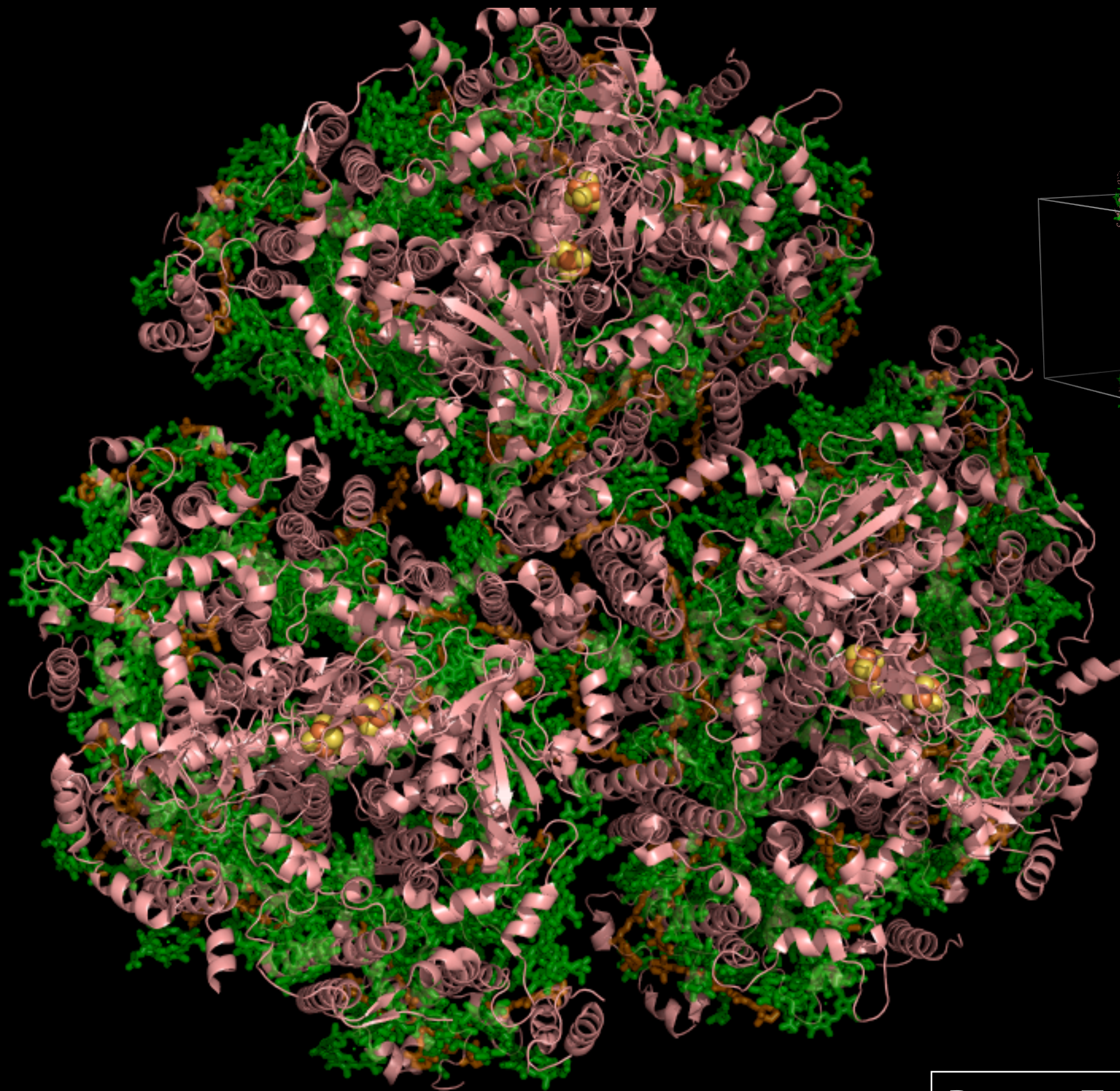
20 fs



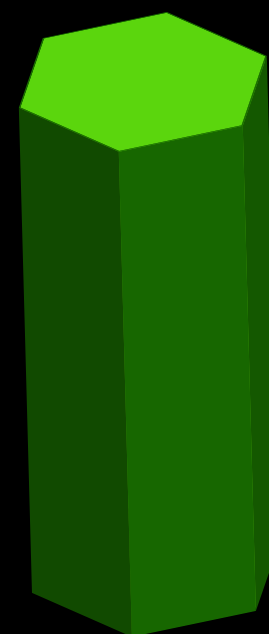
Stefan Hau-Riege, LLNL

FLASH: Wavelength 100 Å
Structures: 100 Å to microns

LCLS: Wavelength 6.8 Å
Structures: 6 Å to microns

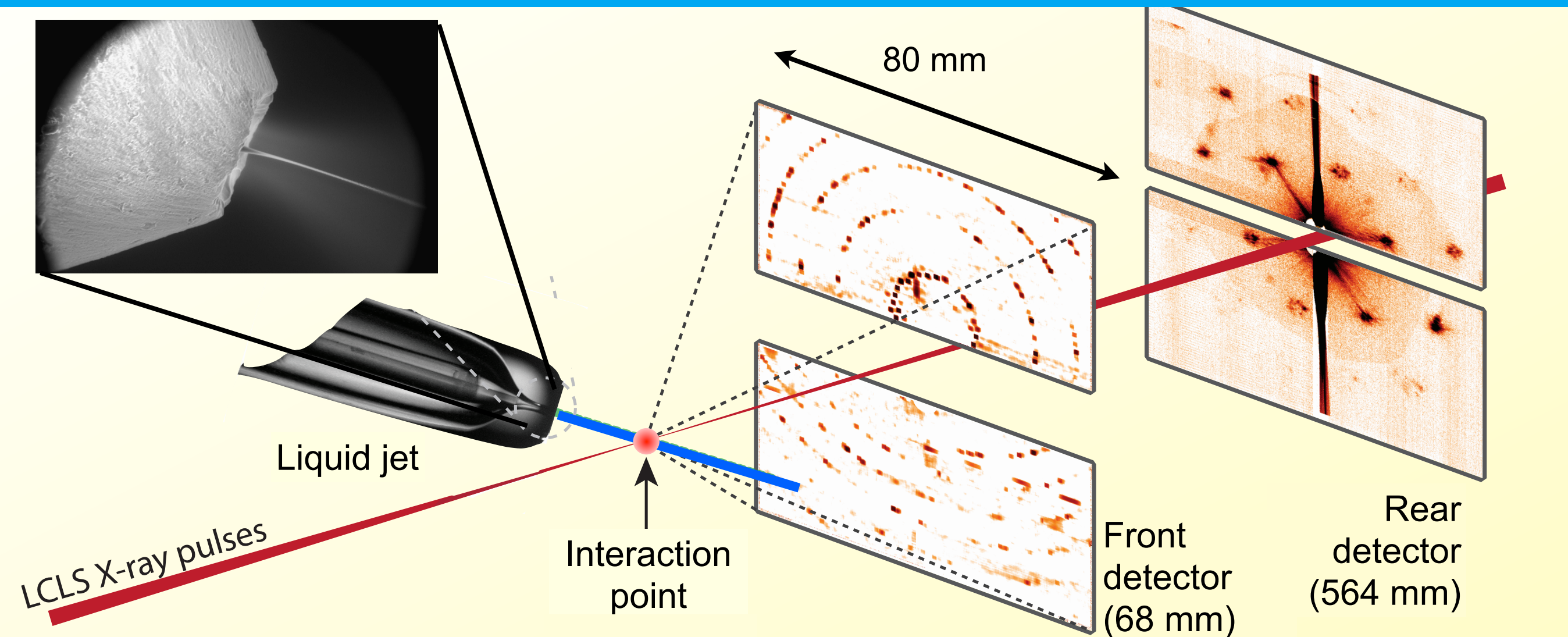


$$a = b = 288 \text{ \AA}$$
$$c = 167 \text{ \AA}$$

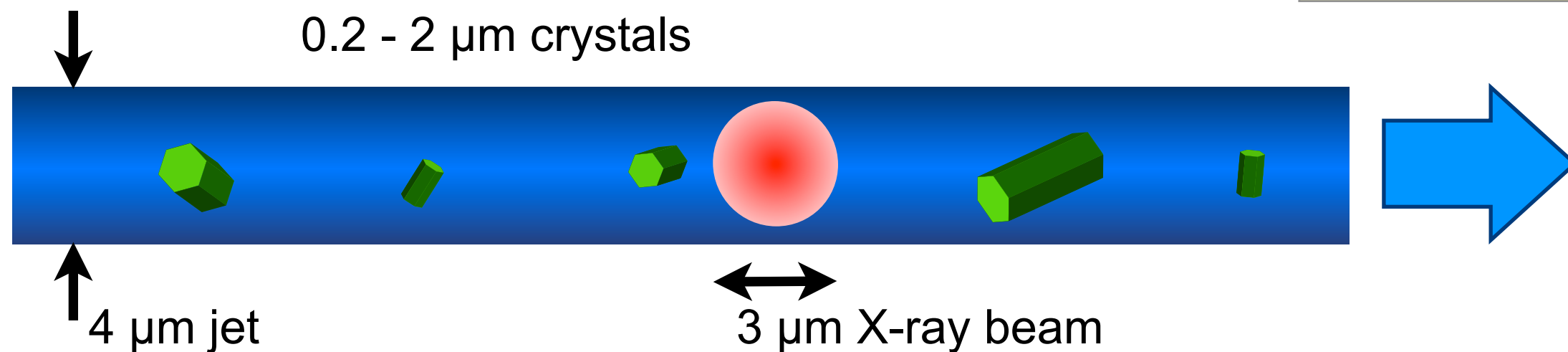


Petra Fromme, ASU

Nanocrystallography is carried out in a flowing water microjet



CAMP Chamber: L. Struder *et al.*



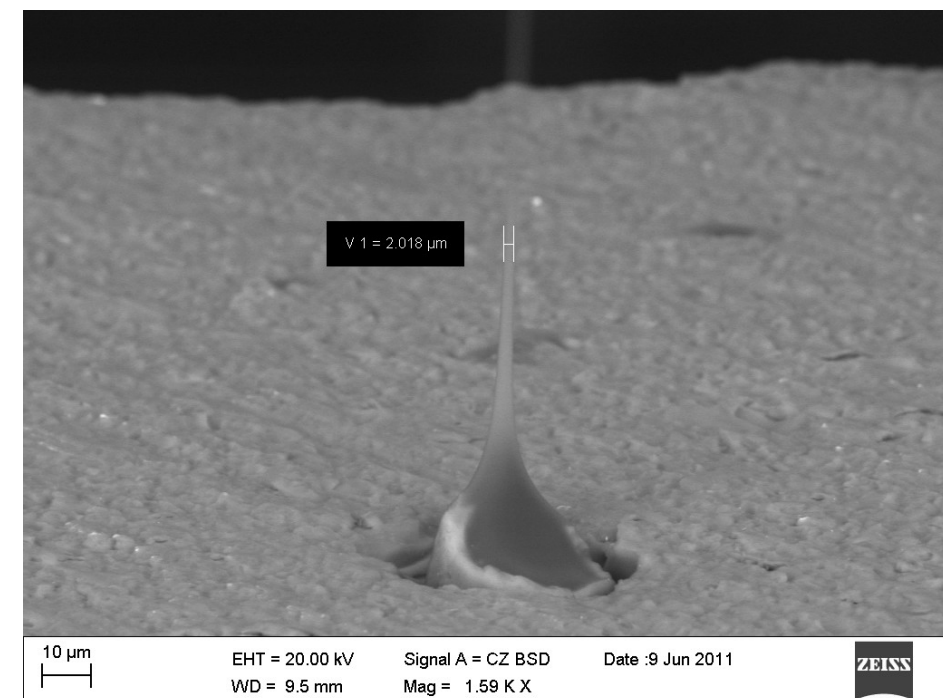
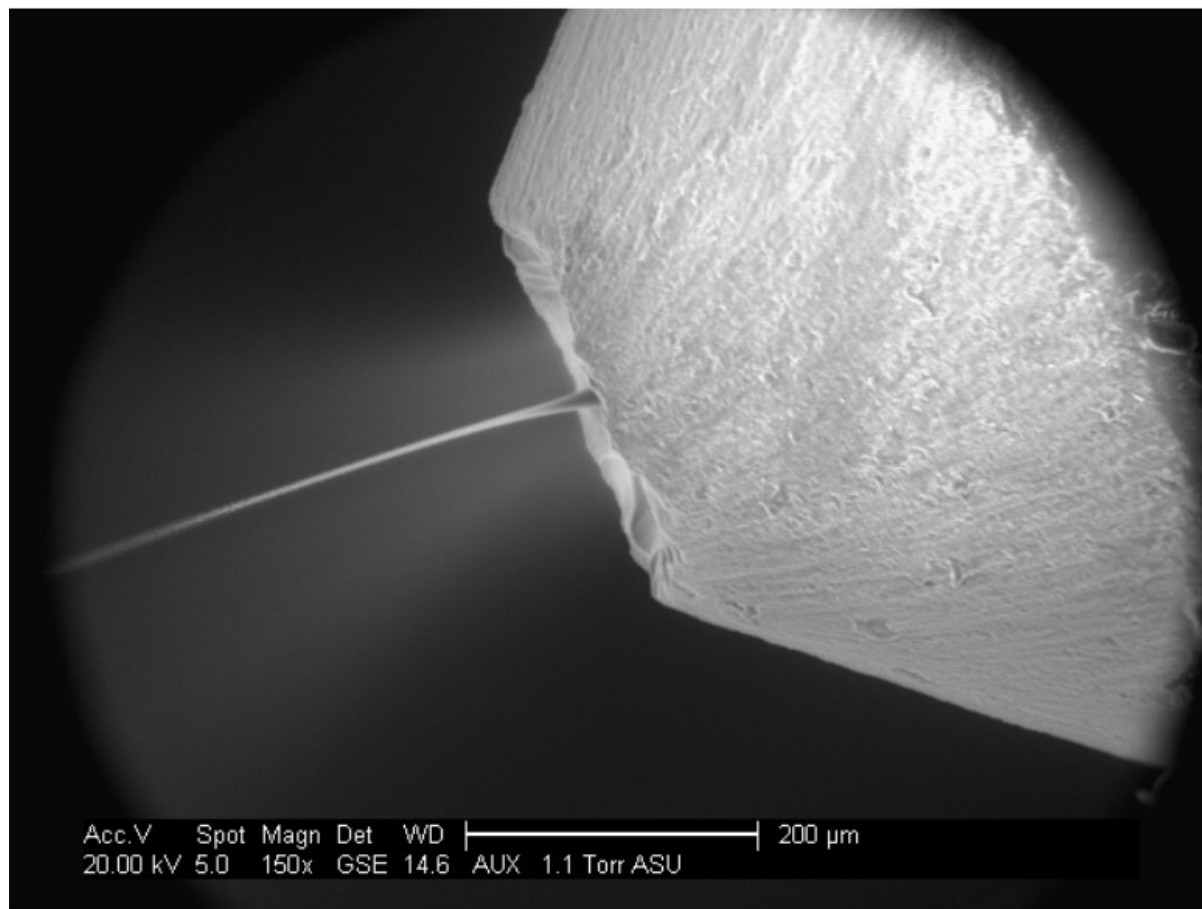
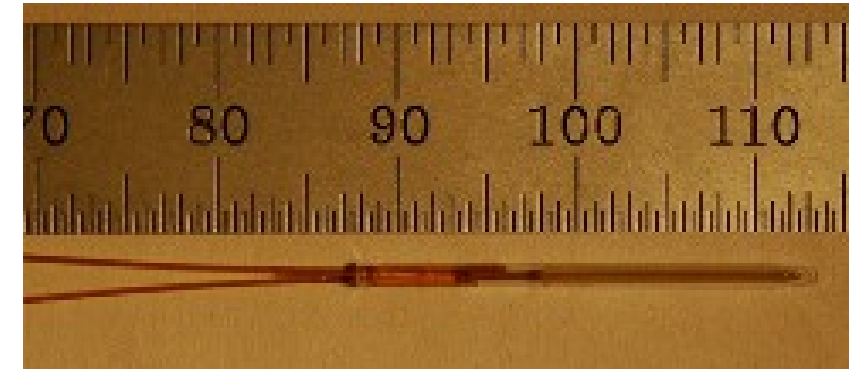
Samples are delivered to the beam in a liquid jet



- > Sample delivery (“injection”) technology is **critical** to the success of serial crystallography and many other FEL experiments

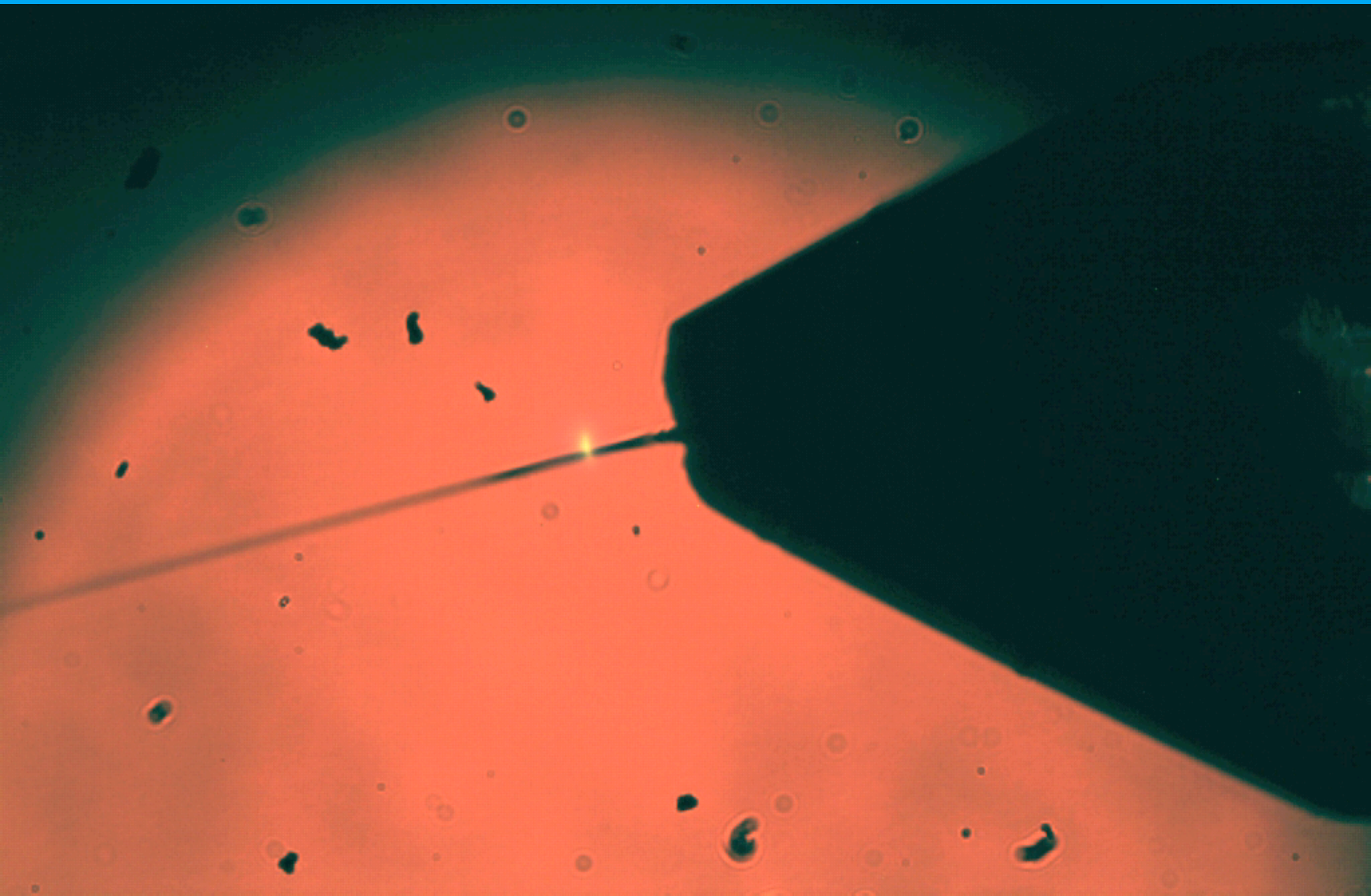
Gas dynamic nozzle creates liquid streams with diameters down to 200 nm.

“Droplet on demand” offers potential reductions in sample consumption of an **order of magnitude**.

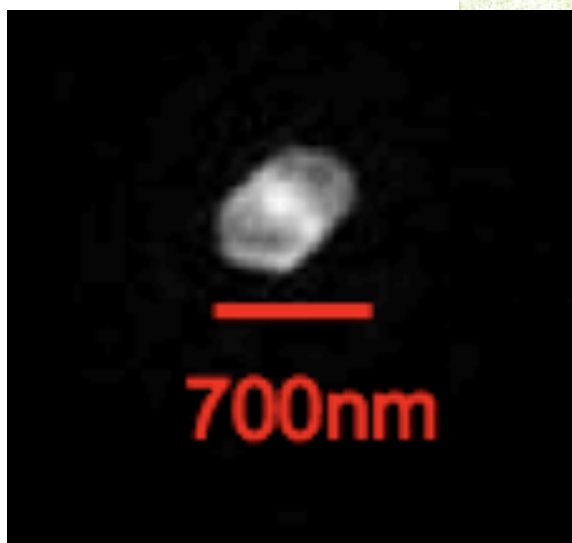
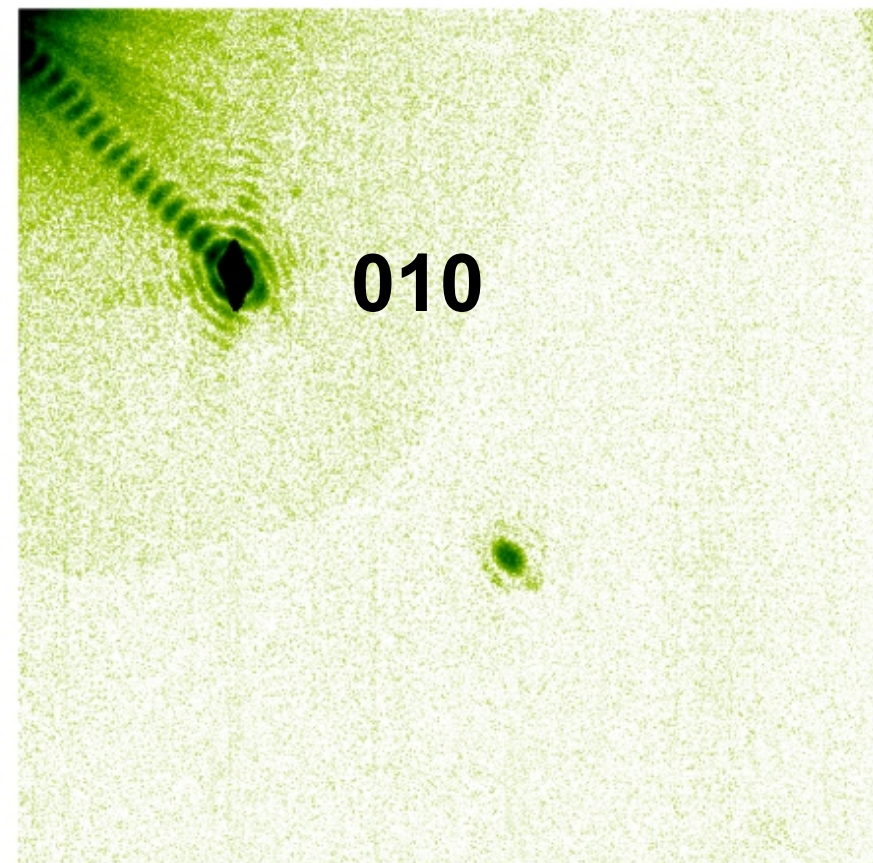
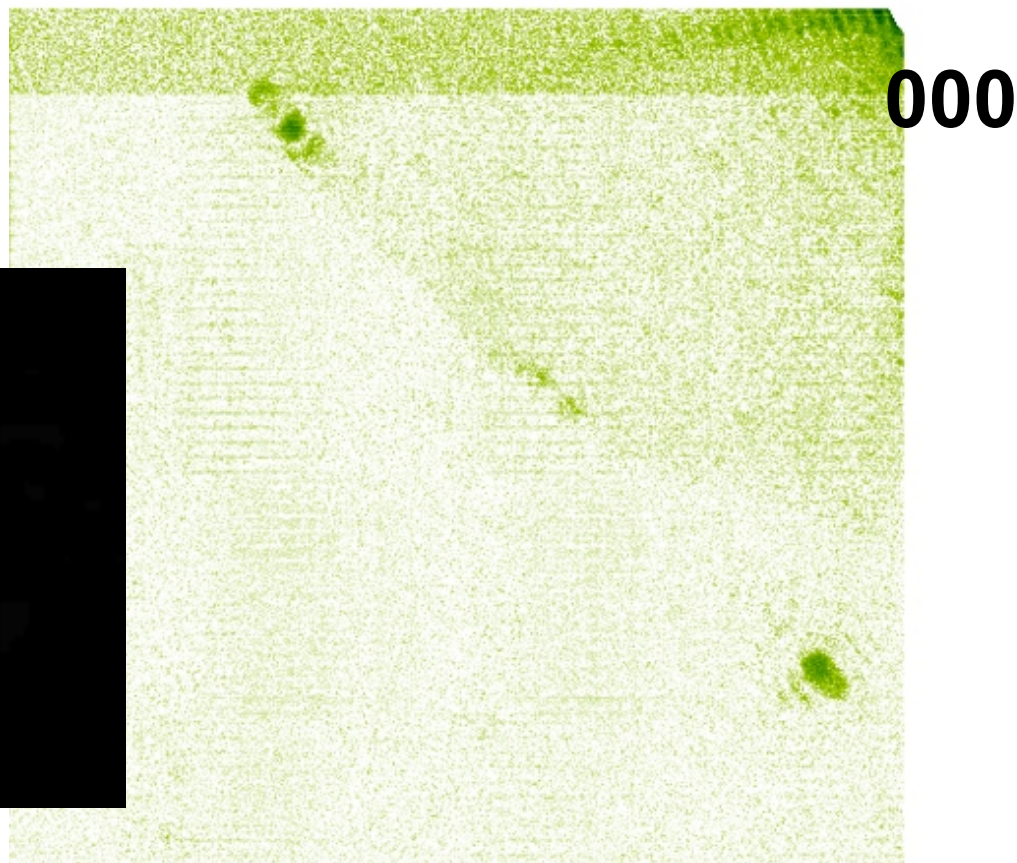
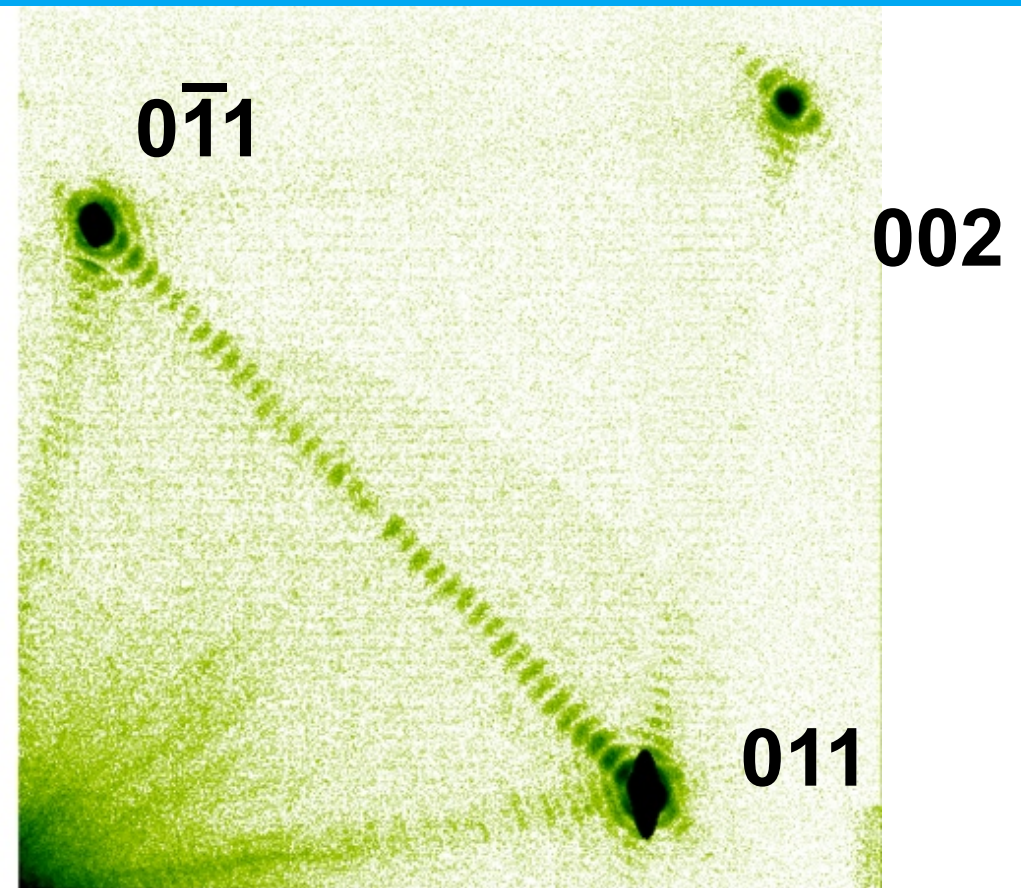
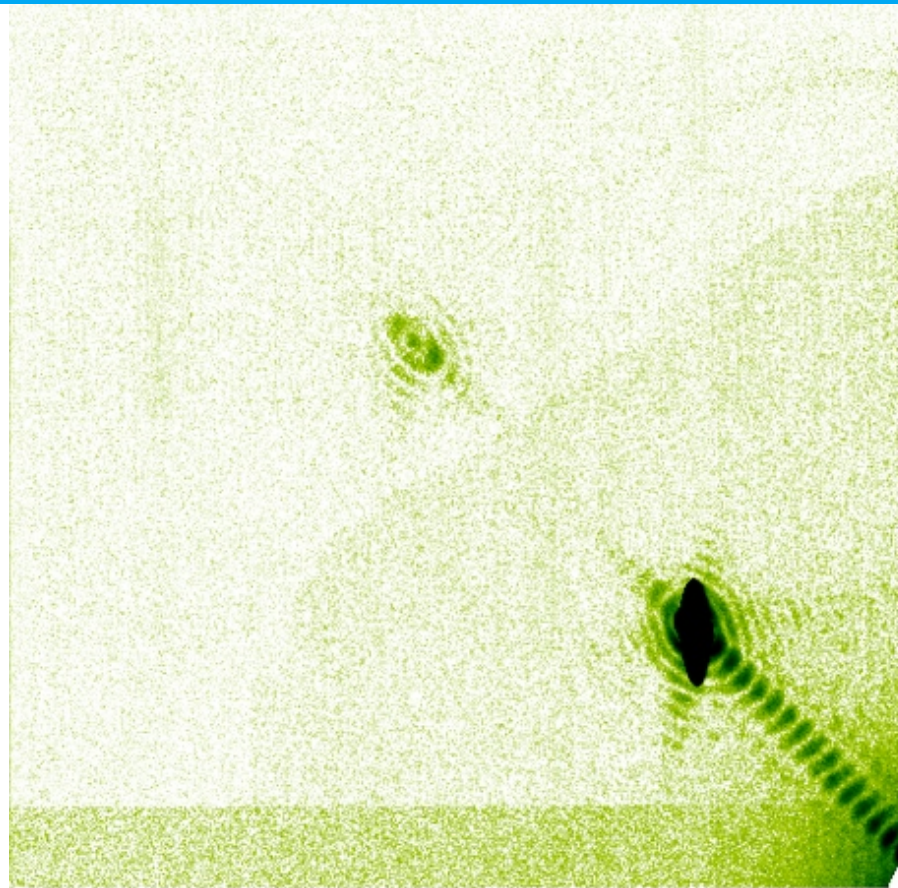


Dan DePonte, CFEL

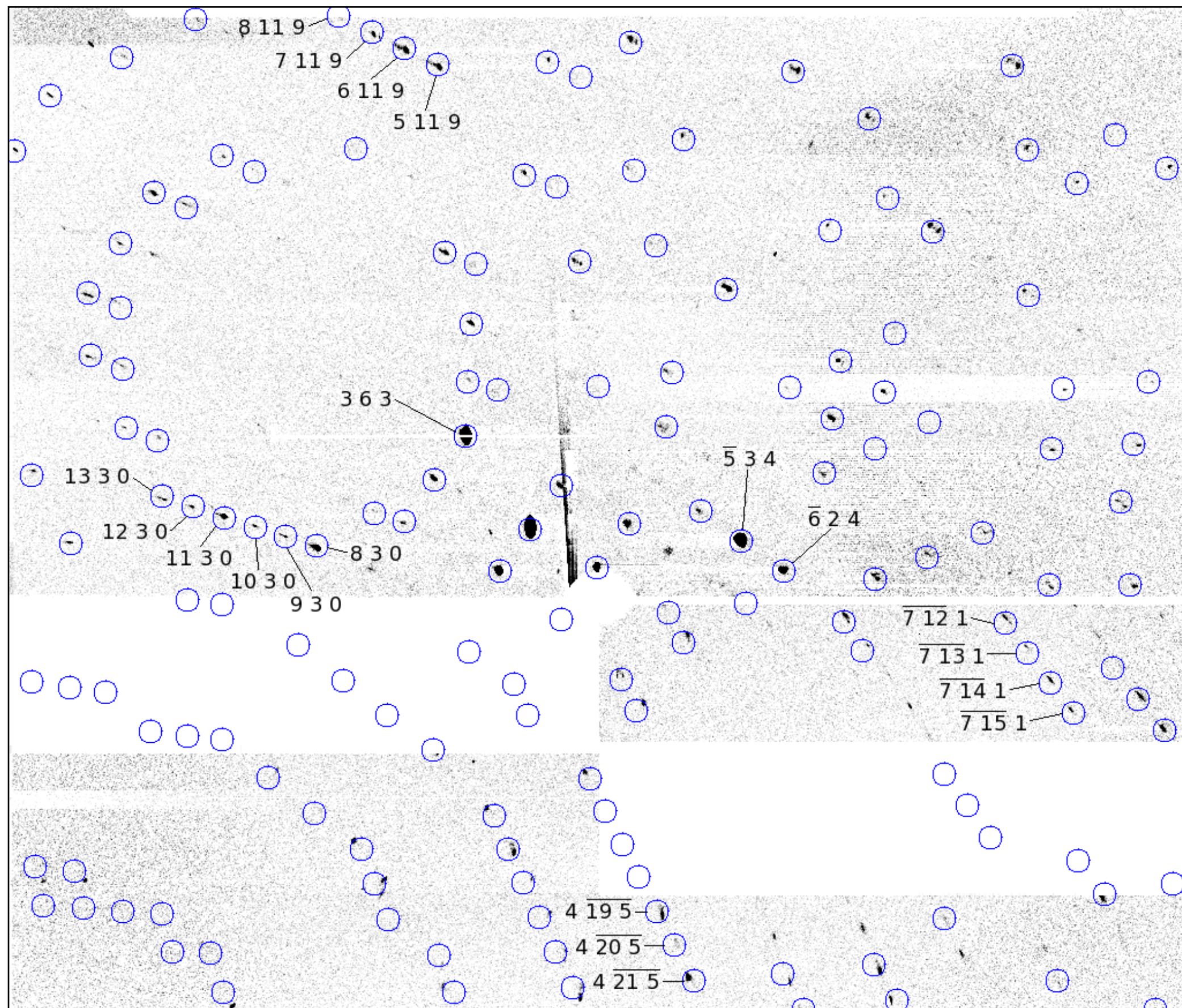
**Optical emission is observed for dose rates
above about 20 MGy/fs**



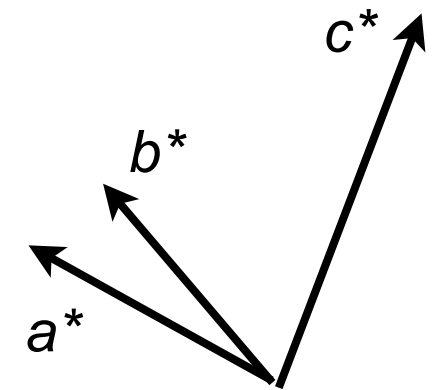
The crystal shape can be used to obtain additional information about the molecular transform

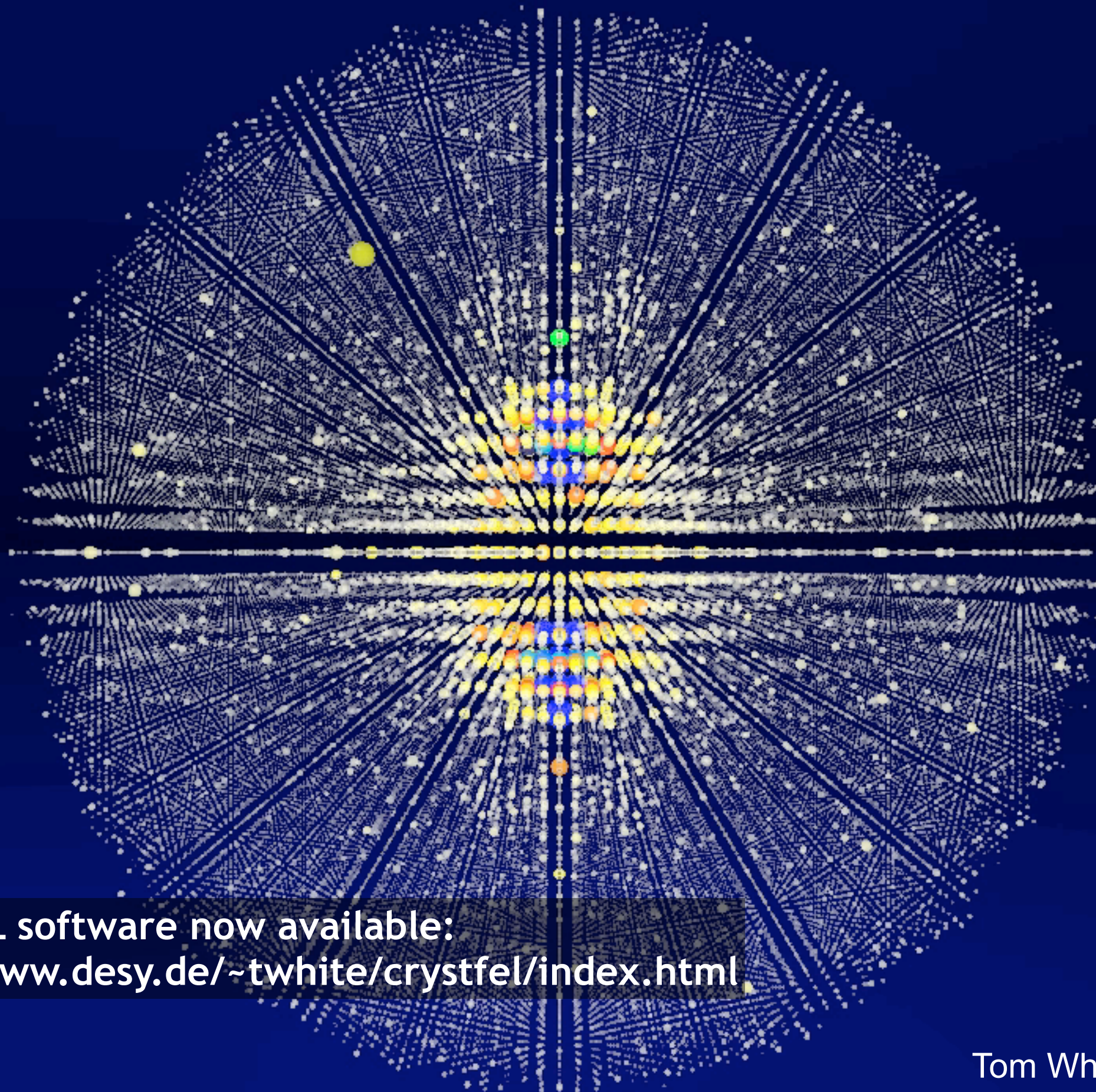


Each pattern is indexed



Tom White (CFEL)
Rick Kirian (ASU)





CrystFEL software now available:
<http://www.desy.de/~twhite/crystfel/index.html>

Tom White (CFEL)

We have a new DESY system for processing and storage



LCLS Data

Dec 2009:

1 week
30 Hz
>20 TB data
>6,000,000 patterns

May-June 2010:

4 experiments
5 weeks
60 Hz
>120 TB data

Jan-Feb 2011:

2 weeks
120 Hz
> 250 TB data



SGI Altix

72 physical cores
360GB RAM
Shared memory
Direct connected storage

Data Direct Networks

SFA 10000

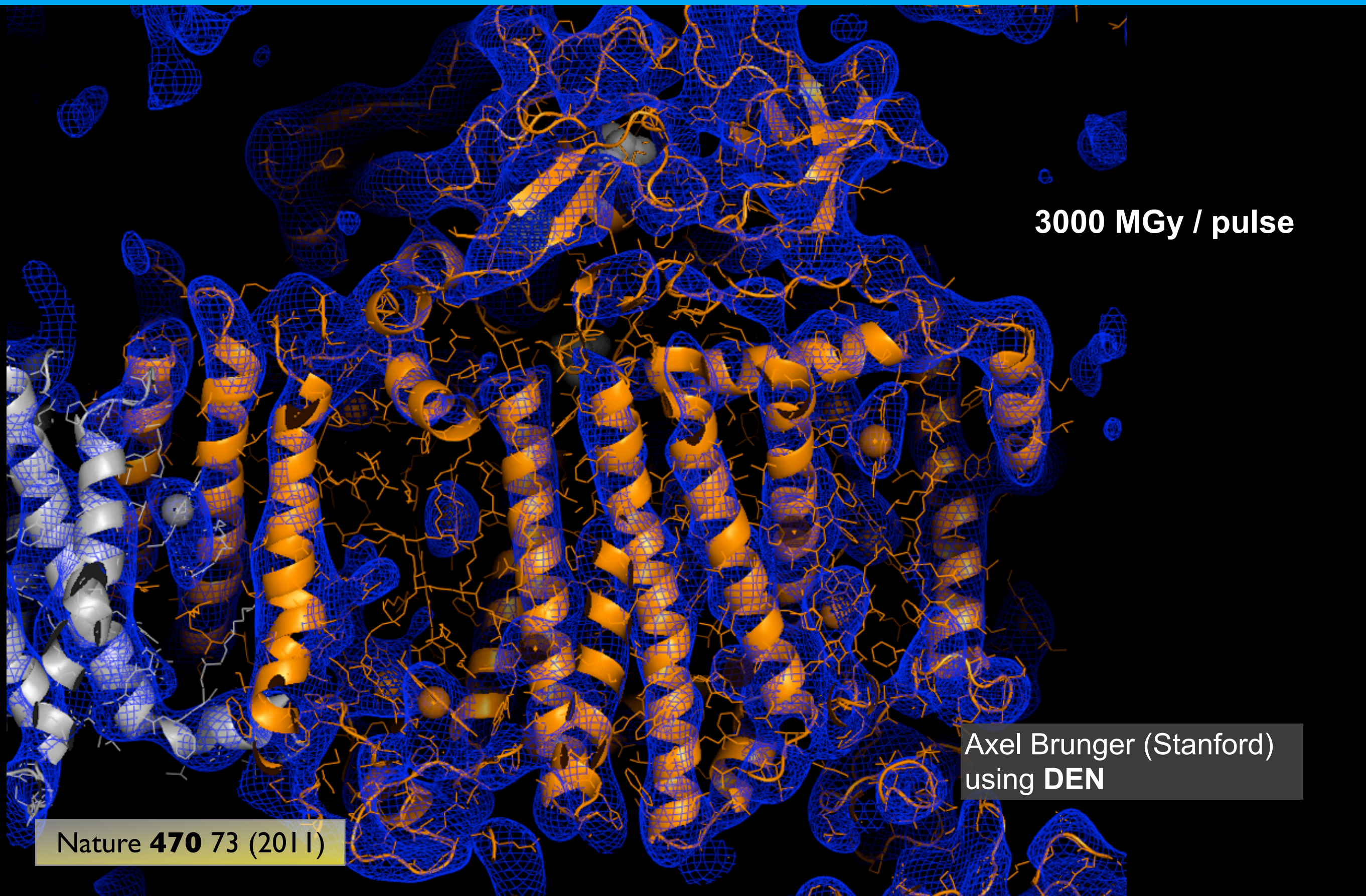
60-bay HDD / 4U unit
~1 PB/rack (formatted)
(600 x 2 TB HDDs)



Anton Barty, Tom White

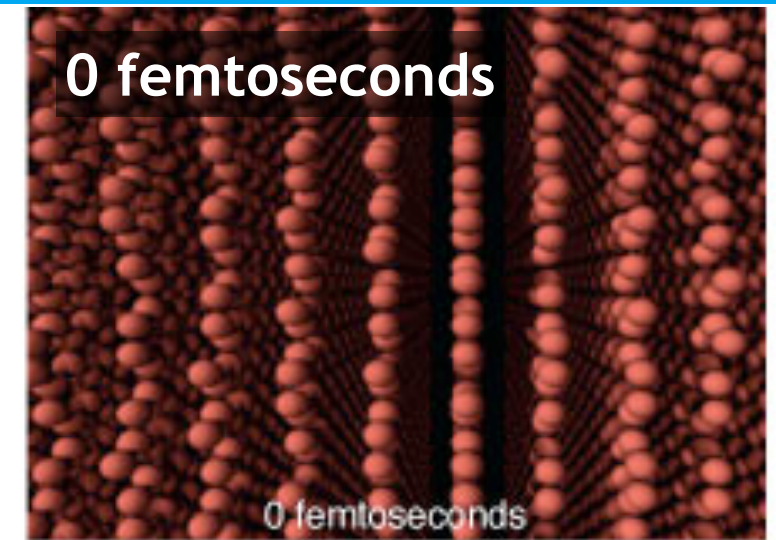
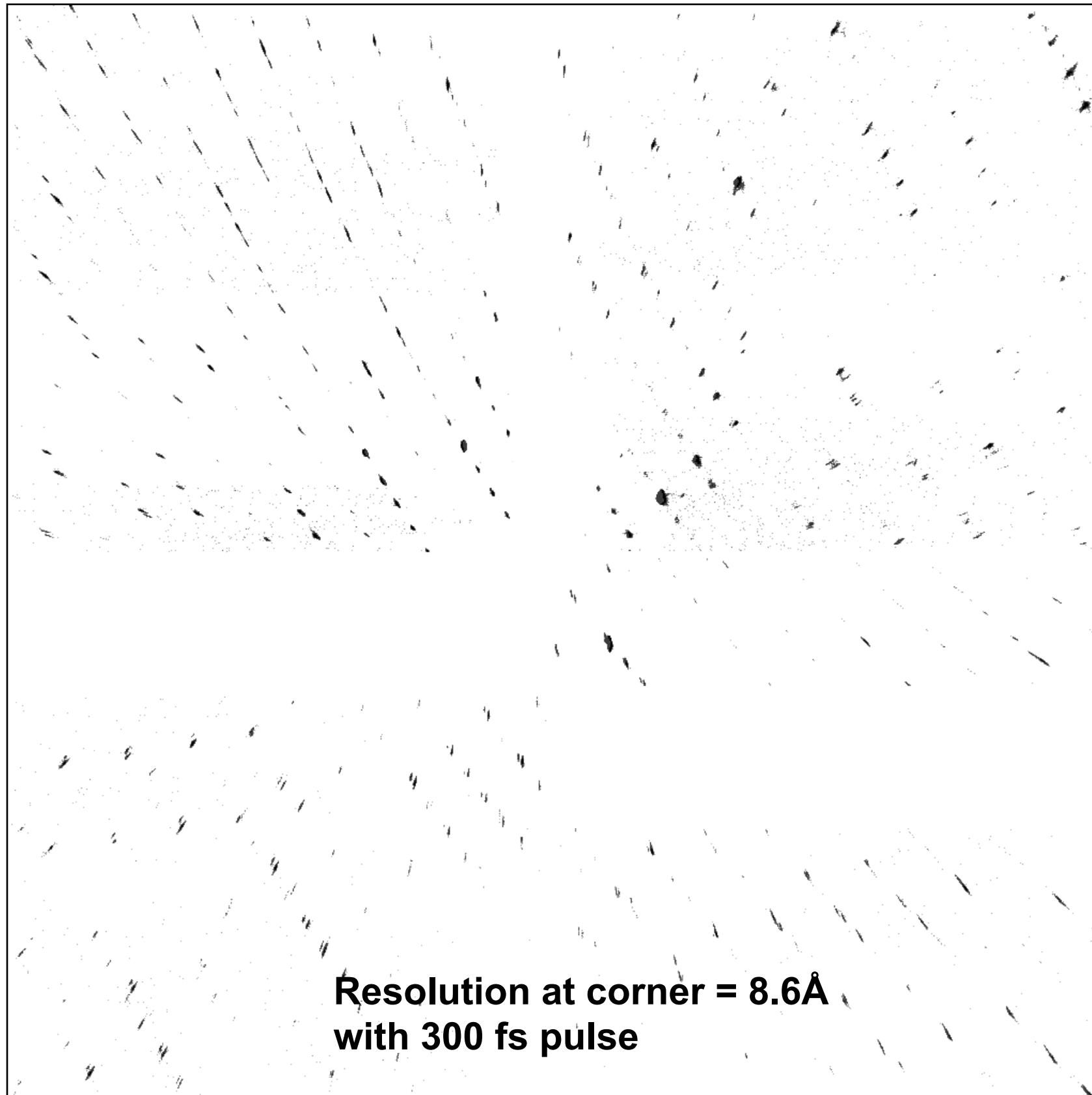
Can process 30 patterns / second

Molecular replacement reconstructs the 8.5Å structure

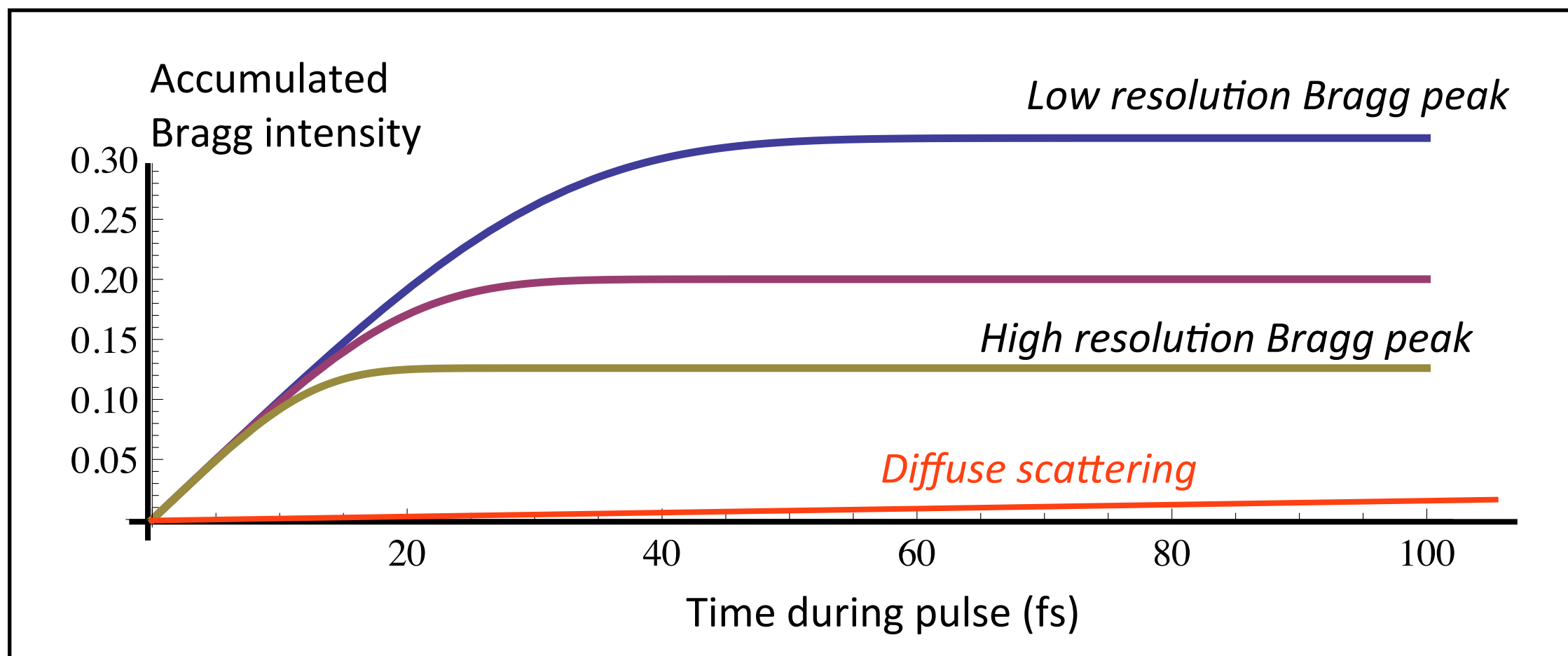
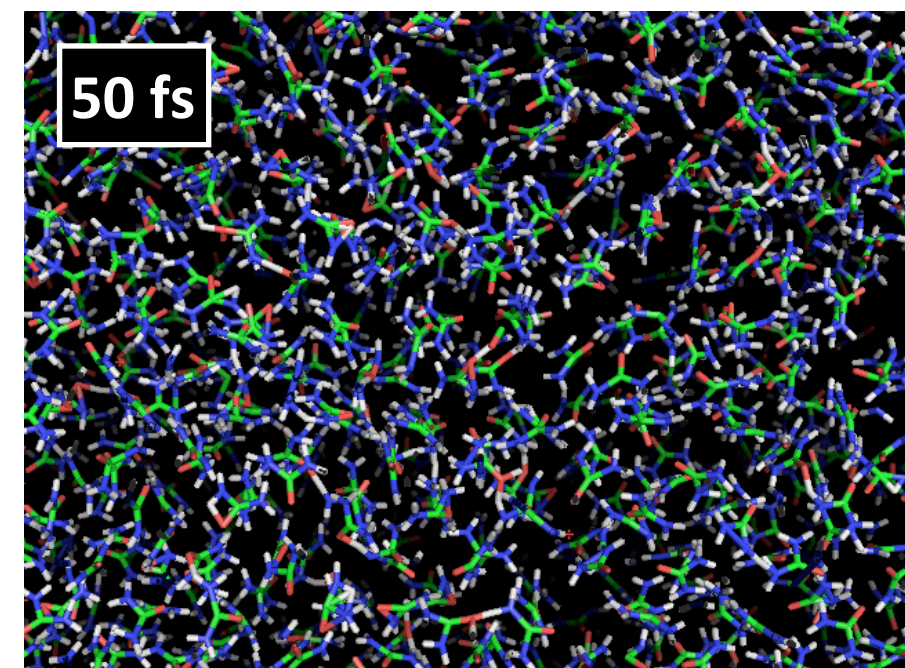
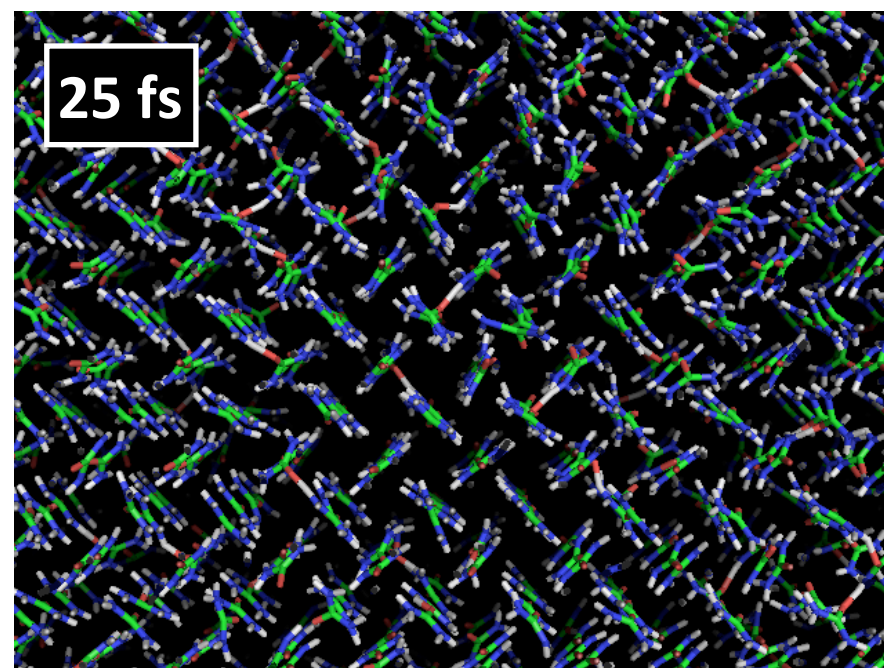
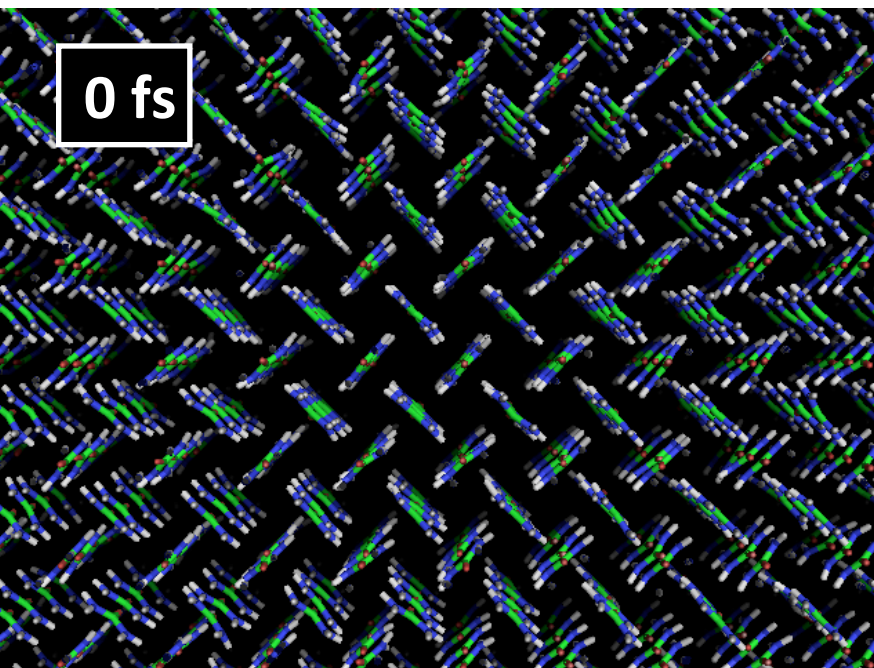


Nature **470** 73 (2011)

Bragg peaks are observed even with 300 fs pulses

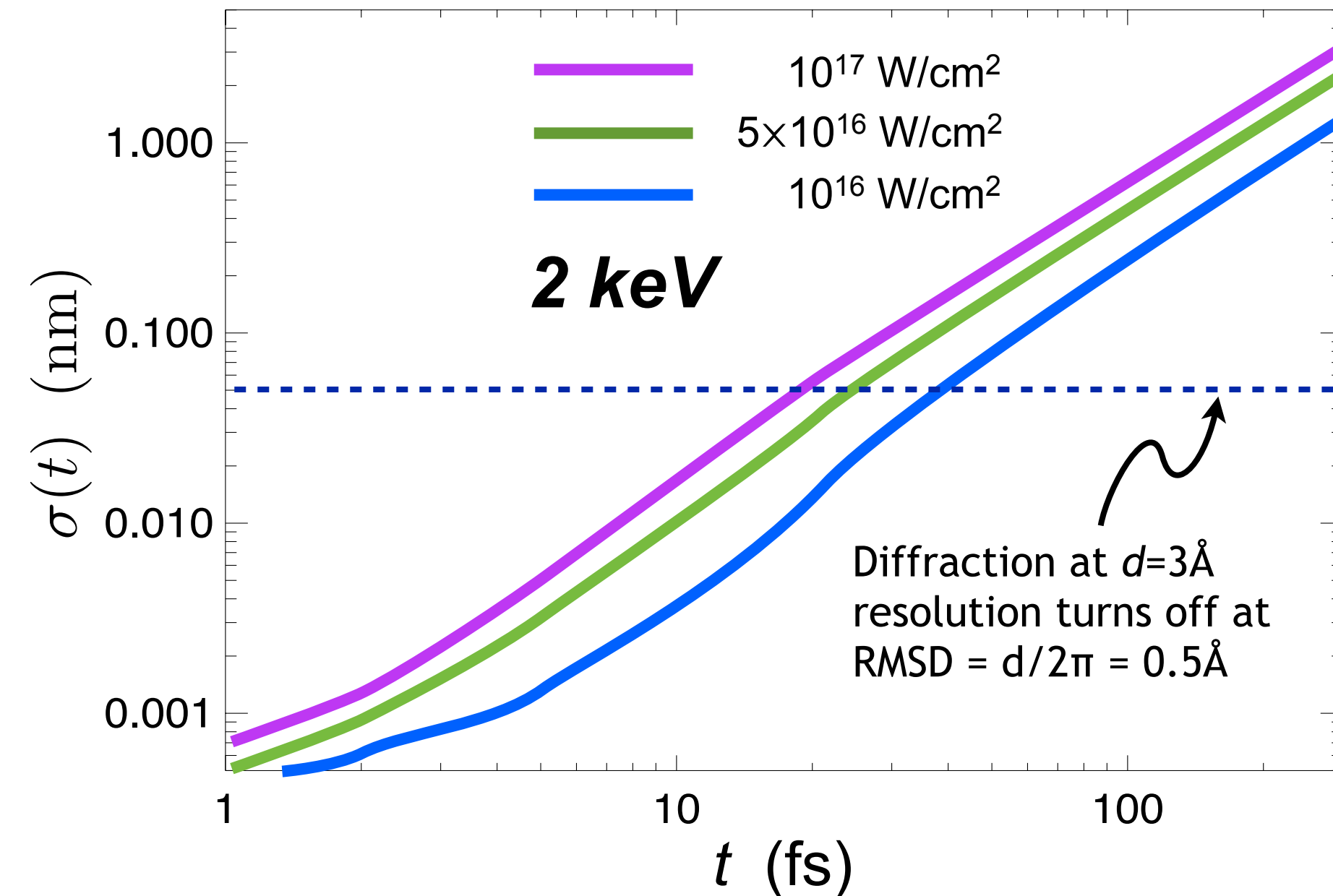


A crystal only gives Bragg diffraction when it is a crystal!



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

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



Ion diffusion: **temperature**

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

collision frequency

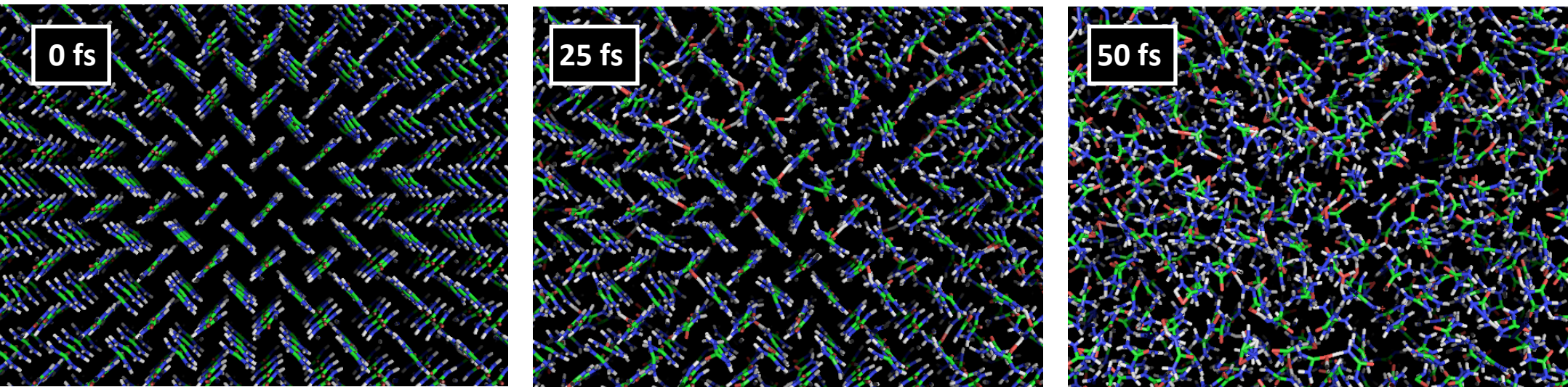
RMS displacement:

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

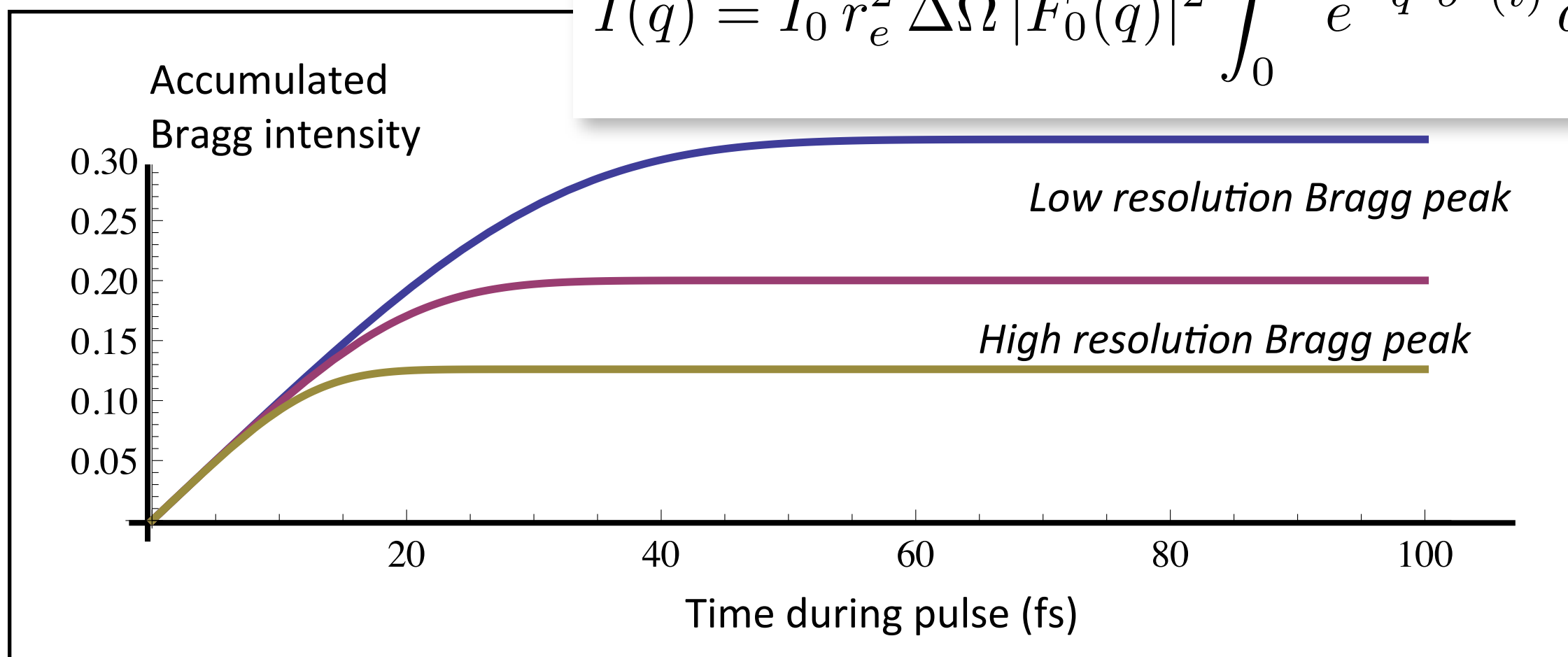
$$\propto t^{3/2}$$

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

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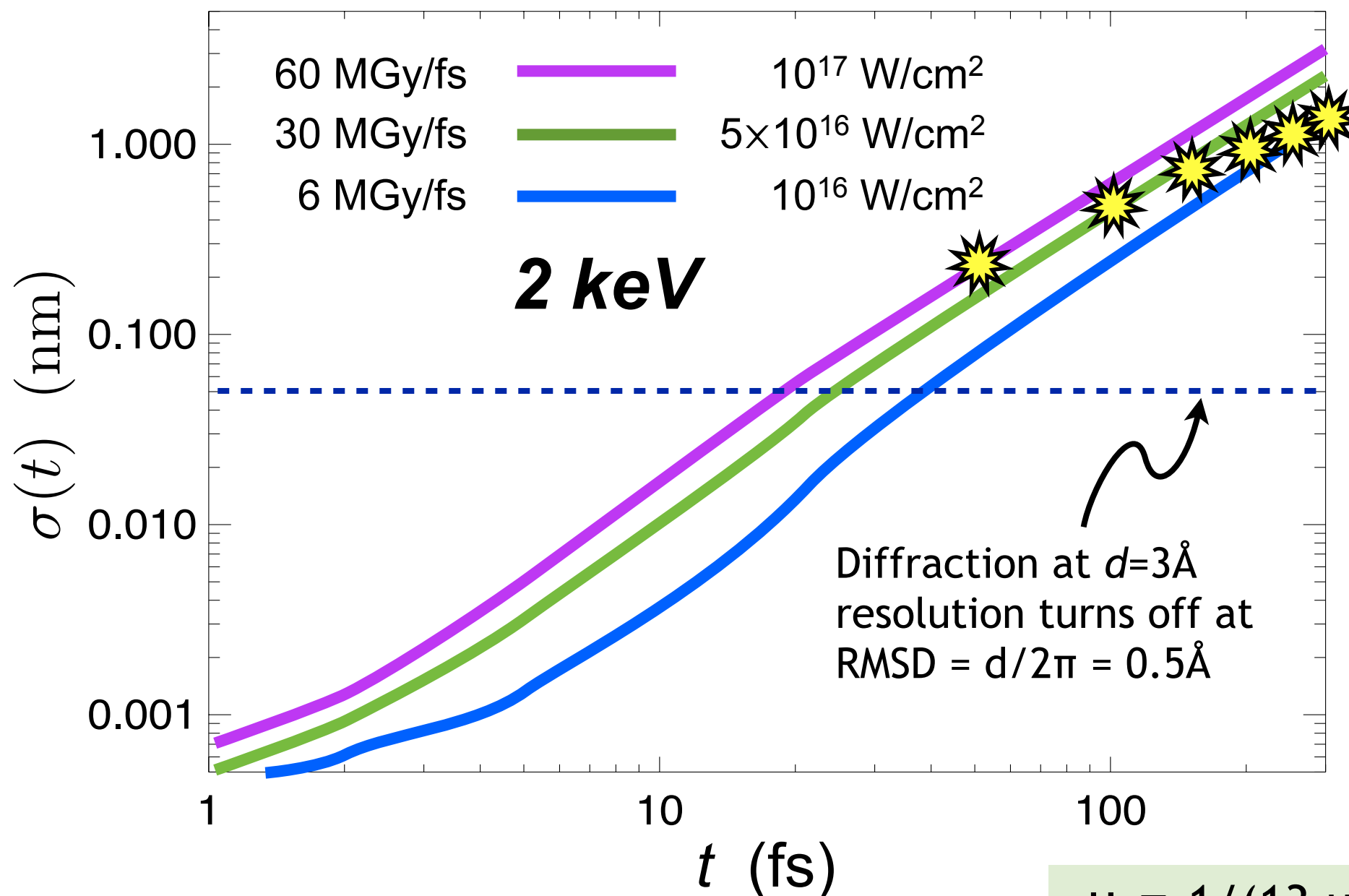
$$\propto t^{3/2}$$

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

Dose rate

rate of energy absorbed / mass

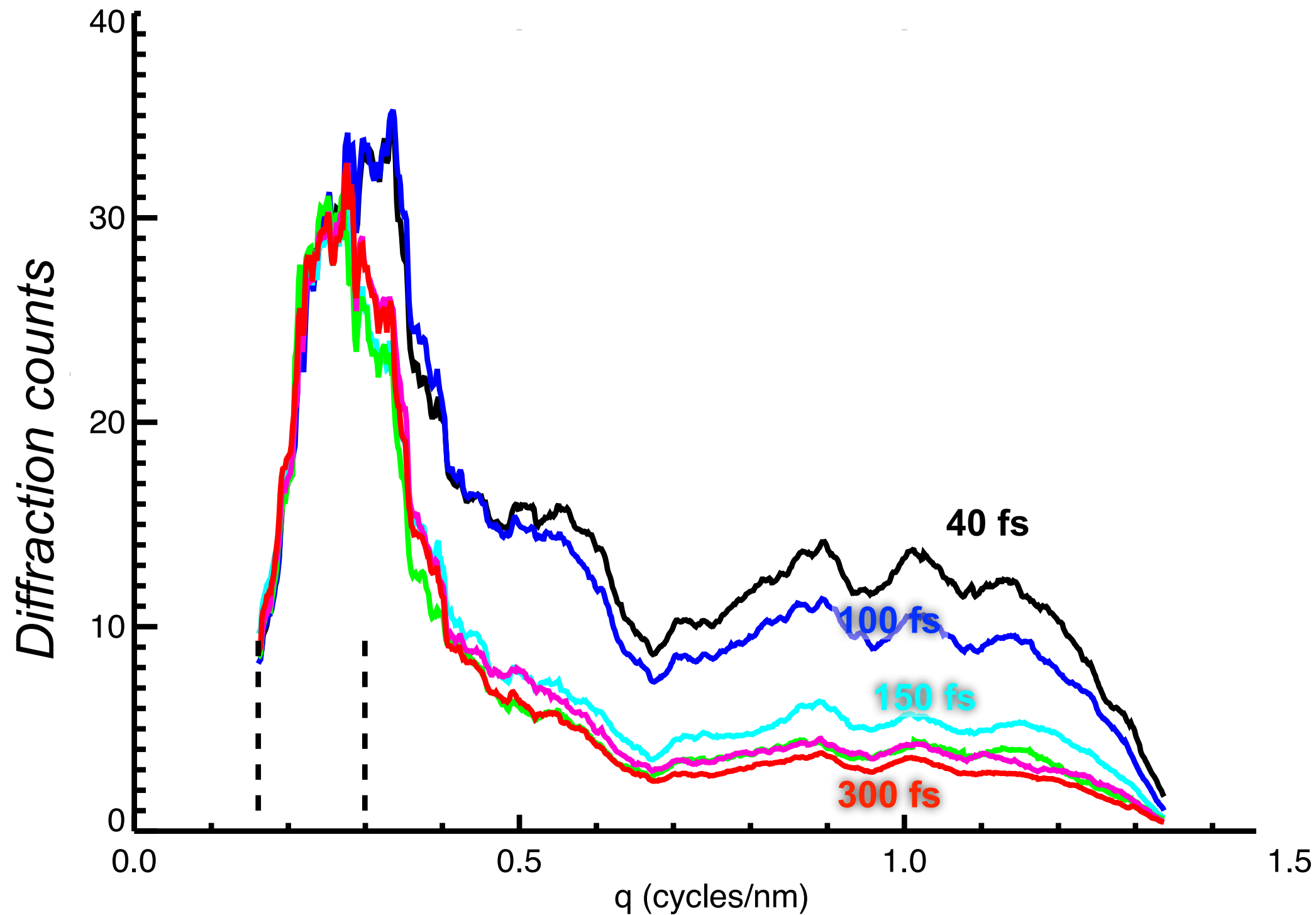
$$= I_0 \cdot \mu / \rho$$



$$\mu = 1/(13 \text{ }\mu\text{m}) \text{ at } 2 \text{ keV}$$

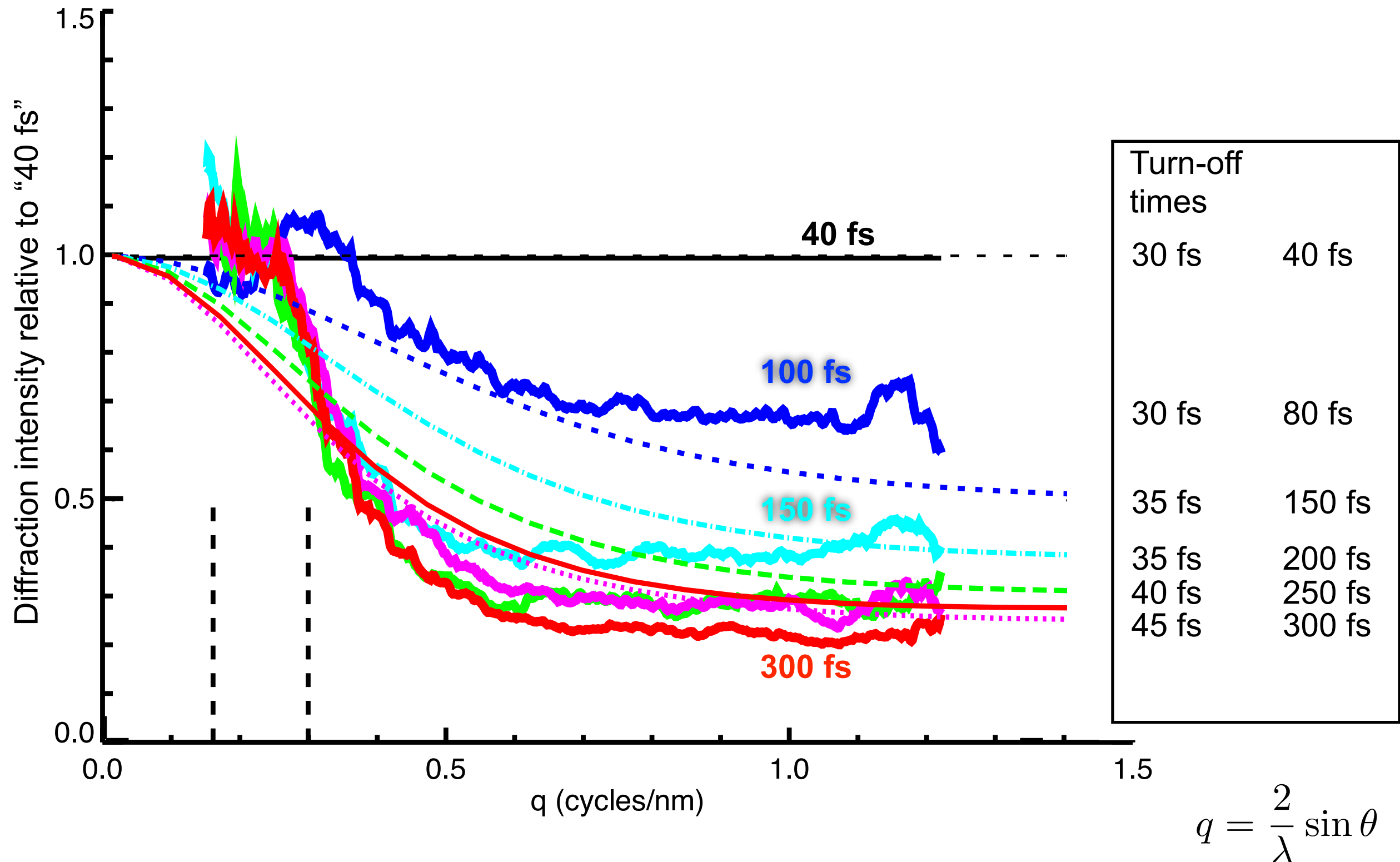
$$\mu = 1/(850 \text{ }\mu\text{m}) \text{ at } 8 \text{ keV}$$

We see a degradation of the sample at longer pulse durations

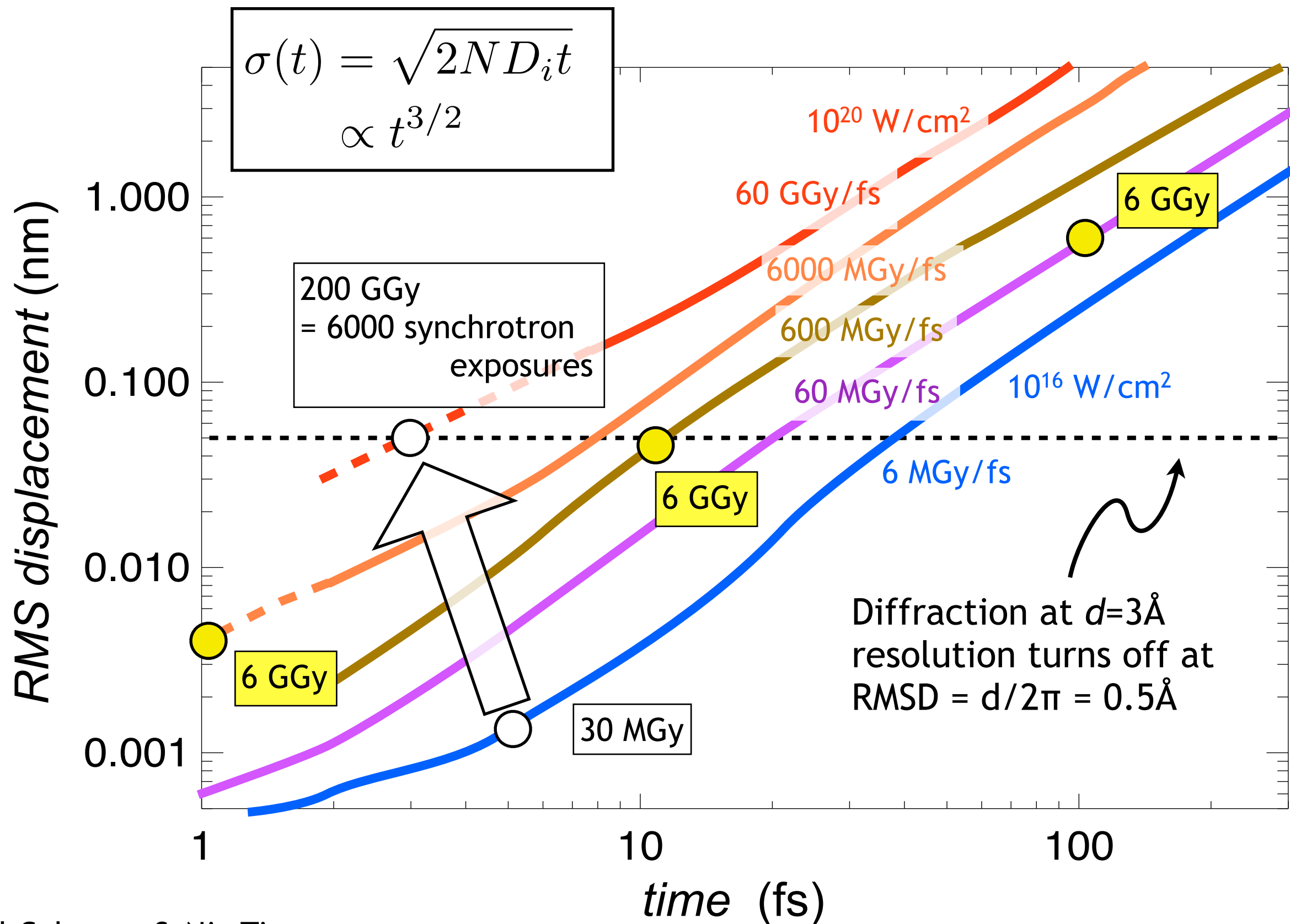


$$q = \frac{2}{\lambda} \sin \theta$$

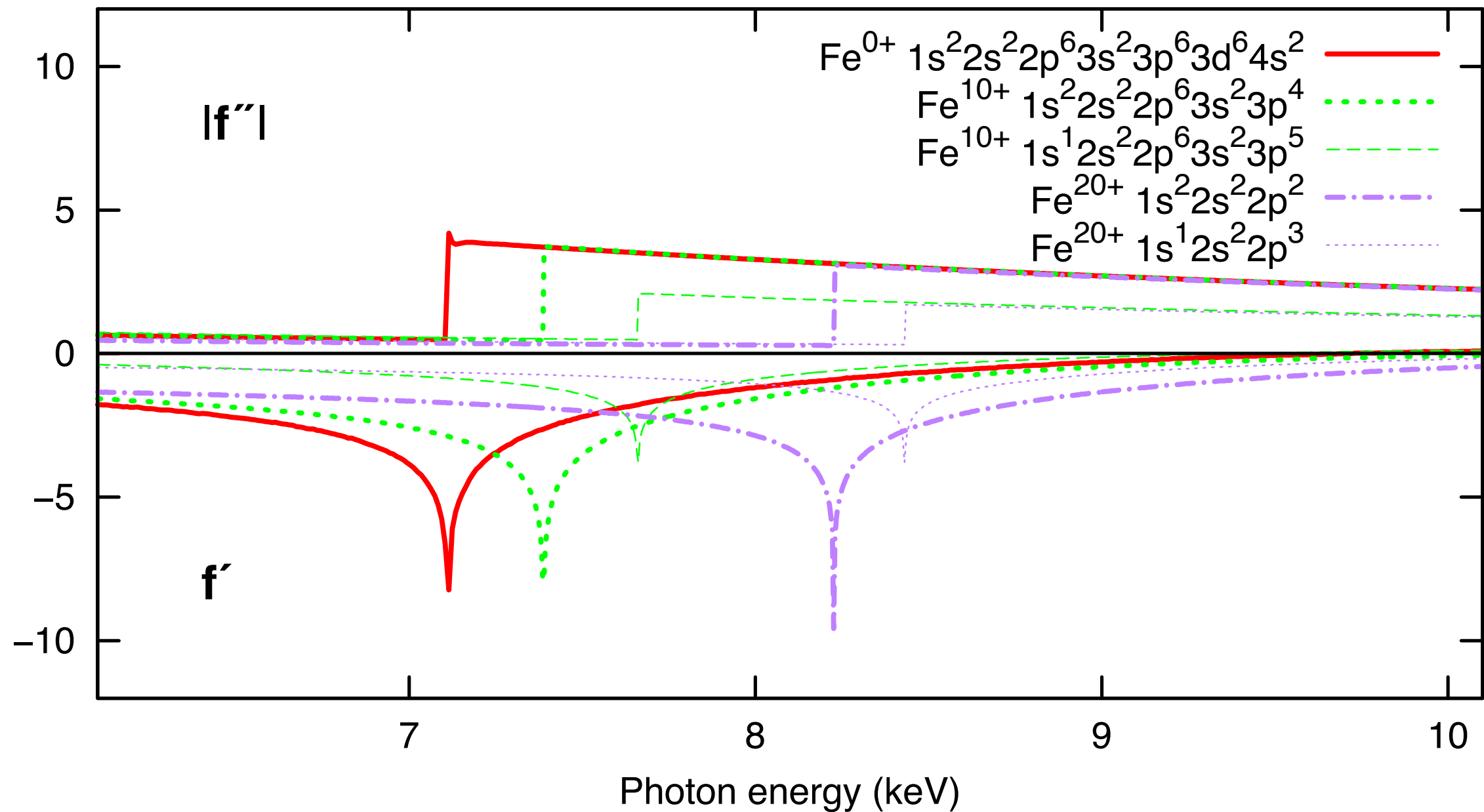
Only the first 30 fs contributes to the diffraction



The explosion accelerates during the pulse



Ionized states have higher binding energies

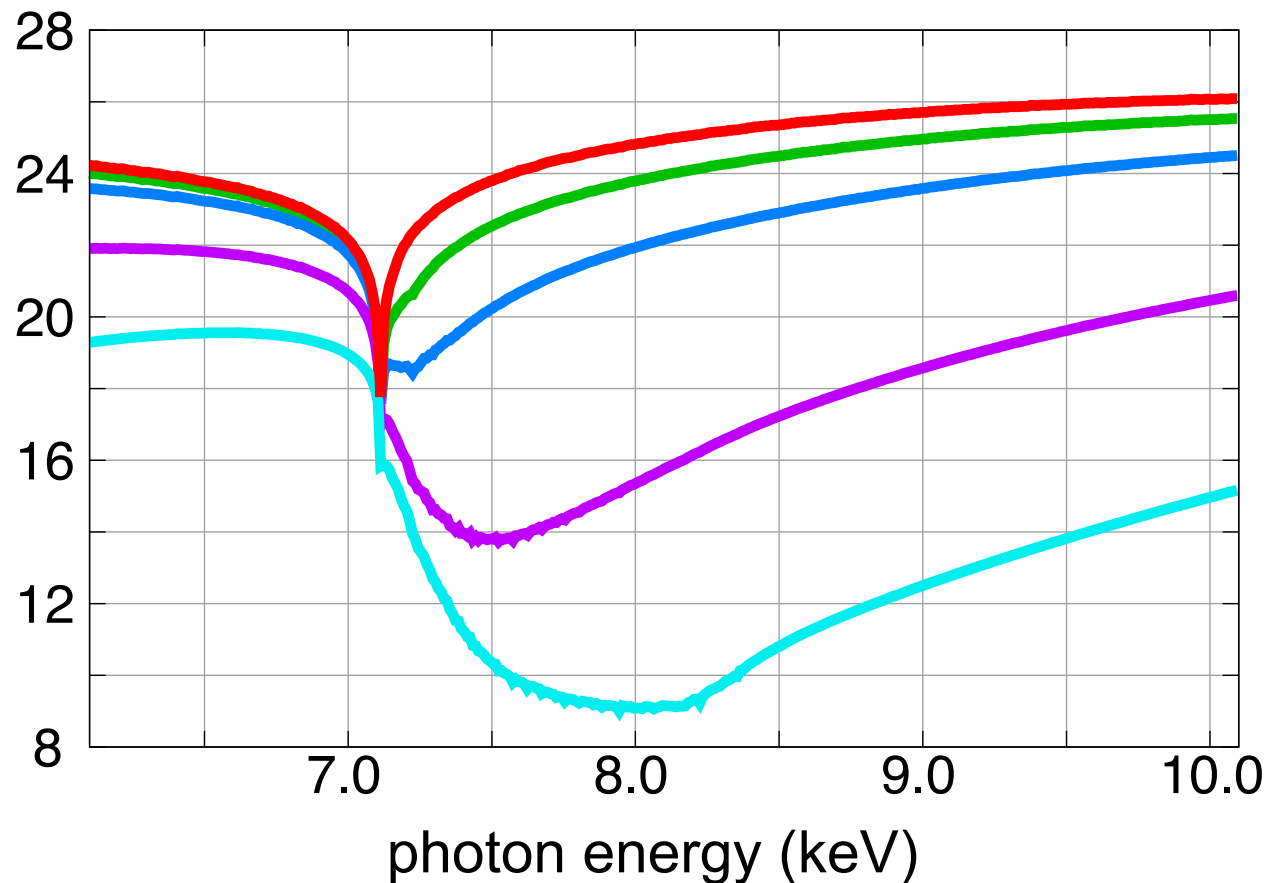


S.-K. Son, H.N.C., R. Santra,
PRL **107**, 218102 (2011).

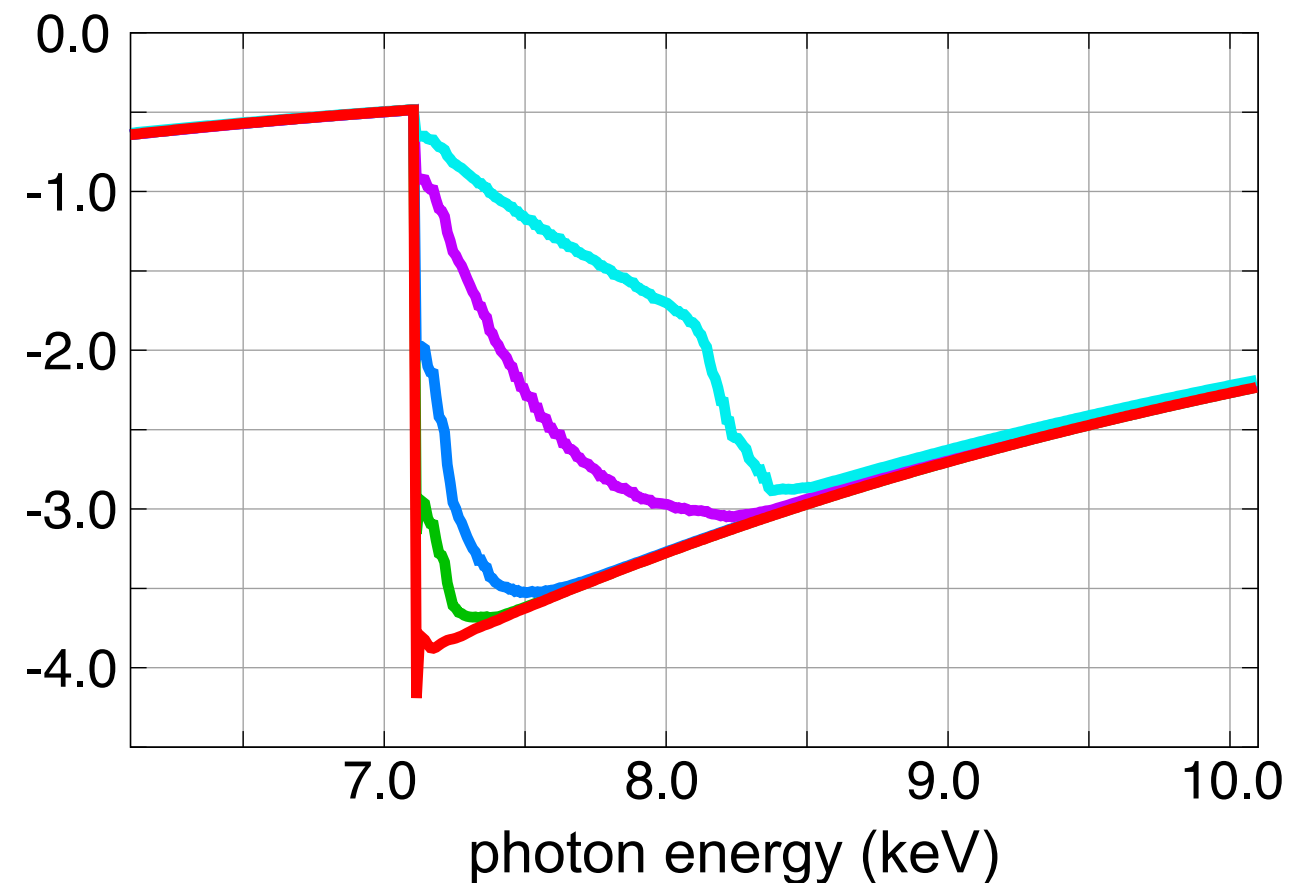
Calculations show that anomalous signals are enhanced by high X-ray intensity

Effective scattering factors for Fe with 2 mJ pulse
Average ionization by end of pulse is +14 for highest fluence

$b(\lambda) \rightarrow f^0 + f'$



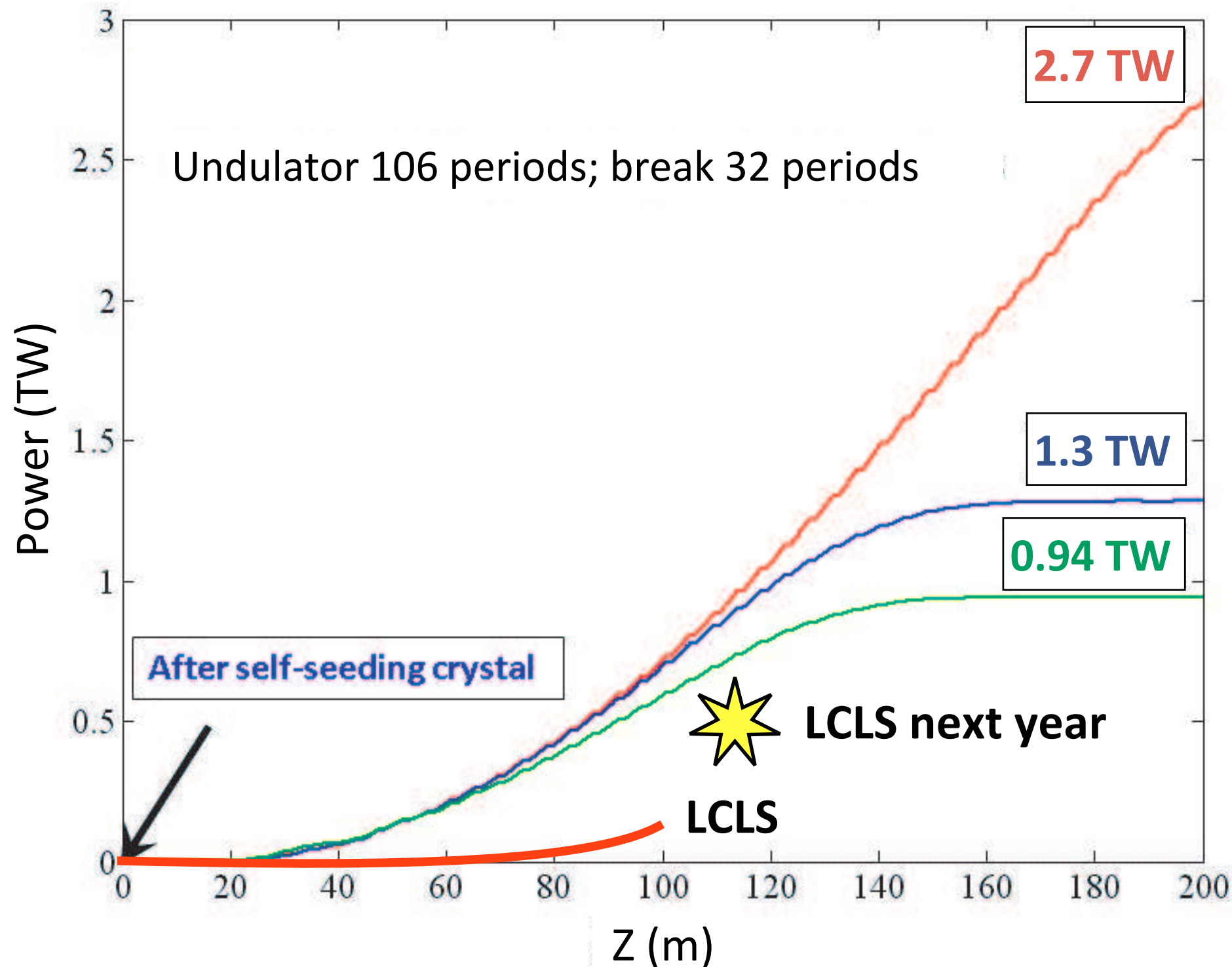
$c(\lambda) \rightarrow f''$



- Undamaged
- 1.6×10^{17} W/cm² 1.6 MGy/fs
- 5×10^{17} W/cm² 5 MGy/fs
- 2×10^{18} W/cm² 20 MGy/fs
- 2×10^{19} W/cm² 200 MGy/fs

S.-K. Son, H.N.C., R. Santra,
PRL 107, 218102 (2011).

Tapered undulators could increase peak power by a factor of 50

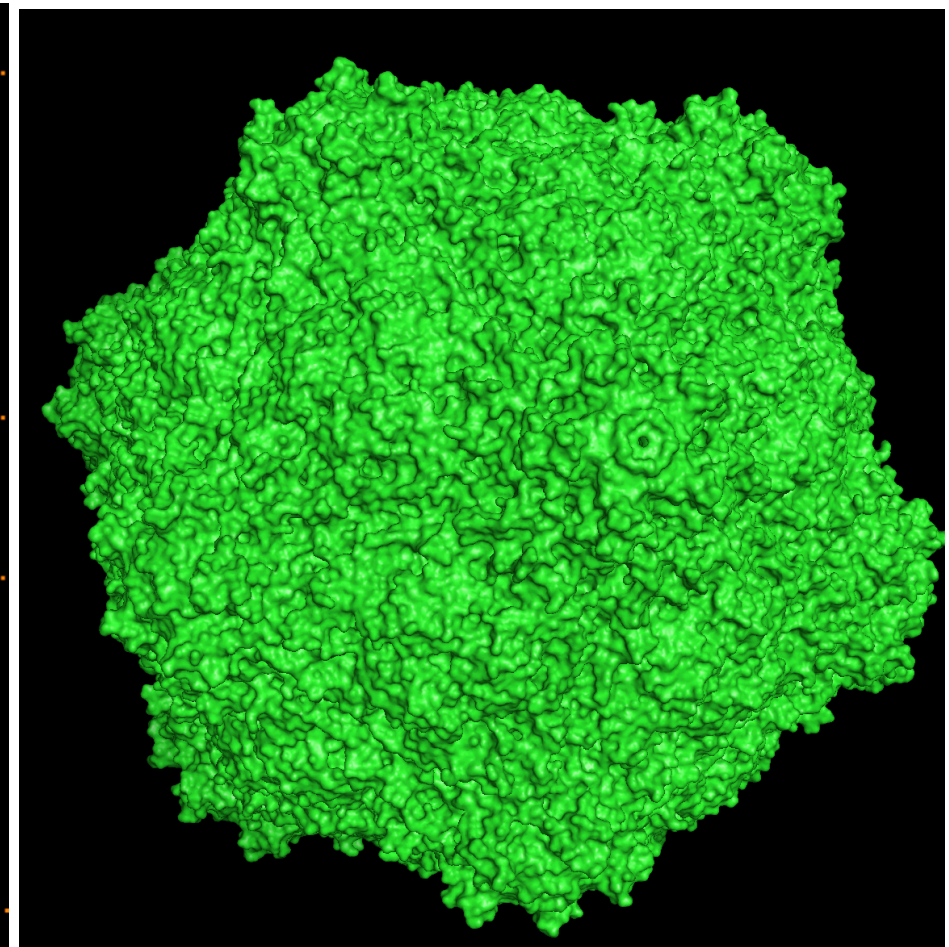
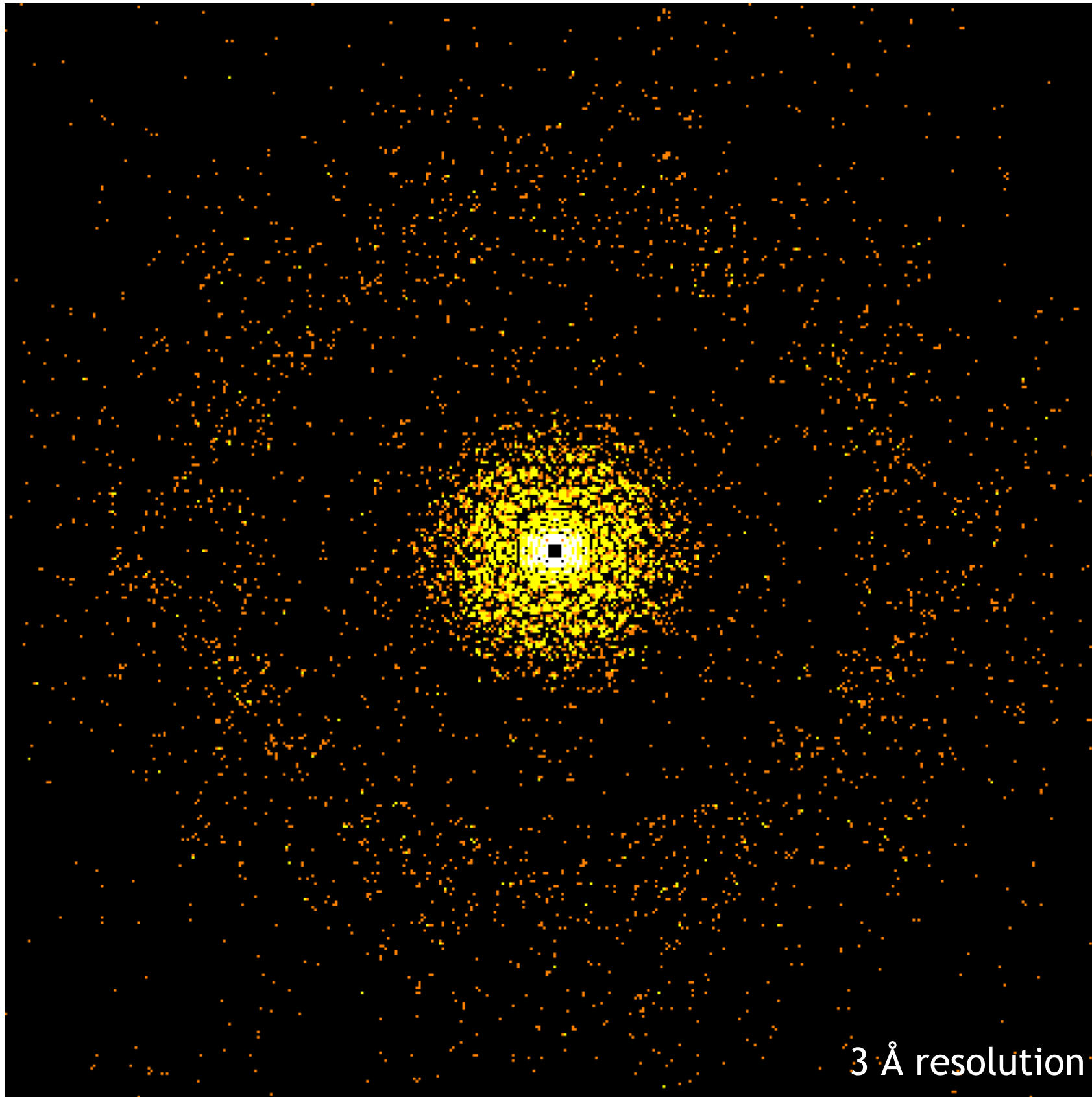


1 TW focused to $1 \mu\text{m}^2$:
 10^{20} W/cm^2

W.M. Fawley *et al*
LCLS Tech note 11-3
(Sept 2011)

G. Geloni,
V. Kocharyan, and
E. Saldin. J. Mod.
Opt. **58**, 1391
(2011)

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



← 28 nm →

10^{14} ph/ μm^2

60 GGy

6000 MGy/fs $\times$ 10 fs

RMS displacement: 0.5 Å
half electrons ionized

Sample delivery of single particles is challenging

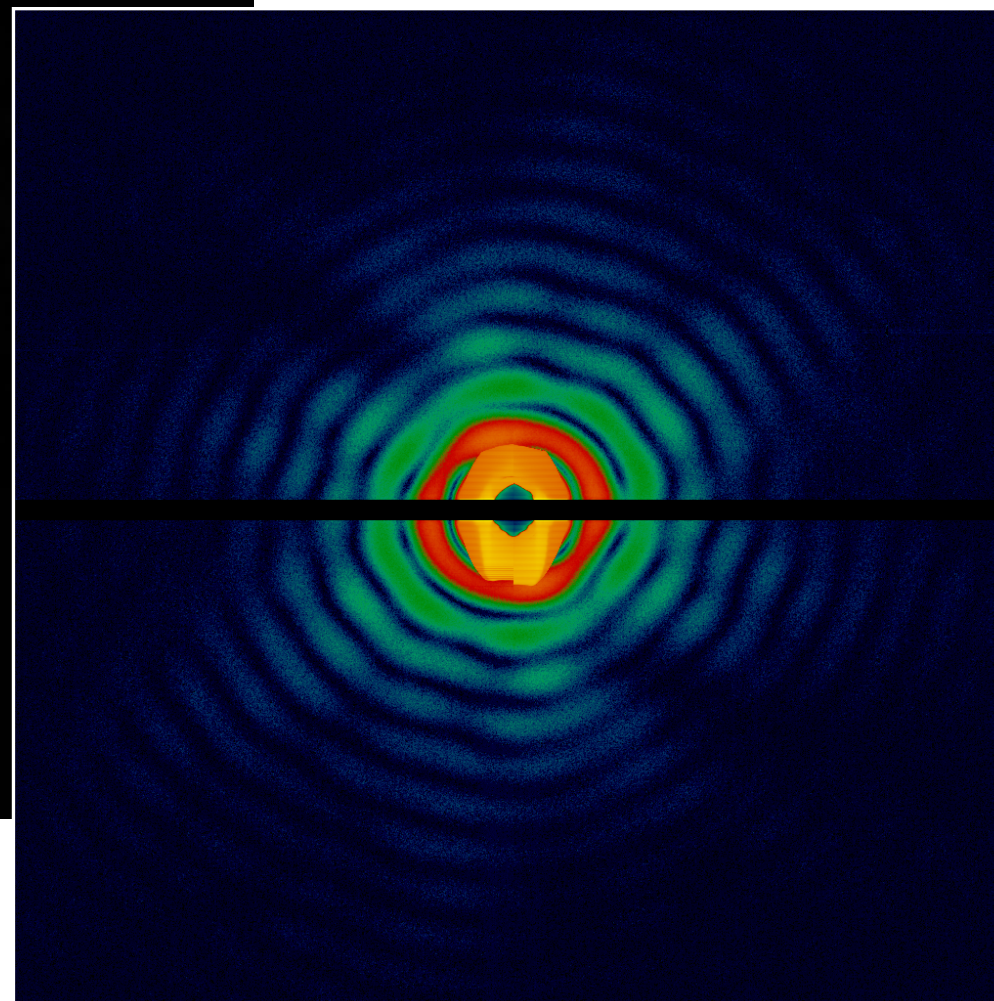
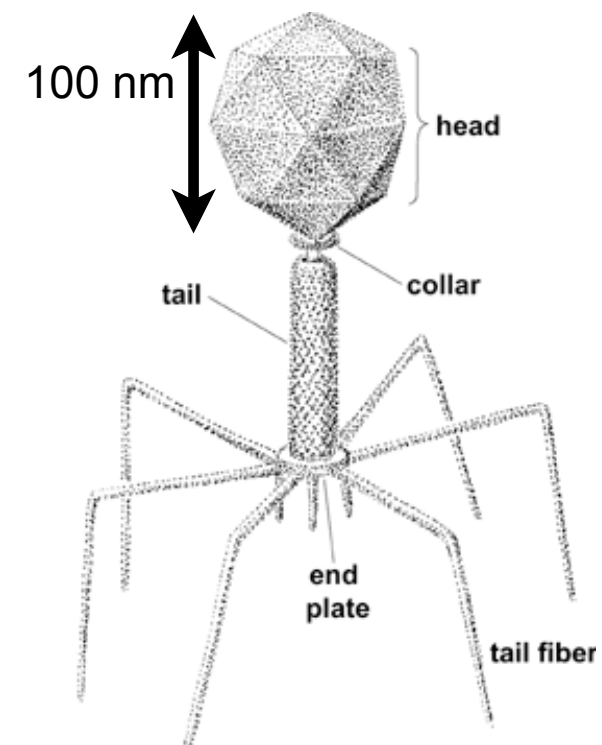


2010_Jun21_r0178_140404_90345

2010_Jun21_r0176_135059_69759

100 nm

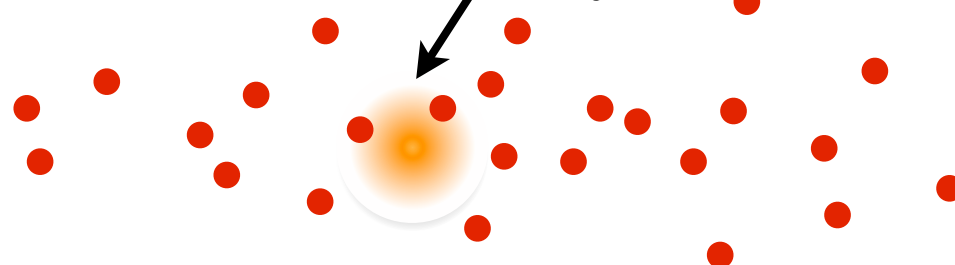
2010_Jun20_r0149_155821_22485



Aerosol jet



x-ray beam



Summary

- ★ “Diffraction before destruction” holds to 1.8 Å resolution
- ★ We can combine millions of serial diffraction measurements into a dataset of average 3D structure factors
- ★ No effect of radiation damage is yet observed in refined protein structures
- ★ Isotropic atomic displacements terminate the diffraction
- ★ 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

