Multiwavelength anomalous diffraction at high x-ray intensity

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Workshop on Resonant Elastic X-ray Scattering in Condensed Matter
Oxford, UK / July 16, 2013

Overview

- MAD for phase problem
- XFEL for femtosecond x-ray nanocrystallography
- Possible to use MAD with XFEL?
- Electronic damage to heavy atoms
- MAD with XFEL: generalized Karle-Hendrickson equation
- Conclusion

Acknowledgment

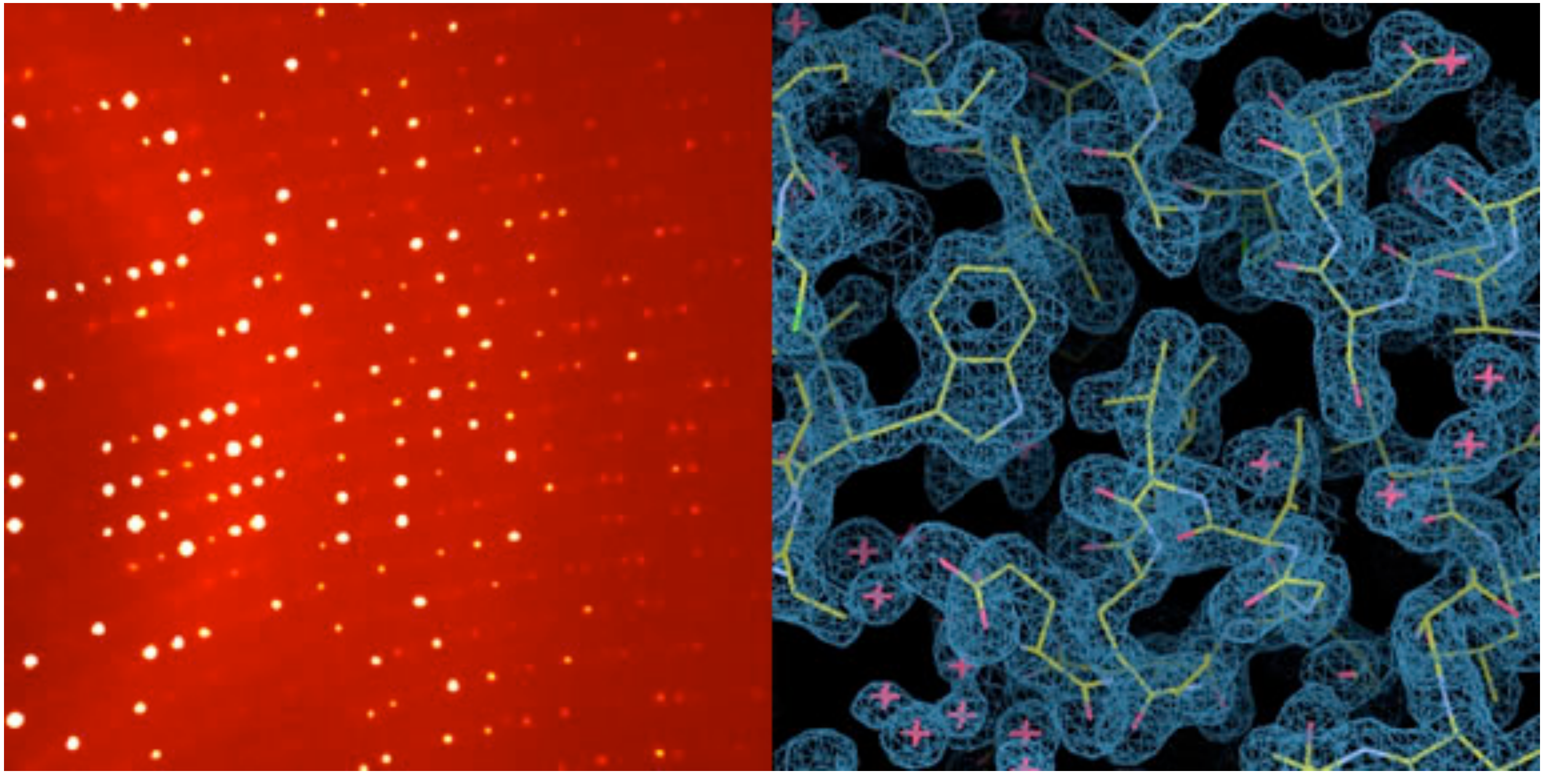
CFEL Theory Division

Robin Santra

CFEL Coherent Imaging Division

Henry Chapman

Structural determination of macromolecules



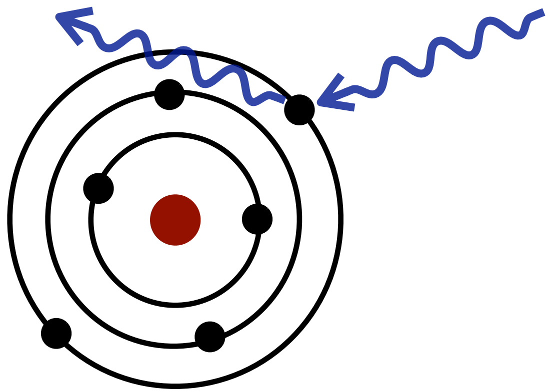
Picture taken from http://www.sandiego.edu/cas/chemistry/newsletter/

X-ray scattering

- Elastic x-ray scattering form factor

$$f^0(\mathbf{Q}) = \int d^3r\ \rho(\mathbf{r})\ e^{i\mathbf{Q}\cdot\mathbf{r}}$$

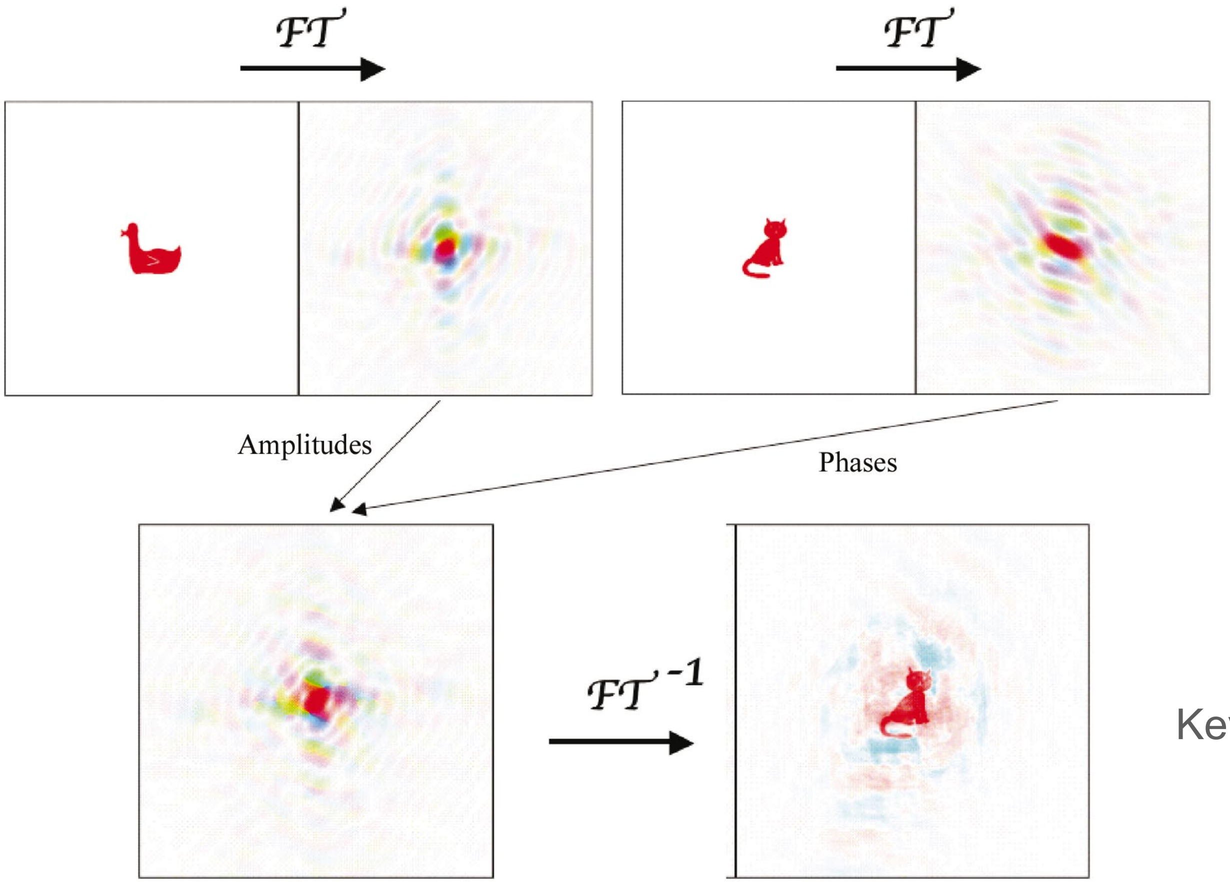
$$\frac{d\sigma(\mathbf{Q})}{d\Omega} = \left(\frac{d\sigma}{d\Omega}\right)_T \left|f^0(\mathbf{Q})\right|^2$$



- **Phase problem**: a fundamental obstacle in constructing an electronic density map from x-ray diffraction

$$f^0(\mathbf{Q}) = \int d^3r\ \rho(\mathbf{r})\ e^{i\mathbf{Q}\cdot\mathbf{r}} = \left|f^0(\mathbf{Q})\right|\ e^{i\phi^0(\mathbf{Q})}$$

Why are phases important?



Taylor, *Acta Cryst.* **D59**, 1881 (2003).
Kevin Cowtan's Book of Fourier: http://www.ysbl.york.ac.uk/~cowtan/fourier/fourier.html

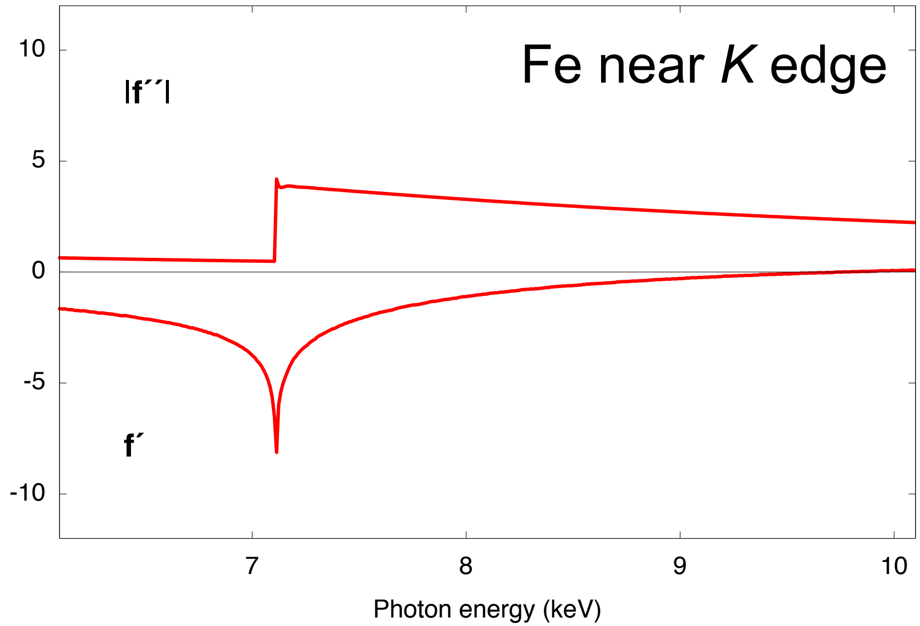
cat's phases + duck's amplitudes → reconstruction of the cat

Phasing method

- Many phasing methods have been proposed and applied.
  - Molecular replacement (MR)
  - Single / multiple isomorphous replacement (SIR / MIR)
  - SIR / MIR with anomalous scattering (SIRAS / MIRAS)
  - Multi-wavelength anomalous diffraction (MAD)
  - Single-wavelength anomalous diffraction (SAD)
- molecular replacement: phases borrowed from a similar molecule, but structural determination severely biased
- *ab initio* phasing: without knowing a similar structure, mainly employing anomalous scattering of heavy atoms

Multiwavelength Anomalous Diffraction

- Resonant elastic x-ray scattering: $f(\mathbf{Q},\omega) = f^0(\mathbf{Q}) + f'(\omega) + if''(\omega)$

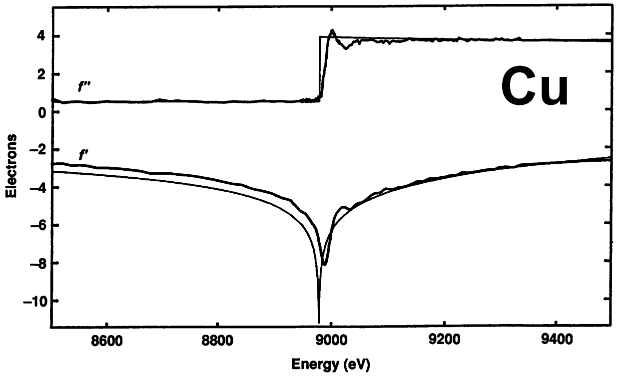


- MAD phasing: The Karle-Hendrickson equation provides a simple way for phasing from the contrast at two or more wavelengths.

Karle, *Int. J. Quant. Chem.* **18**, Suppl. S7, 357 (1980).
Hendrickson, *Trans. Am. Crystalgr. Assoc.* **21**, 11 (1985).

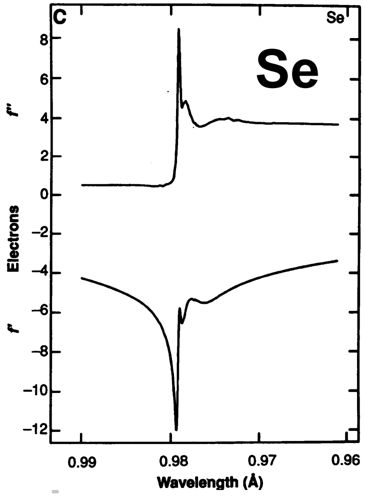
MAD with synchrotron radiation

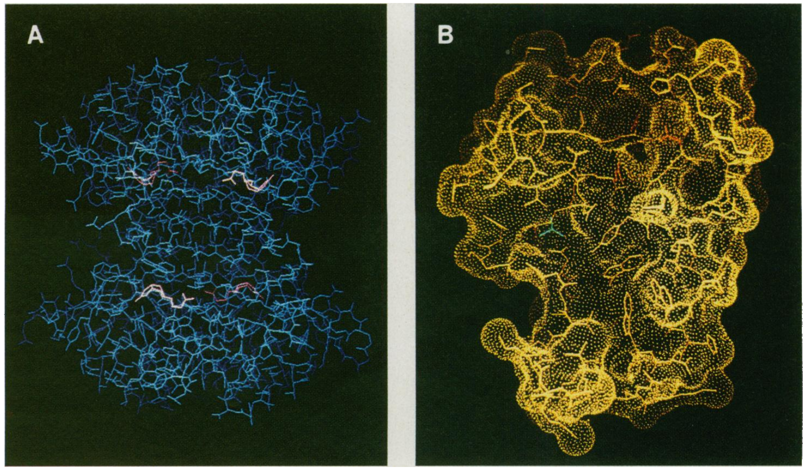
- MAD has been a well-established phasing method with synchrotron radiation since 80's.



Heptahydrido *bis*(diiopropylphenyl)phosphine
Re LIII-edge
Arndt *et al.*, *Nature* **298**, 835 (1982).

Cucumber basic blue protein
Guss *et al.*, *Science* **241**, 806 (1988).





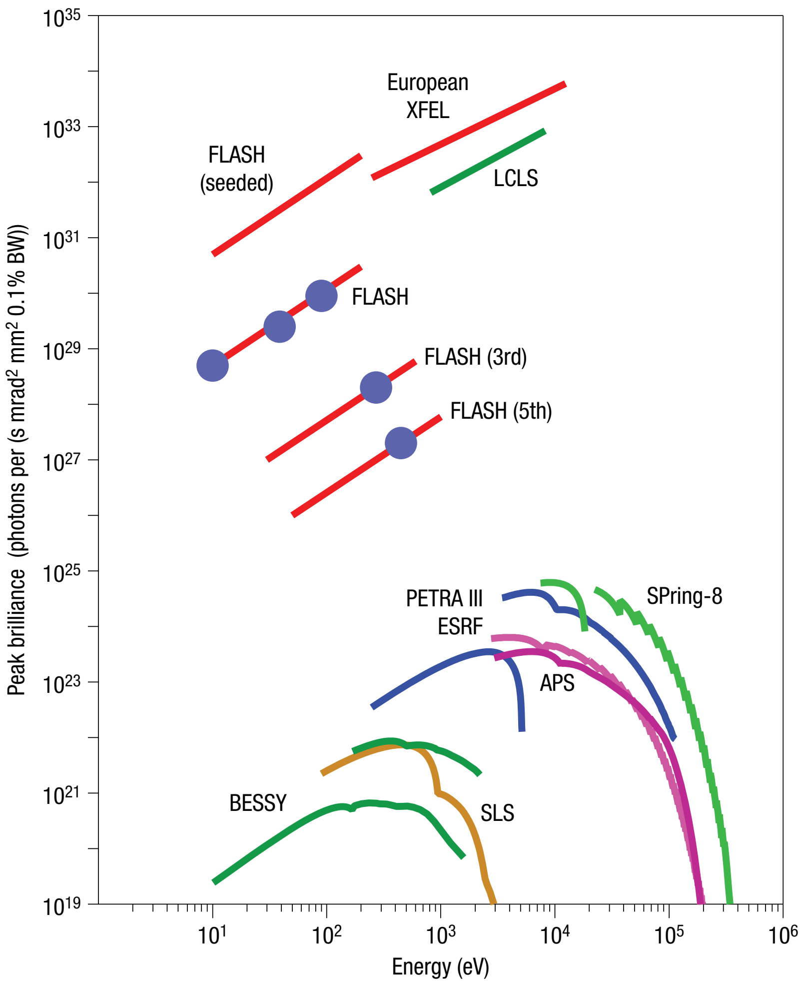
A) Streptavidin
Hendrickson *et al.*, *PNAS* **86**, 2190 (1989).

B) Ribonuclease H
Yang *et al.*, *Science* **249**, 1398 (1990).

Picture taken from Hendrickson, *Science* **254**, 51 (1991).

What is XFEL?

- XFEL: X-ray Free-Electron Laser
- *Ultraintense*
  - synchrotron: at most one photon absorbed per pulse
  - XFEL: many photons absorbed per pulse
  - fluence: ~10^{13} photons per μm^2 per pulse
  - peak intensity: ~10^{18} W/cm^2
- *Ultrafast*
  - pulse duration: femtoseconds or sub-fs



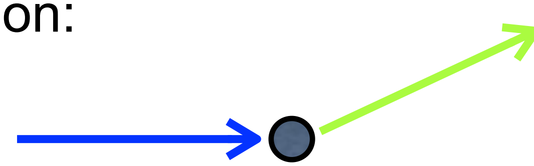
Ackermann *et al.*, *Nature Photon.* **1**, 336 (2007).

Where are XFELs?

- FLASH at DESY, Germany (2004)
- LCLS at SLAC, USA (2009)
- SACLA at RIKEN Harima, Japan (2011)
- PAL XFEL at Pohang, Korea (2015)
- European XFEL, Germany (2015)

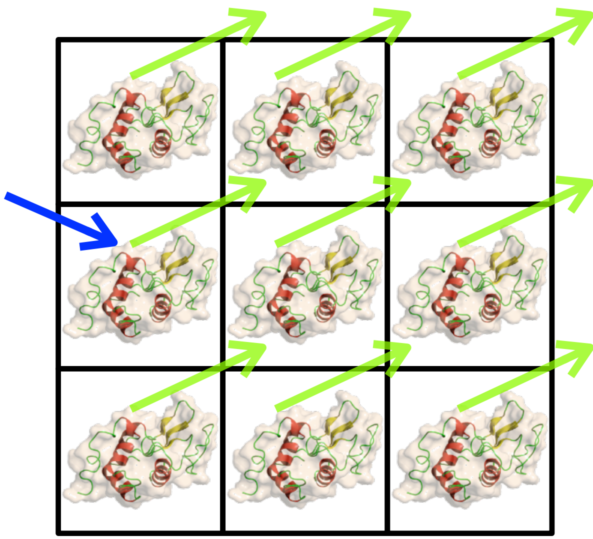
Why need for *ultraintense*

- Carbon at synchrotron radiation:
  12 keV, 10^6 photons
  on 10μm × 10μm

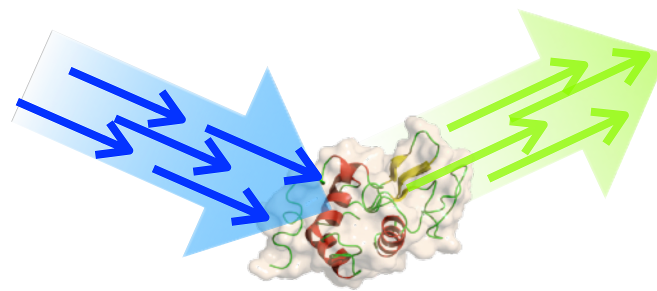


scattering
probability ~ 10^{-12}

- Signal amplification

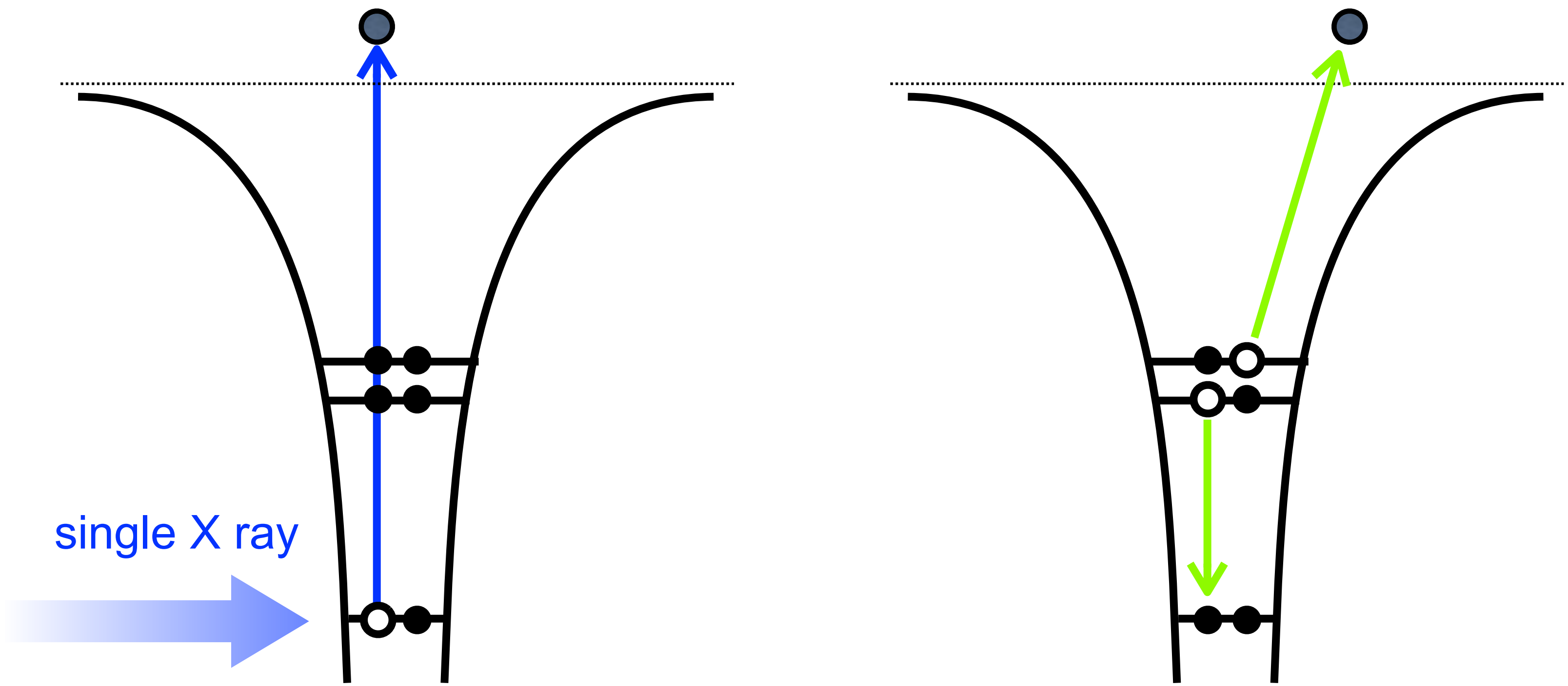


~10^8 molecules in
a μm-sized crystal



high x-ray fluence from XFEL
(×10^8~10^{10} more than
synchrotron radiation)

Photoabsorption by X-rays



photoionization

$C \rightarrow C^{*+} + e^{-}$

Auger decay

$C^{*+} \rightarrow C^{++} + e^{-}$

- Typically absorption cross section is larger than scattering cross section.
- XFEL induces multiphoton multiple ionization dynamics.

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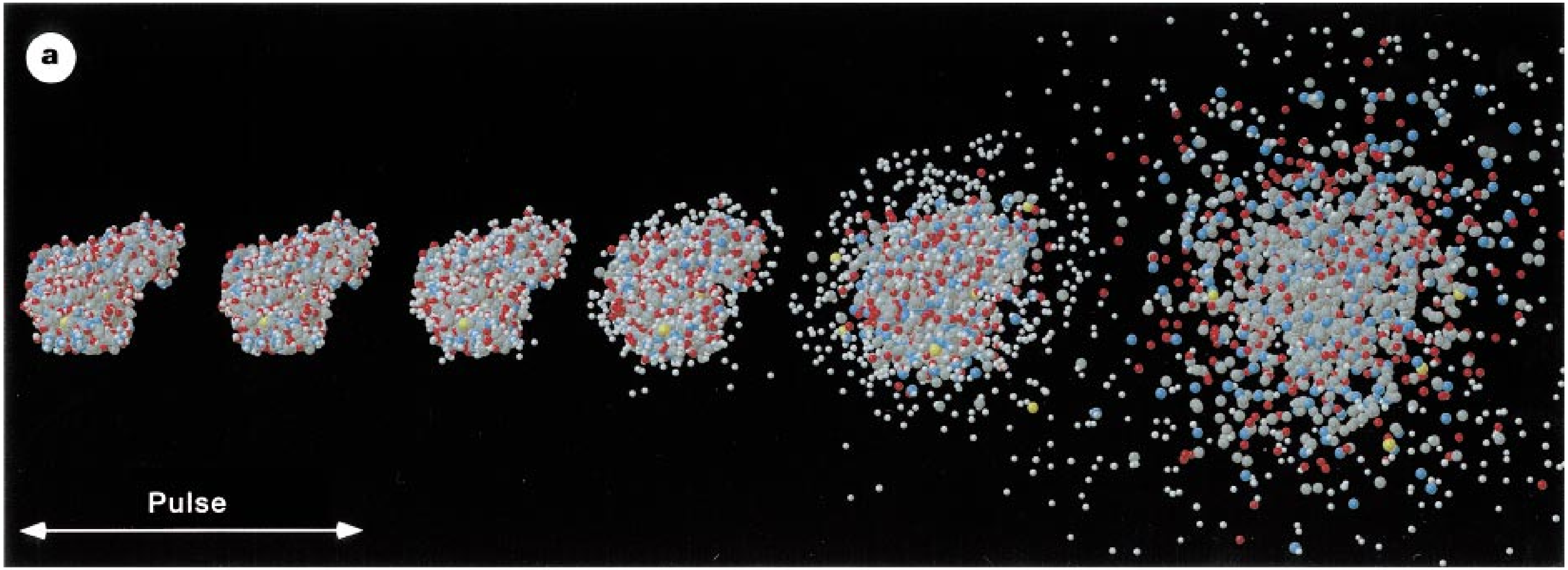
Radiation damage (Coulomb explosion)

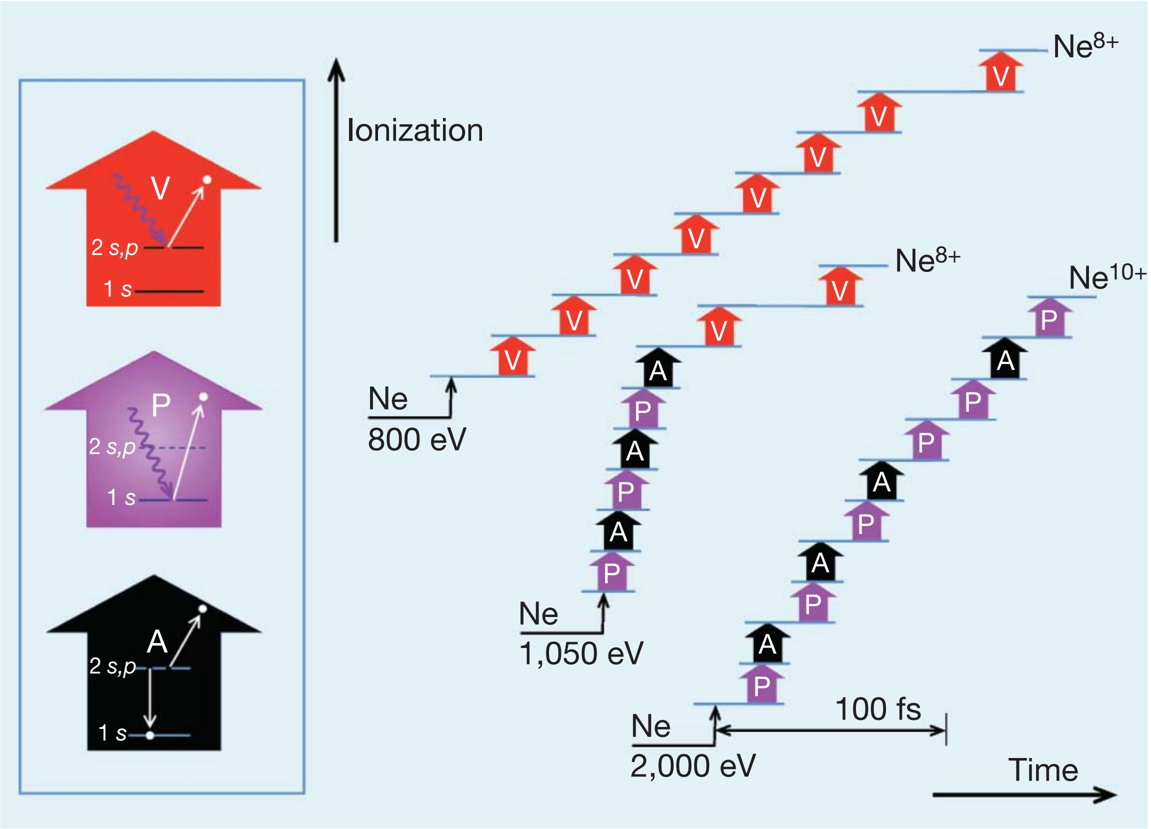


t=−2fs *t*=2fs *t*=5fs *t*=10fs *t*=−20fs *t*=50fs

Neutze *et al.*, *Nature* **406**, 752 (2000)

- Diffraction-before-destruction: needs *ultrafast* pulses (~femtosecond)

Electronic damage during XFEL pulses

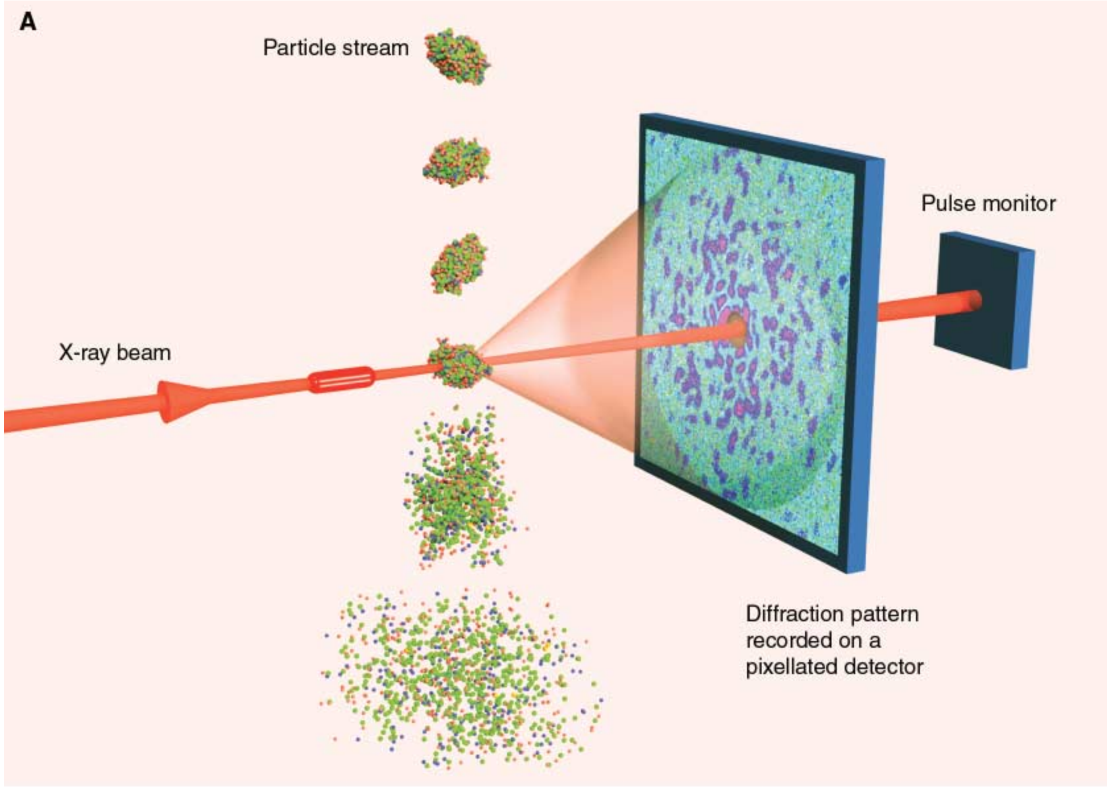


Young *et al.*, *Nature* **466**, 56 (2010).

- Multiphoton multiple ionization via a sequence of one-photon ionizations
- Diffraction-during-ionization: unavoidable electronic damage (~attosec.)

Femtosecond X-ray nanocrystallography

- Growing high-quality crystals is one of major bottlenecks in x-ray crystallography.
- *Ultraintense* and *ultrafast* pulses from XFEL
- Enough signals from *nano-sized crystals* and single molecules
- Single-shot molecular imaging: revolutionary impact on structural biology



Gaffney & Chapman, *Science* **316**, 1444 (2007).

New theory for new experiment

Can we use the MAD phasing with XFEL?

phase problem ➔ **MAD**

growing high-quality crystals ➔ **XFEL**

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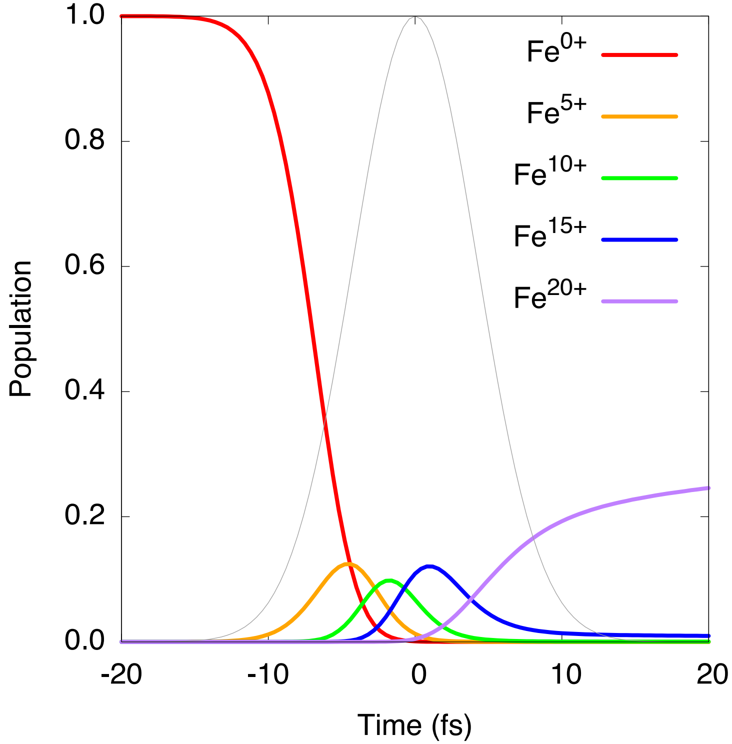
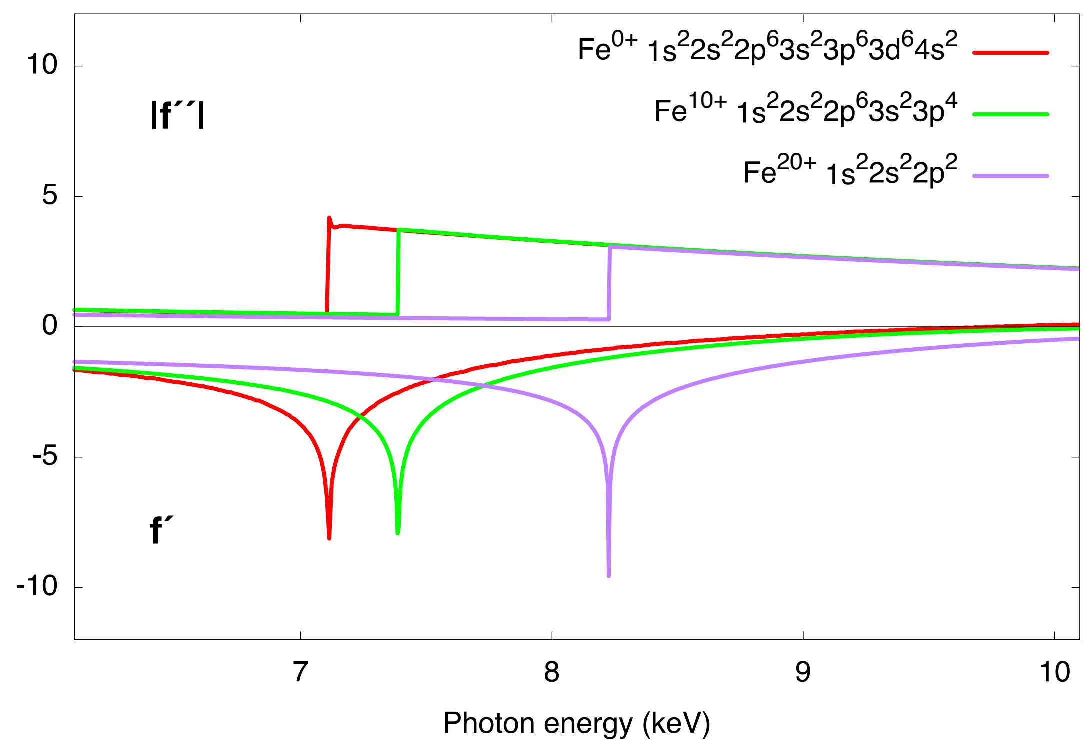
Electronic damage to heavy atoms

Population dynamics of Fe charge states during an XFEL pulse



Dispersion corrections of atomic form factors of Fe and its ions

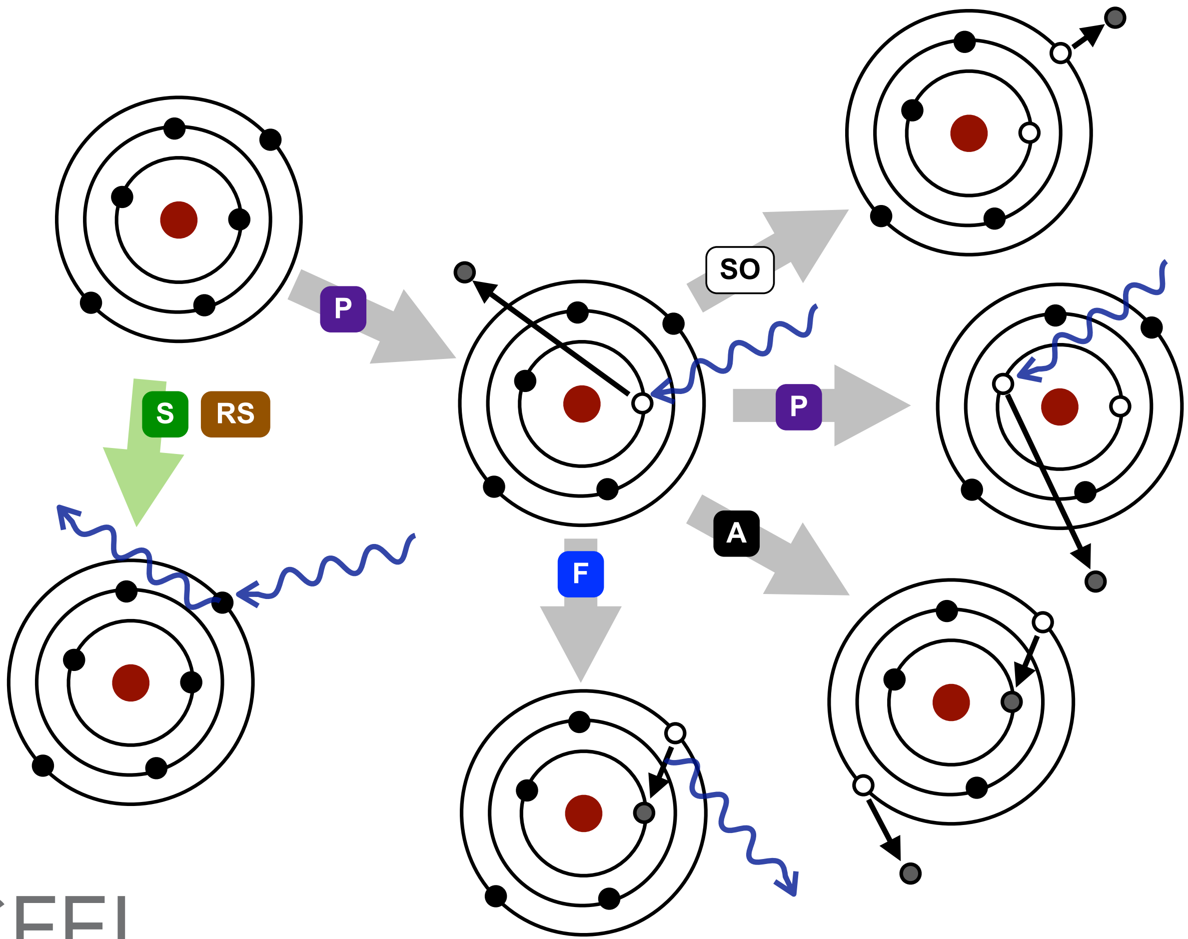


(8 keV, 5×10^{12} photons/μm^2, 10 fs FWHM)

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

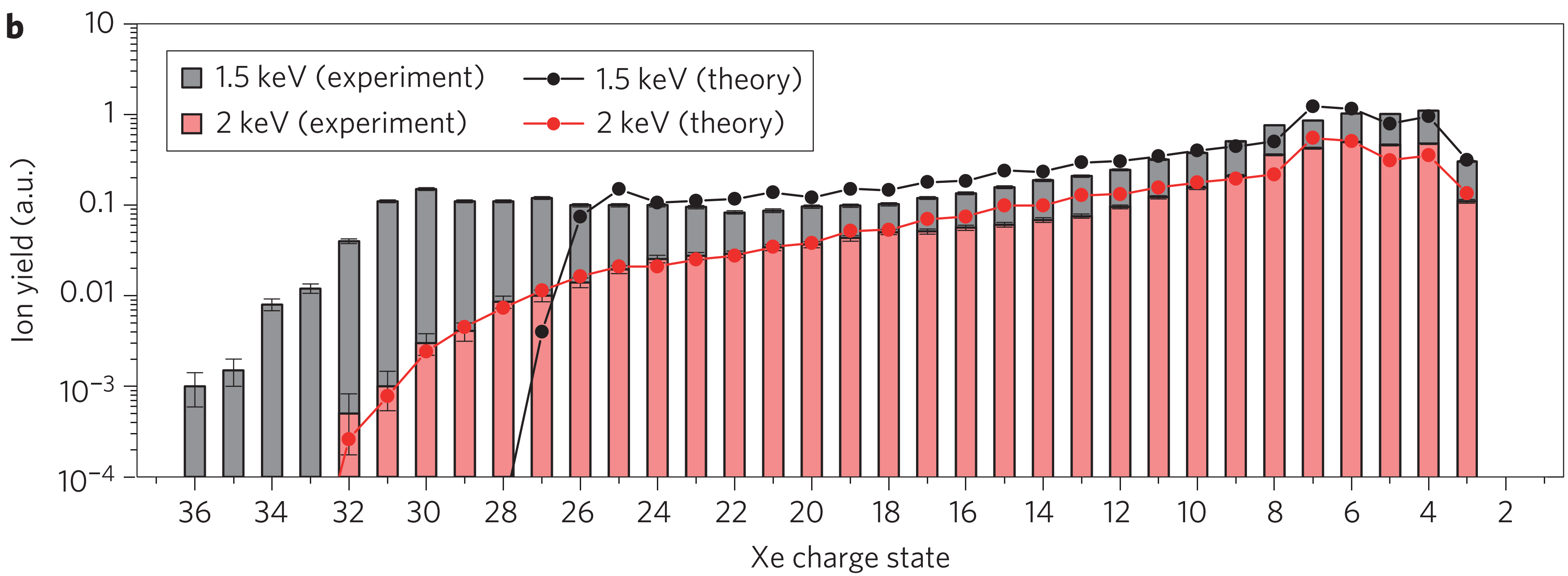
XATOM: x-ray and atomic physics toolkit

- X-ray-induced atomic processes for any given element and configuration
- Rate equation model to simulate ionization and relaxation dynamics



Son, Young & Santra, *Phys. Rev. A* **83**, 033402 (2011).

Xe at LCLS



- Charge state distribution of Xe measured at LCLS
- At 2 keV: good agreement between experiment and theory
- At 1.5 eV: unprecedented high charge states (up to Xe^{36+}) in experiment

Rudek, Son *et al.*, *Nature Photon.* **6**, 858 (2012).

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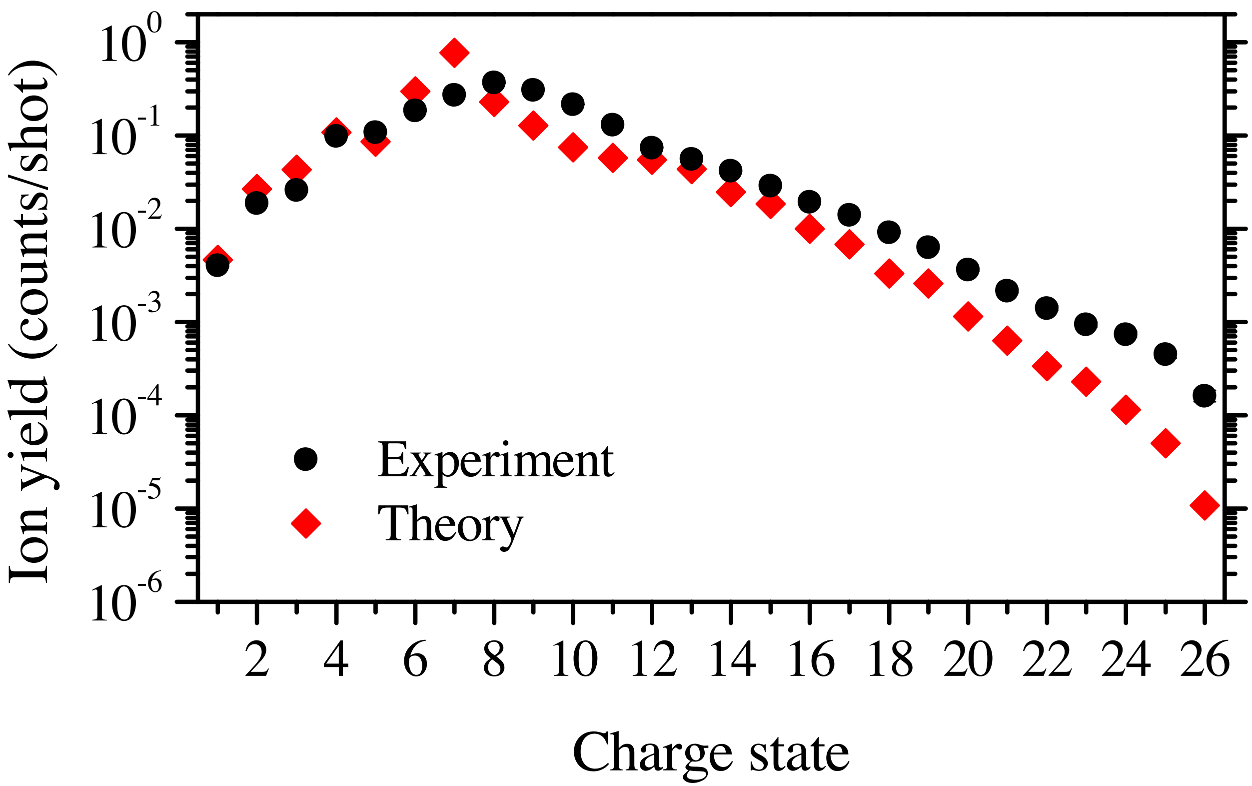
Xe at SACLA



- At 5.5 keV: deep inner-shell (*L*-shell) ionization dynamics good agreement between experiment and theory

Fukuzawa, Son *et al.*, *Phys. Rev. Lett.* **110**, 173005 (2013).

Prior speculations regarding MAD at XFEL

- Unavoidable electronic damage, especially to heavy atoms
- Dramatic change of anomalous scattering for high charge states
- Stochastic electronic damage to heavy atoms would destroy coherent scattering signals in nanocrystals
- MAD would not be an applicable route for phasing at XFEL...?

- We demonstrate the existence of a Karle-Hendrickson-type equation in the high-intensity regime.
- We show that MAD not only works, but also the extensive electronic rearrangements at high x-ray intensity provide a new path to phasing.

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

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Karle-Hendrickson equation

- Karle-Hendrickson eq. represents a set of equations at different ω:

$$\begin{aligned}|F_T(\mathbf{Q},\omega)|^2 = \left|F_T^0(\mathbf{Q})\right|^2 &+ \left|F_A^0(\mathbf{Q})\right|^2 a(\mathbf{Q},\omega)\\ &+ \left|F_T^0(\mathbf{Q})\right|\left|F_A^0(\mathbf{Q})\right| b(\mathbf{Q},\omega)\cos\Delta\phi^0(\mathbf{Q})\\ &+ \left|F_T^0(\mathbf{Q})\right|\left|F_A^0(\mathbf{Q})\right| c(\mathbf{Q},\omega)\sin\Delta\phi^0(\mathbf{Q})\end{aligned}$$

- MAD coefficients (determined theoretically or experimentally):

$$a(\mathbf{Q},\omega) = \frac{f_A'(\omega)^2 + f_A''(\omega)^2}{\{f_A^0(\mathbf{Q})\}^2}, \quad b(\mathbf{Q},\omega) = \frac{2f_A'(\omega)}{f_A^0(\mathbf{Q})}, \quad c(\mathbf{Q},\omega) = \frac{2f_A''(\omega)}{f_A^0(\mathbf{Q})}$$

- 3 unknowns at every **Q**: $\left|F_T^0(\mathbf{Q})\right|, \ \left|F_A^0(\mathbf{Q})\right|, \Delta\phi^0(\mathbf{Q}) \ [= \phi_T^0(\mathbf{Q}) - \phi_A^0(\mathbf{Q})]$
- These 3 unknowns are algebraically solved with 3 measurements.

Karle, *Int. J. Quant. Chem. Quant. Bio. Symp.* **7**, 357 (1980)
Hendrickson, *Trans. Am. Crystalgr. Assoc.* **21**, 11 (1985)

Scattering intensity including elec. damage

$$\frac{dI(\mathbf{Q},\omega)}{d\Omega} = \mathcal{F}C(\Omega)\int_{-\infty}^{\infty} dt\, g(t) \sum_{I} P_I(t) \left| F_P^0(\mathbf{Q}) + \sum_{j=1}^{N_H} f_{I_j}(\mathbf{Q},\omega) e^{i\mathbf{Q}\cdot\mathbf{R}_j} \right|^2$$

$$I = (I_1, I_2, \cdots I_{N_H}), \quad P_I(t) = \prod_{j=1}^{N_H} P_{I_j}(t)$$

$$f_{I_j}(\mathbf{Q},\omega) = f_{I_j}^0(\mathbf{Q}) + f_{I_j}'(\omega) + i f_{I_j}''(\omega)$$

- All changes among N_H heavy atoms are included.
- *P*: protein, *H*: heavy atoms; only heavy atoms scatter anomalously and undergo damage dynamics during an x-ray pulse.
- Heavy atoms are ionized independently.
- Only one species of heavy atoms is considered.

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

Generalized Karle-Hendrickson equation

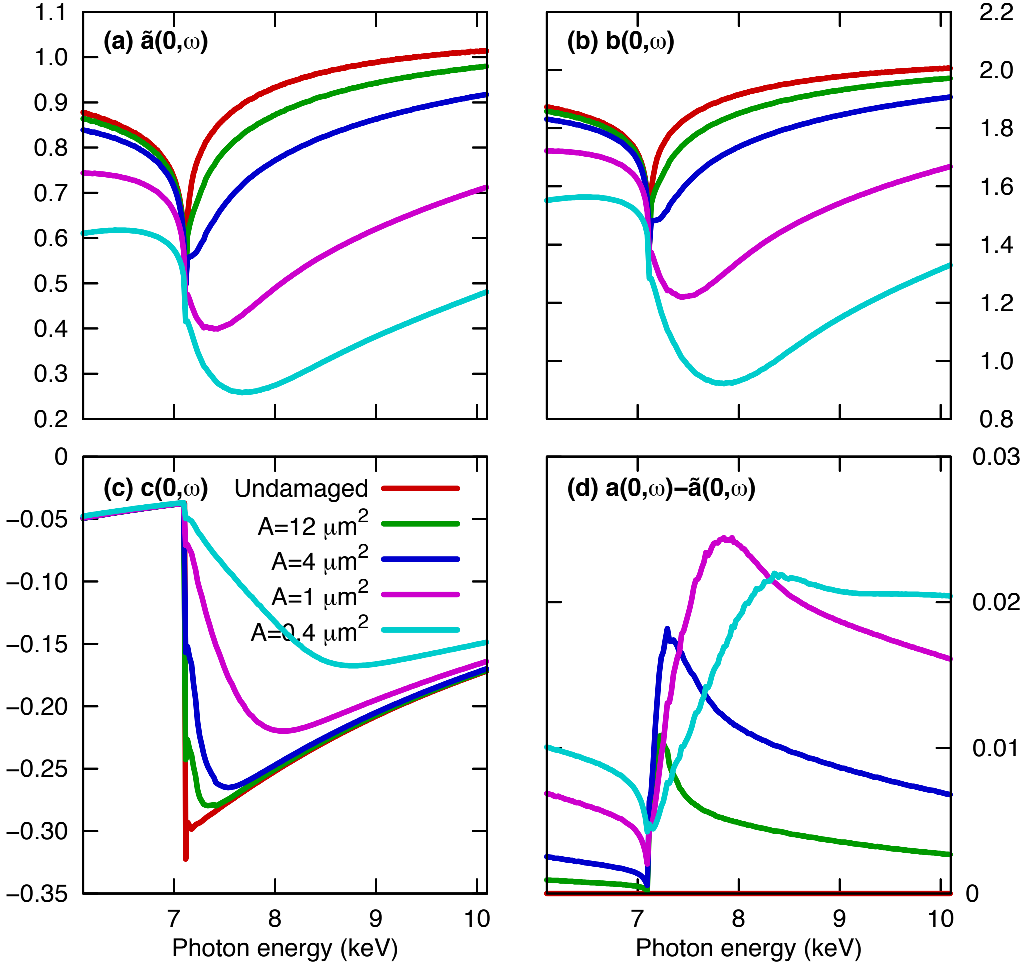
$$\frac{dI(\mathbf{Q},\omega)}{d\Omega} = \mathcal{F}C(\Omega)\Big[\left|F_P^0(\mathbf{Q})\right|^2 + \left|F_H^0(\mathbf{Q})\right|^2 \tilde{a}(\mathbf{Q},\omega)$$
$$+ \left|F_P^0(\mathbf{Q})\right| \left|F_H^0(\mathbf{Q})\right| b(\mathbf{Q},\omega) \cos\Delta\phi^0(\mathbf{Q})$$
$$+ \left|F_P^0(\mathbf{Q})\right| \left|F_H^0(\mathbf{Q})\right| c(\mathbf{Q},\omega) \sin\Delta\phi^0(\mathbf{Q})$$
$$+ N_H \left|f_H^0(\mathbf{Q})\right|^2 \{a(\mathbf{Q},\omega) - \tilde{a}(\mathbf{Q},\omega)\}\Big]$$

- MAD coefficients: $a(\mathbf{Q},\omega)$, $b(\mathbf{Q},\omega)$, $c(\mathbf{Q},\omega)$, and $\tilde{a}(\mathbf{Q},\omega)$
  → measured or calculated with time evolution of config. populations
  e.g.) $\tilde{a}(\omega) = \frac{1}{\{f_H^0\}^2}\int_{-\infty}^{\infty} dt\, g(t) \left|\sum_{I_H} P_{I_H}(t) f_{I_H}(\omega)\right|^2$
- 3 unknowns: $\left|F_P^0(\mathbf{Q})\right|$, $\left|F_H^0(\mathbf{Q})\right|$, $\Delta\phi^0(\mathbf{Q})$ $[= \phi_P^0(\mathbf{Q}) - \phi_H^0(\mathbf{Q})]$
  → solvable with measurements at 3 different wavelengths.

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

MAD coefficients

Fe in an x-ray pulse of 2×10^{12} photons and 10 fs FWHM



- dynamical behavior of heavy atoms calculated by XATOM
- bleaching effect: minimum deepened and edge broadened → easy to choose wavelengths
- **MAD works**: enhanced contrast at different wavelengths
- potential new phasing methods

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

Brand-new phasing method

- **SIR** (single isomorphic replacement): atomic replacement in sample preparation; native vs. derivative
- **RIP** (radiation-damage induced phasing): chemical rearrangement during the x-ray pulses; S–S bond vs. bond breaking
- **MAD** (multi-wavelength anomalous diffraction): $\Delta F_{\Delta\lambda}$
- **SAD** (single-wavelength anomalous diffraction): $\Delta F_{\pm}$

New phasing method: neither **SIR** nor **RIP**

Fluences rather than wavelengths: neither **MAD** nor **SAD**

Son, Chapman & Santra, *Phys. Rev. Lett.* **107**, 218102 (2011).

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Conclusion

- MAD phasing method in extreme conditions of ionizing radiations
- Combination of ultrafast electronic dynamics at the atomic level and imaging of macromolecules by intense x-ray pulses
- Existence of a generalized Karle-Hendrickson equation for the MAD method at high x-ray intensity
- Bleaching effect on the scattering strength to be beneficial to the phasing method
- A new opportunity for solving the phase problem in femtosecond nanocrystallography with XFELs

→ A breakthrough in structural biology

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Dr. Zoltan Jurek
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Take-home message

XFEL goes MAD.