Multiwavelength anomalous diffraction at high x-ray intensity

Sang-Kil Son,[1] Henry N. Chapman,[1,2] and Robin Santra[1,2]
[1] Center for Free-Electron Laser Science, DESY, Hamburg, Germany
[2] Department of Physics, University of Hamburg, Hamburg, Germany

---

Ultrafast Dynamic Imaging of Matter, Banff, Alberta, Canada
July 1–3, 2012

HELMHOLTZ
ASSOCIATION

CFEL
SCIENCE

Center for Free-Electron Laser Science
CFEL is a scientific cooperation of the three organizations:
DESY – Max Planck Society – University of Hamburg

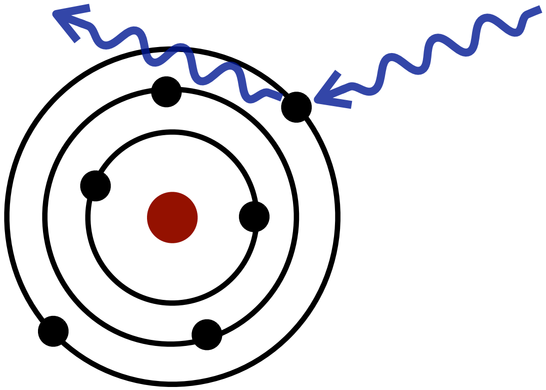
DESY

X-ray scattering

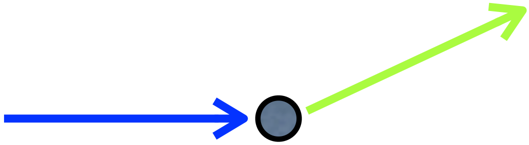
- Elastic x-ray scattering form factor

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

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

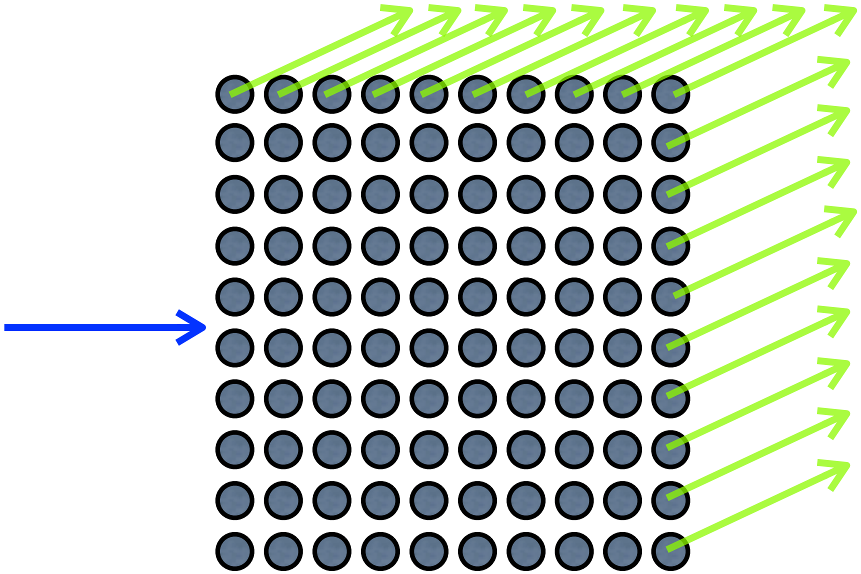


- Carbon at synchrotron radiation: 12 keV, 10^6 photons on 10μm × 10μm

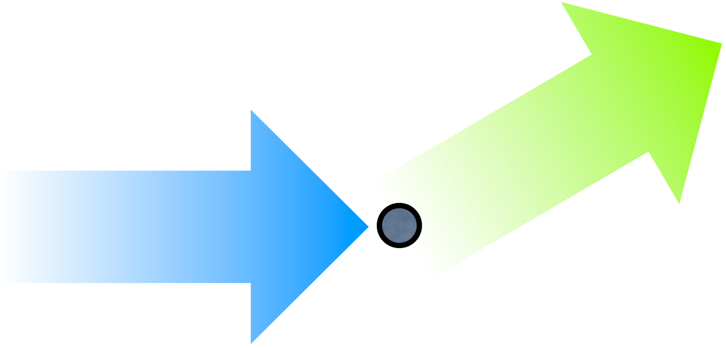


scattering
probability ~ 10^{-12}

Why X-ray free-electron laser



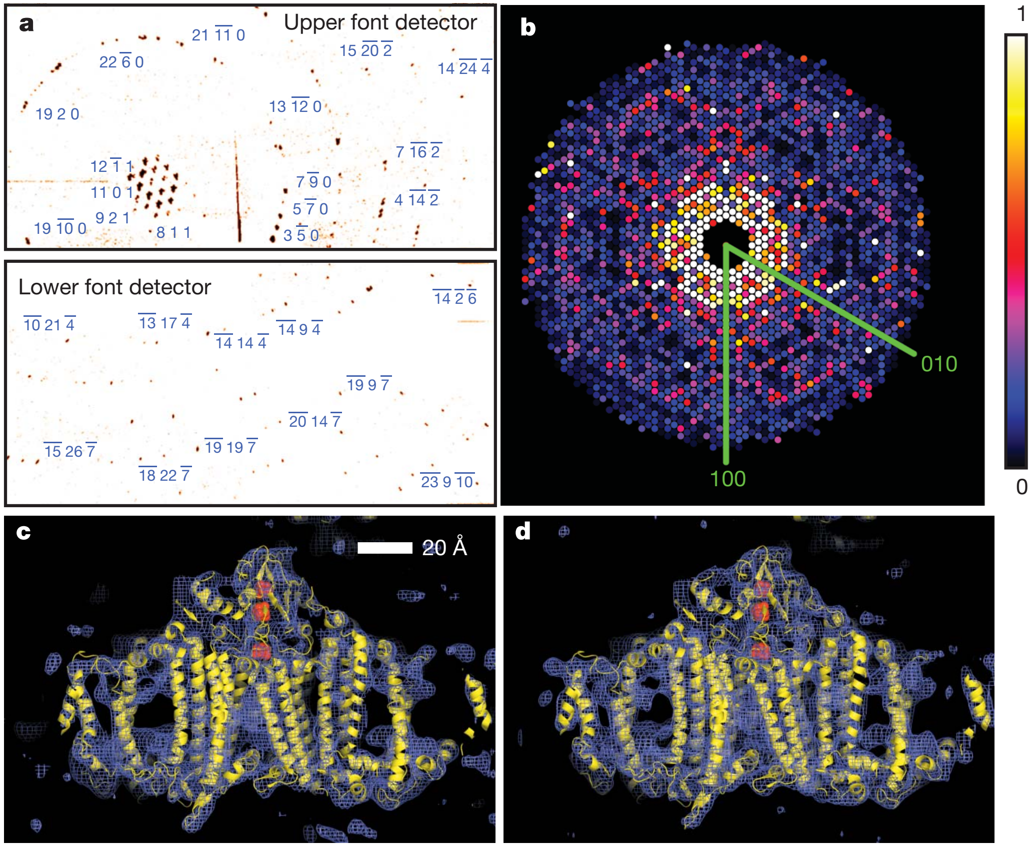
~10^8 molecules in a
µm-sized crystal



high x-ray fluence from XFEL
(×10^6 more than synchrotron radiation)

Femtosecond X-ray nanocrystallography

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



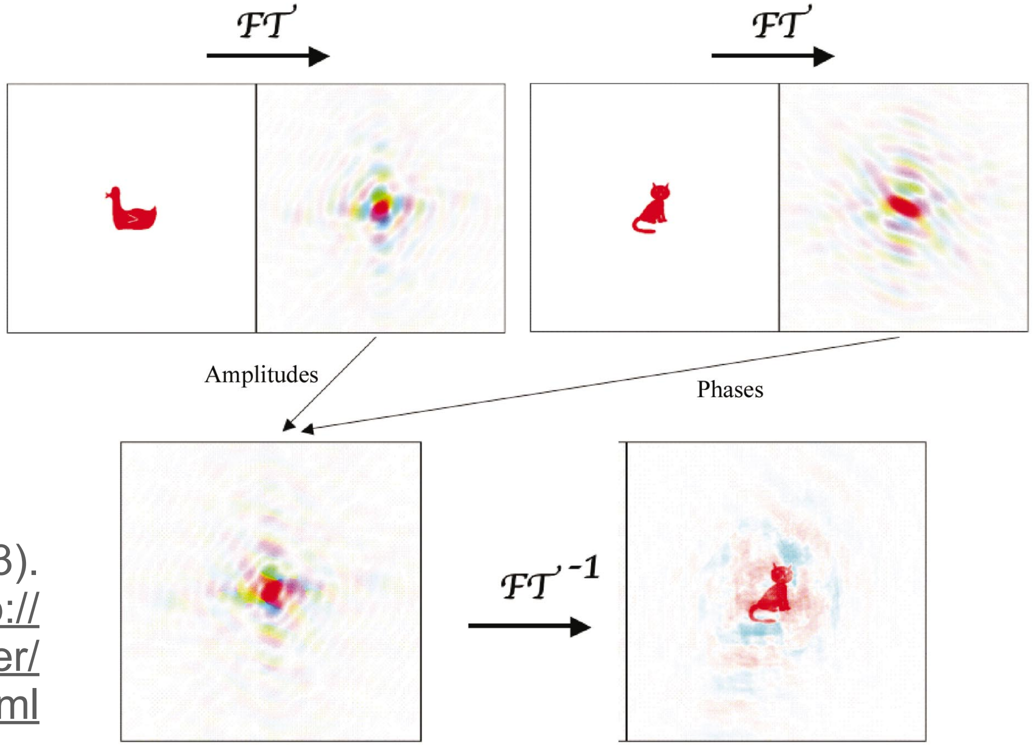
Chapman *et al.*, *Nature* **470**, 73 (2011).

Phase problem

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

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

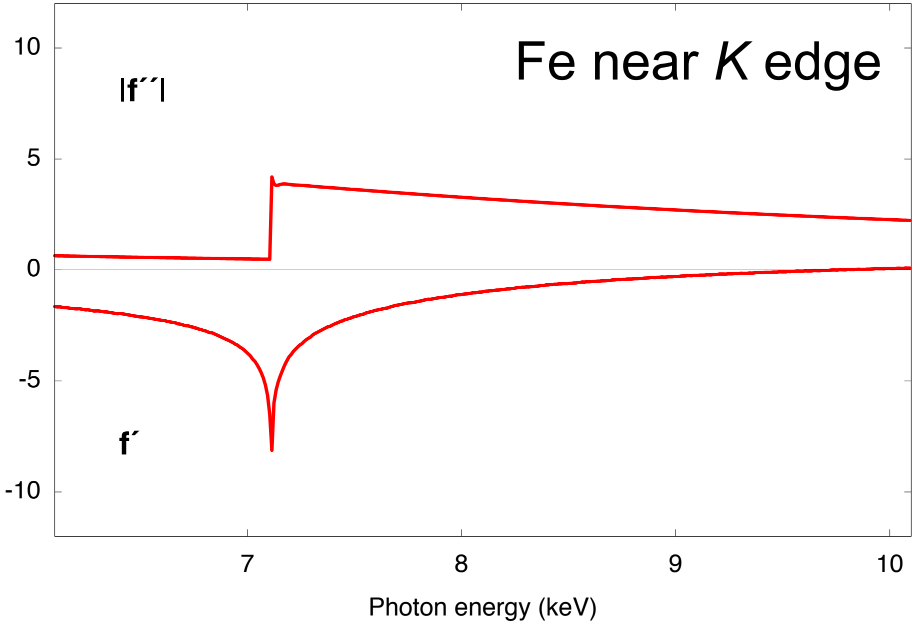
- Phases are essential for structural determination, but they are lost in measurement.



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

Multiwavelength Anomalous Diffraction

- Dispersion correction: $f(\mathbf{Q},\omega) = f^0(\mathbf{Q}) + f'(\omega) + i f''(\omega)$

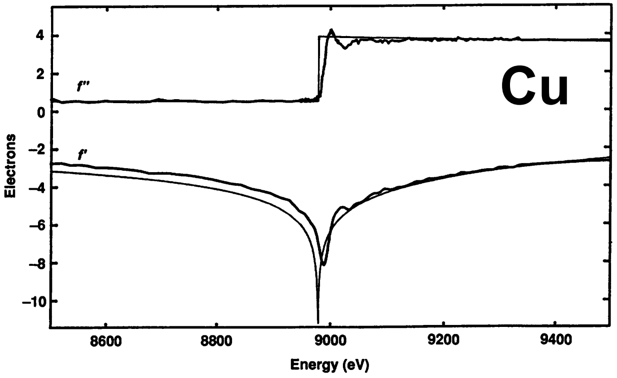


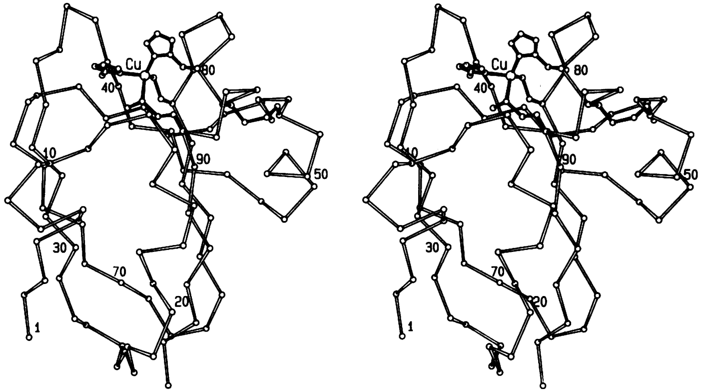
- MAD phasing: The Karle-Hendrickson equation provides a simple way for phasing from the contrast at two or more wavelengths.

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

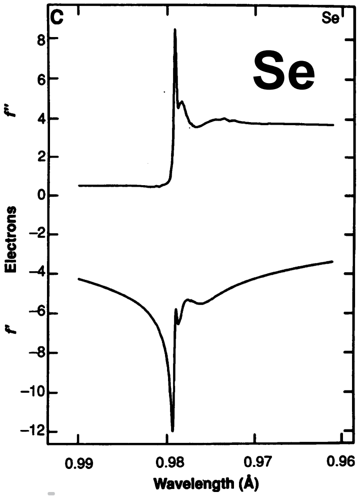
MAD with synchrotron radiation

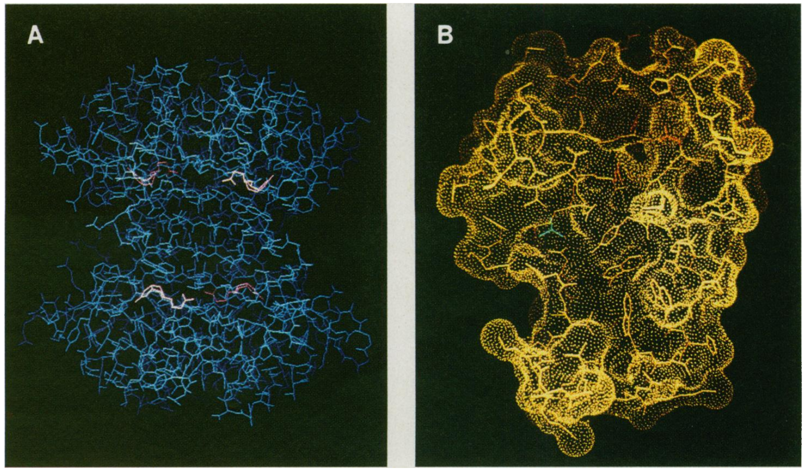
- MAD has been a well-established phasing method with synchrotron radiation since late 80’s.





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).

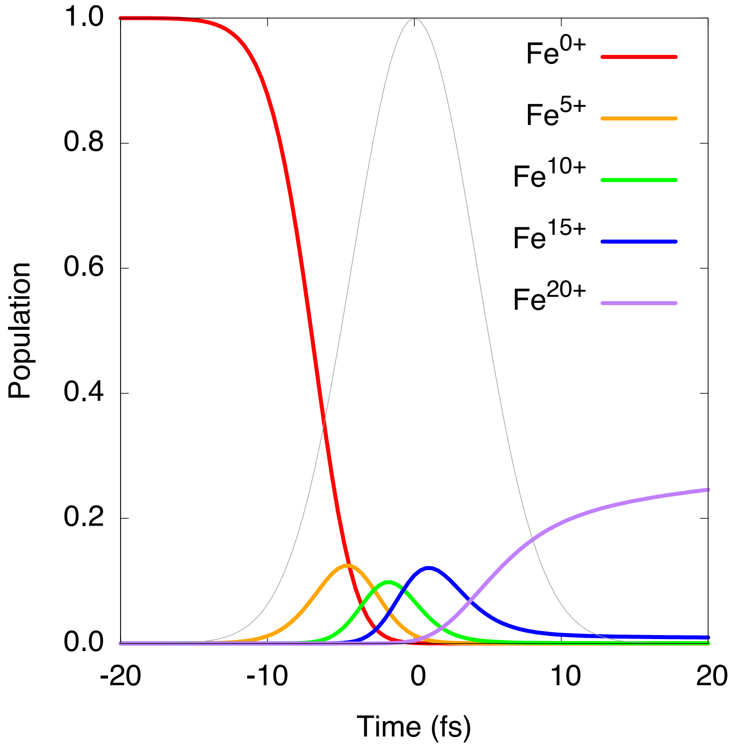
New theory for new experiment

Can we use the MAD phasing with XFEL?

phase problem ➔ **MAD**

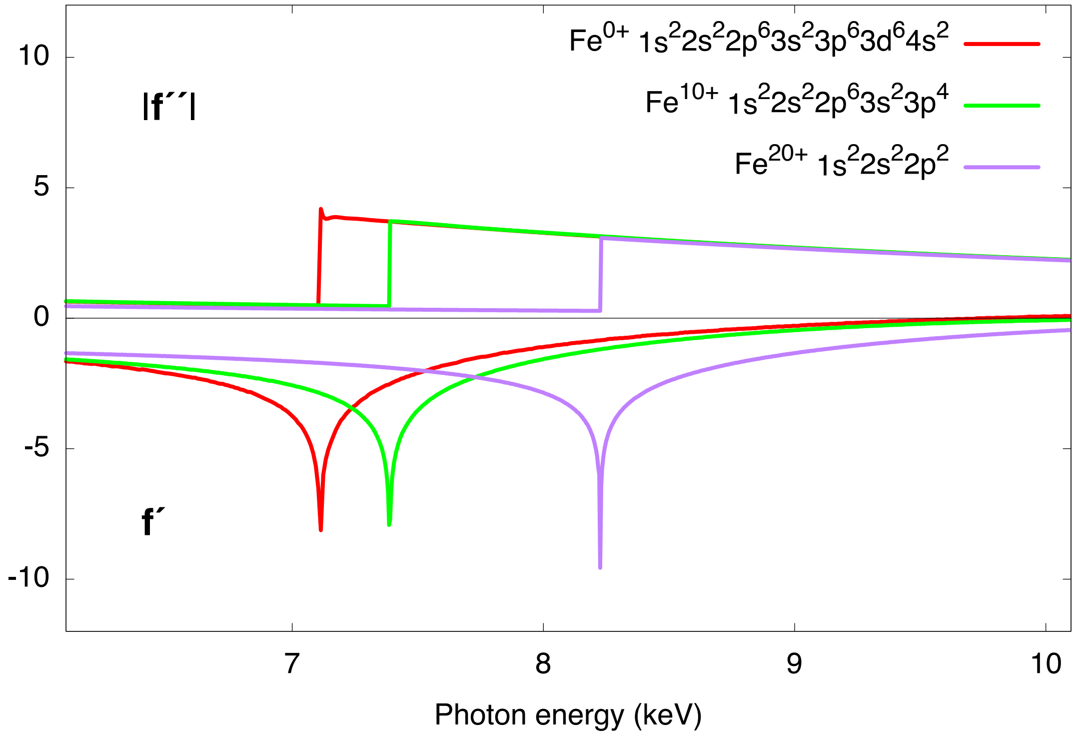
growing high-quality crystals ➔ **XFEL**

Electronic damage to heavy atoms



Population dynamics of Fe charge states during an XFEL pulse

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

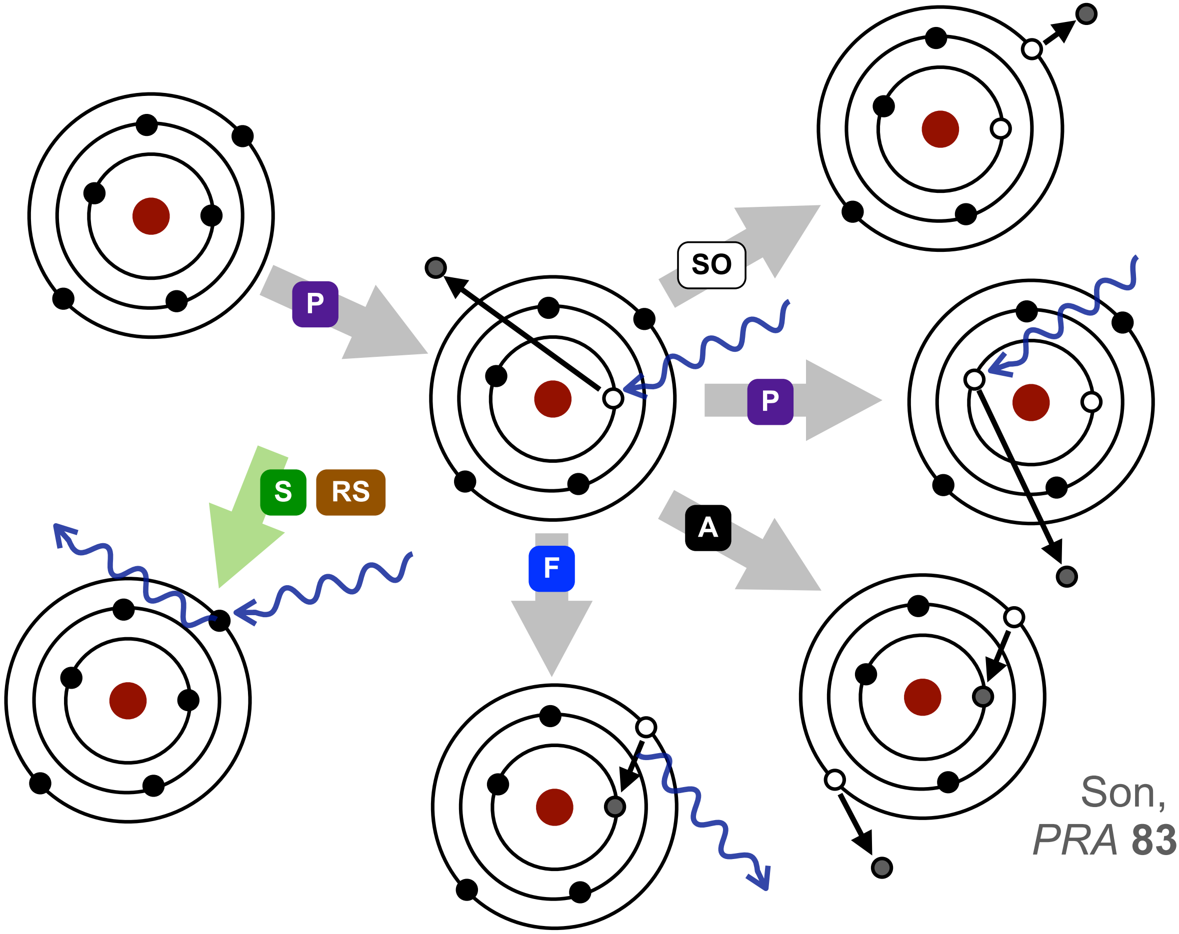


Dispersion corrections of atomic form factors of Fe and its ions

Son, Chapman & Santra, *PRL* **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,
PRA **83**, 033402 (2011).

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, *PRL* **107**, 218102 (2011).

Scattering intensity including elec. damage

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

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

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

- 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, *PRL* **107**, 218102 (2011).

Generalized Karle-Hendrickson equation

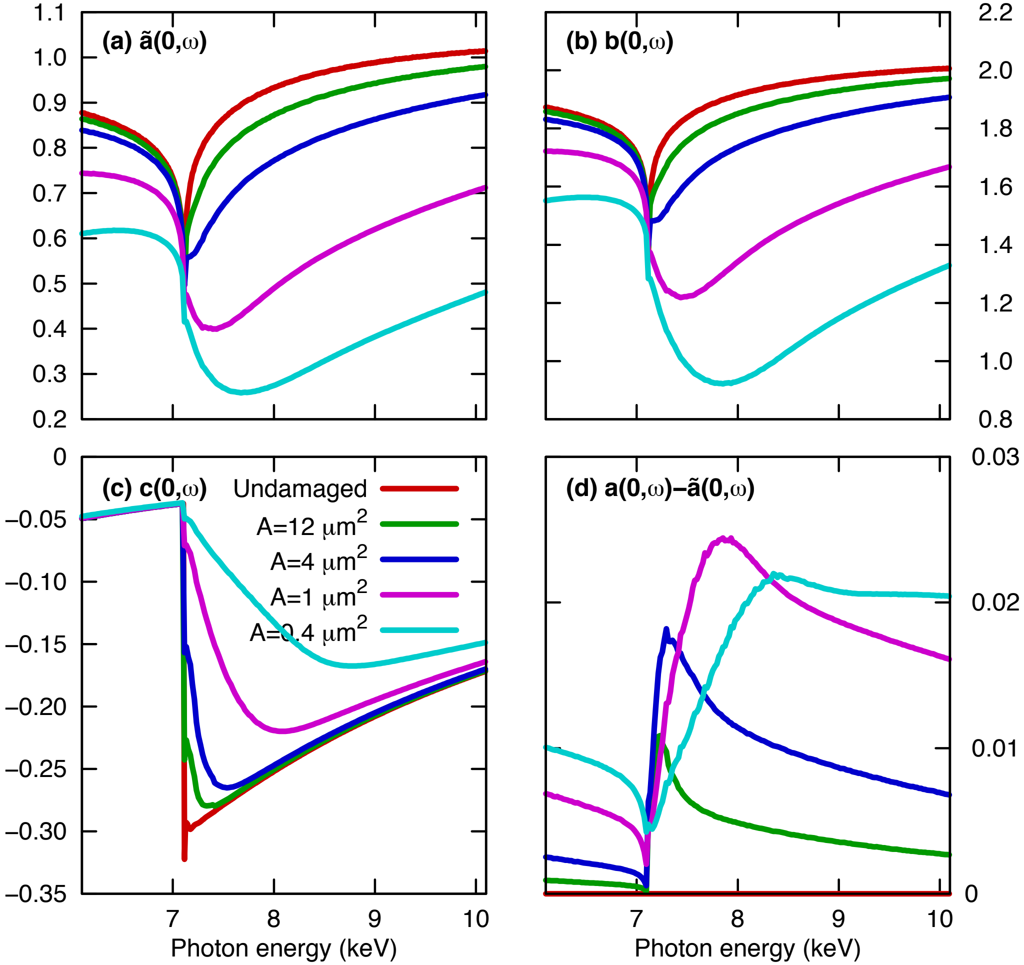
$$\begin{aligned}\frac{dI(\mathbf{Q},\omega)}{d\Omega} = \mathcal{F}C(\Omega)\Big[\big|F_P^0(\mathbf{Q})\big|^2 &+ \big|F_H^0(\mathbf{Q})\big|^2\tilde{a}(\mathbf{Q},\omega)\\ &+ \big|F_P^0(\mathbf{Q})\big|\,\big|F_H^0(\mathbf{Q})\big| b(\mathbf{Q},\omega)\cos\Delta\phi^0(\mathbf{Q})\\ &+ \big|F_P^0(\mathbf{Q})\big|\,\big|F_H^0(\mathbf{Q})\big|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

- MAD coefficients: $a(\mathbf{Q},\omega),\ b(\mathbf{Q},\omega),\ c(\mathbf{Q},\omega),\ \text{and}\ \tilde{a}(\mathbf{Q},\omega)$
  → measured or calculated with time evolution of config. populations
- 3 unknowns: $\big|F_P^0(\mathbf{Q})\big|,\ \big|F_H^0(\mathbf{Q})\big|,\ \Delta\phi^0(\mathbf{Q})\ \left[= \phi_P^0(\mathbf{Q}) - \phi_H^0(\mathbf{Q})\right]$
  → solvable with measurements at 3 different wavelengths.

Son, Chapman & Santra, *PRL* **107**, 218102 (2011).

MAD coefficients

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



- calculated by XATOM
- bleaching effect: minimum deepened and edge broadened
- **MAD works**: enhanced contrast at different wavelengths
- ***alternative phasing method*** similar to SIR (single isomorphic replacement) or RIP (radiation-damage induced phasing)

Son, Chapman & Santra, *PRL* **107**, 218102 (2011).

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

Acknowledgment

CFEL Theory Division

Take-home message

FEL goes MAD.