Multi-wavelength anomalous diffraction (MAD) phasing method at high intensity

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New Science Opportunities at FLASH
Hamburg, Germany / October 13, 2011

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CFEL is a scientific cooperation of the three organizations:
DESY – Max Planck Society – University of Hamburg

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Overview

> **MAD:** phase problem

> **FEL:** single-shot imaging / radiation damage

> **MAD at FEL**

> **MAD at FLASH**

- MAD: Multi-wavelength Anomalous Diffraction
- FEL: Free-Electron Laser

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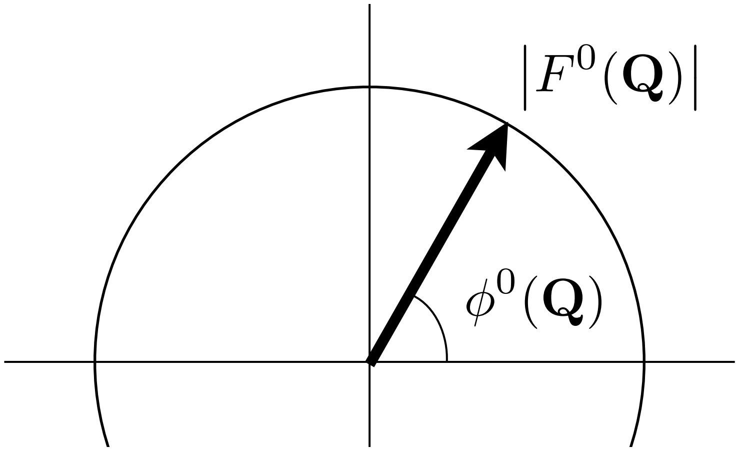
Phase problem

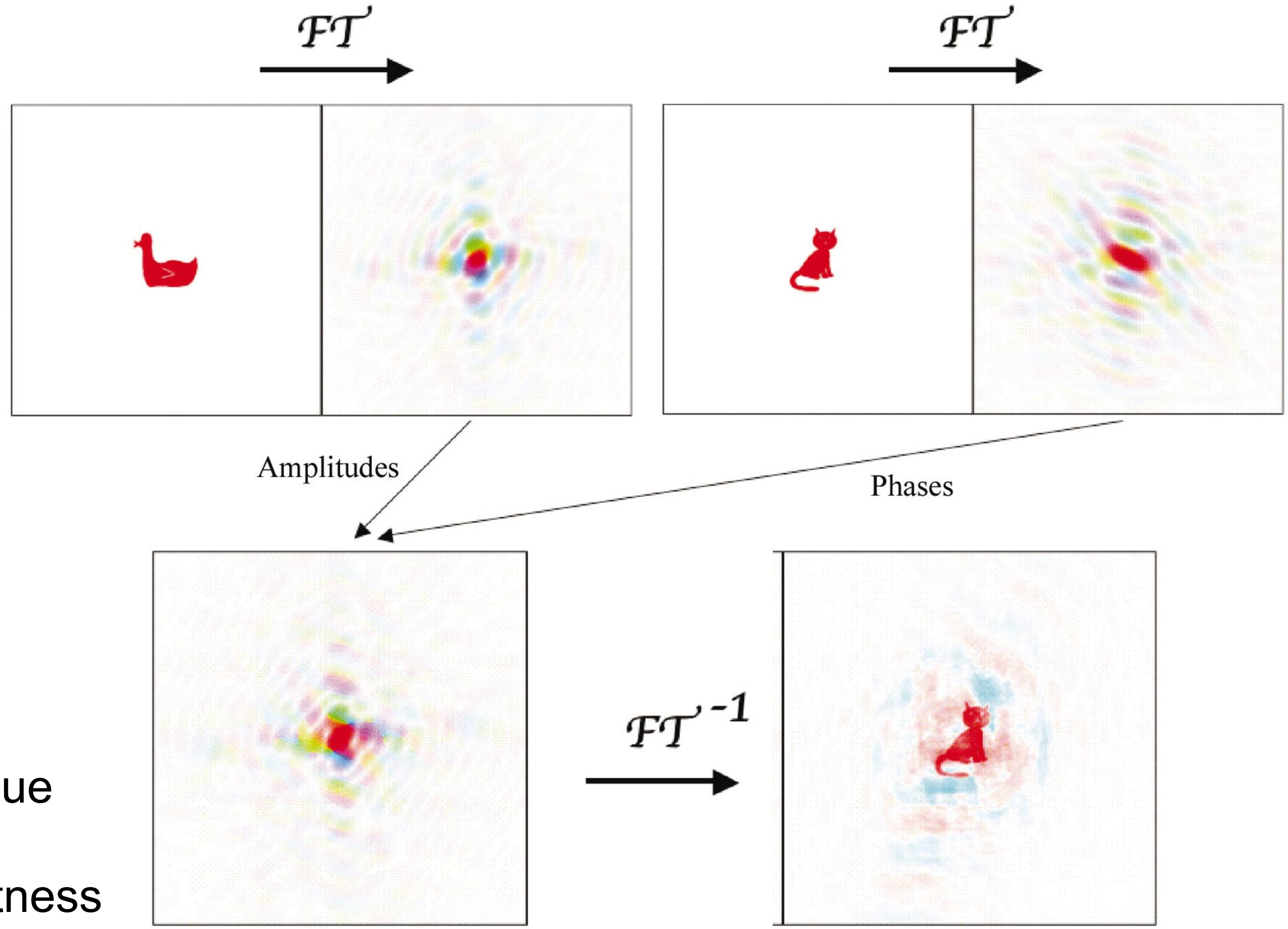
The phase problem is a fundamental obstacle in constructing an electronic density map from x-ray diffraction.

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

- $\rho(\mathbf{r})$: electronic density that we want to know
- $|F^0(\mathbf{Q})|$: → scattering intensity that we can measure
- $e^{i\phi^0(\mathbf{Q})}$: phases that we lose in measurement



Why are phases important?



phase → hue
magnitude
→ brightness

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

Phasing method

- Many phasing methods have been proposed and applied.
  - Direct method
  - 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)
- Why is MAD advantageous?
  - No atomic replacement; Different datasets obtained by physical changes (wavelength) rather than by chemical changes (replacement)
  - Algebraically solved; No need for iterative phase retrieval algorithm

Taylor, *Acta Cryst.* **D59**, 1881 (2003)

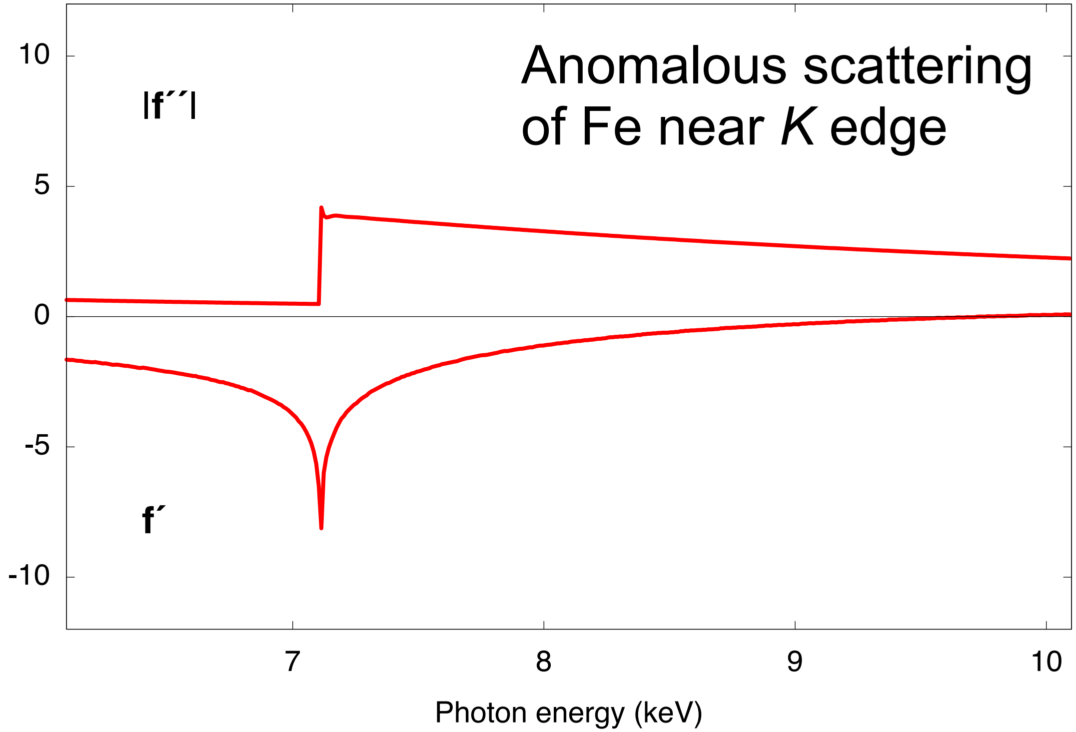
Anomalous scattering

Resonant elastic x-ray scattering (dispersive correction)

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

$$f'(\omega) = -\frac{1}{2\pi^2\alpha}\mathcal{P}\int_0^\infty \frac{\omega'^2}{\omega'^2-\omega^2}\sigma_\mathrm{P}(\omega')d\omega'$$

$$f''(\omega) = -\frac{\omega}{4\pi\alpha}\sigma_\mathrm{P}(\omega)$$

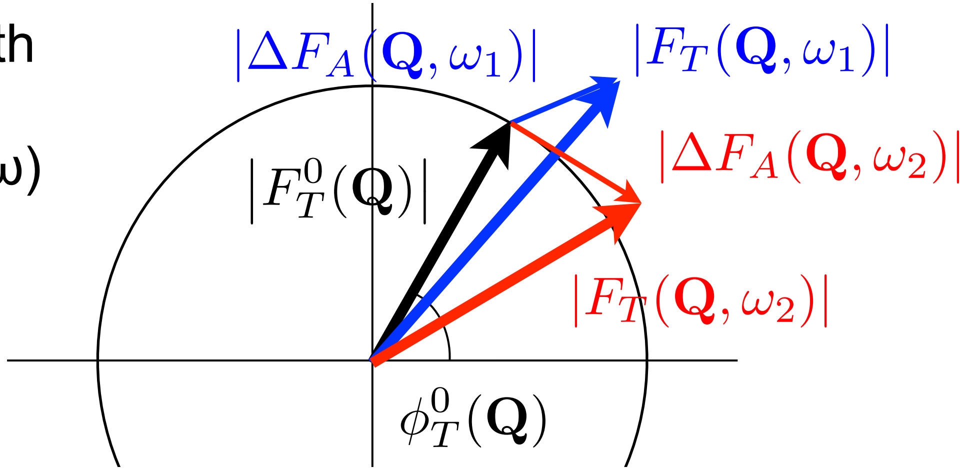


MAD phasing

The anomalous scattering at different wavelengths provides a simple way to solve the phase problem.

$$F_T(\mathbf{Q},\omega) = F_T^0(\mathbf{Q}) + \Delta F_A(\mathbf{Q},\omega)$$
$$= F_T^0(\mathbf{Q}) + F_A^0(\mathbf{Q}) \left(\frac{f'_A(\omega)}{f_A^0(\mathbf{Q})} + i\,\frac{f''_A(\omega)}{f_A^0(\mathbf{Q})} \right)$$

phase diagram with two wavelengths (photon energies ω)



Karle-Hendrickson equation

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

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

- MAD coefficients (determined theoretically or experimentally):

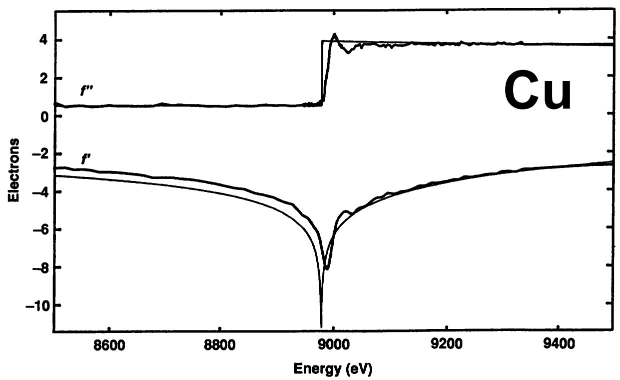
$$
a(\omega) = \frac{f_A'(\omega)^2 + f_A''(\omega)^2}{\left(f_A^0\right)^2}, \quad b(\omega) = \frac{2 f_A'(\omega)}{f_A^0}, \quad c(\omega) = \frac{2 f_A''(\omega)}{f_A^0}
$$

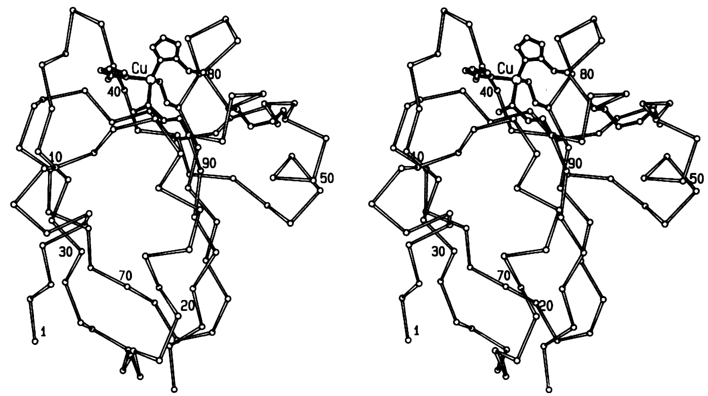
- 3 unknowns at every single **Q**: $\left|F_T^0\right|, \ \left|F_A^0\right|, \Delta\phi^0 (= \phi_T^0 - \phi_A^0)$
- These 3 unknowns are algebraically solved with 3 measurements.

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

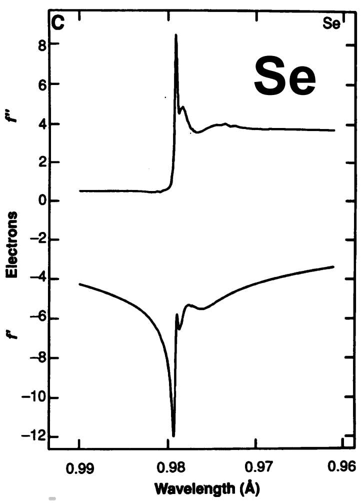
MAD with synchrotron radiation

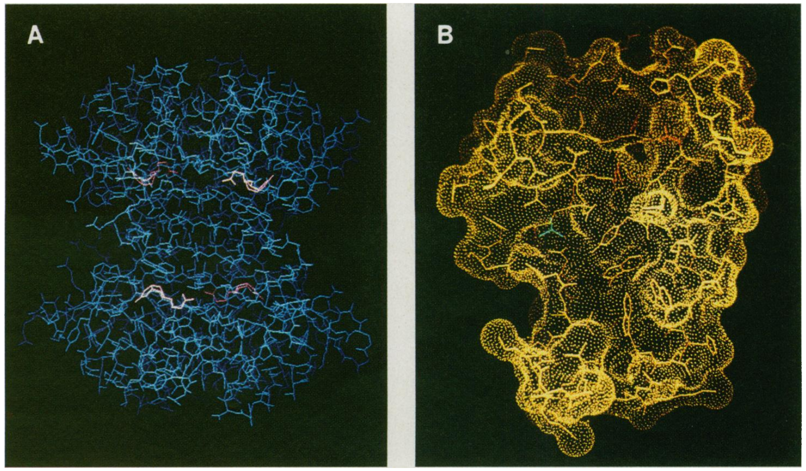
- MAD has been a well-established phasing method with synchrotron radiation since late 80's.





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)

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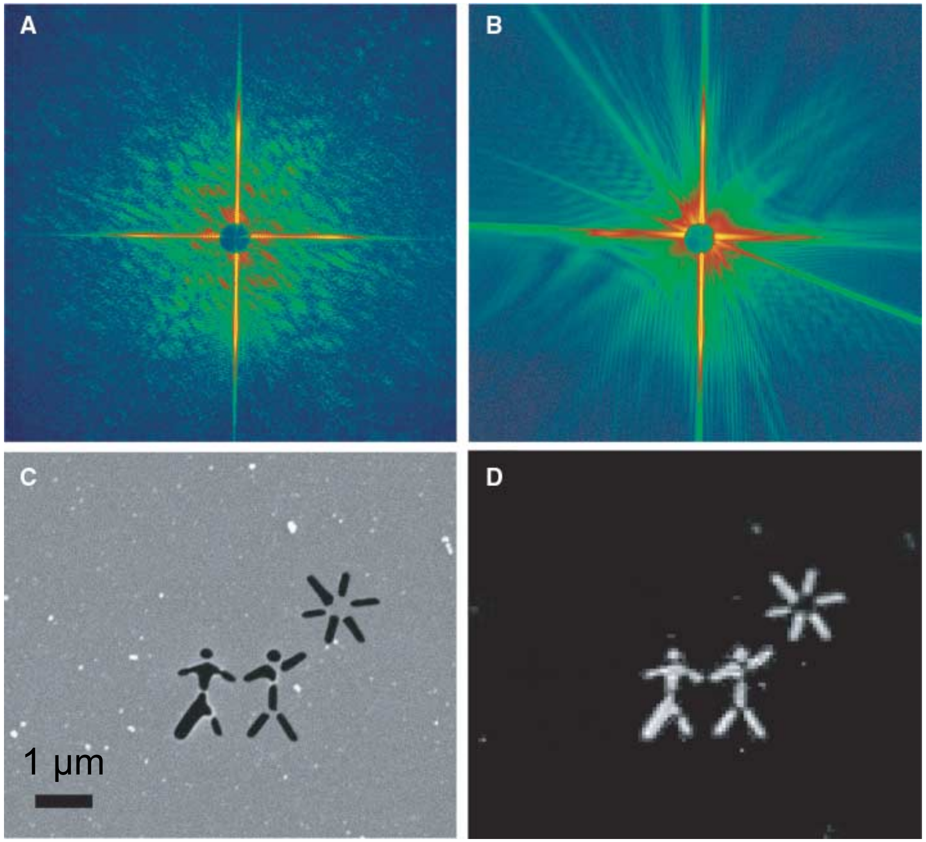
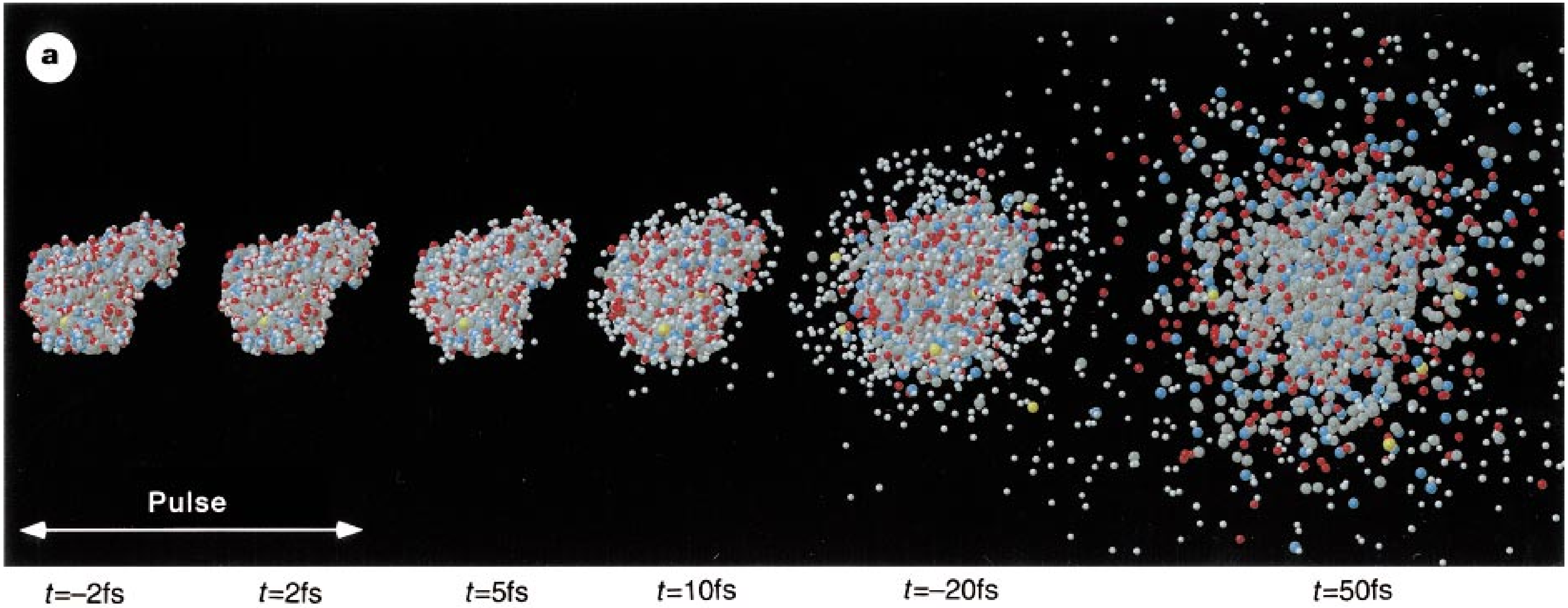
Free-electron laser

- Another major bottleneck in x-ray crystallography: crystallization
- Unprecedented high x-ray fluence from FEL: single molecules and nano-sized crystals
- The phase problem remains largely unsolved.



Chapman *et al.*, *Nature Phys.* **2**, 839 (2006)
Picture taken from Gaffney & Chapman, *Science* **316**, 1444 (2007)

Radiation damage



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

> *Diffraction-before-destruction*: molecular Coulomb explosion suppressed by using ultrafast x-ray FEL pulses within femtosecond timescales

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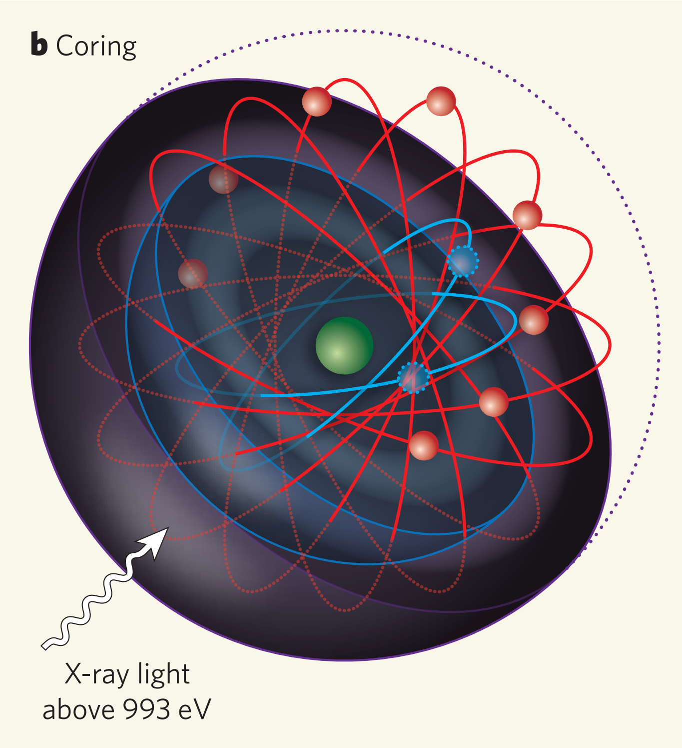
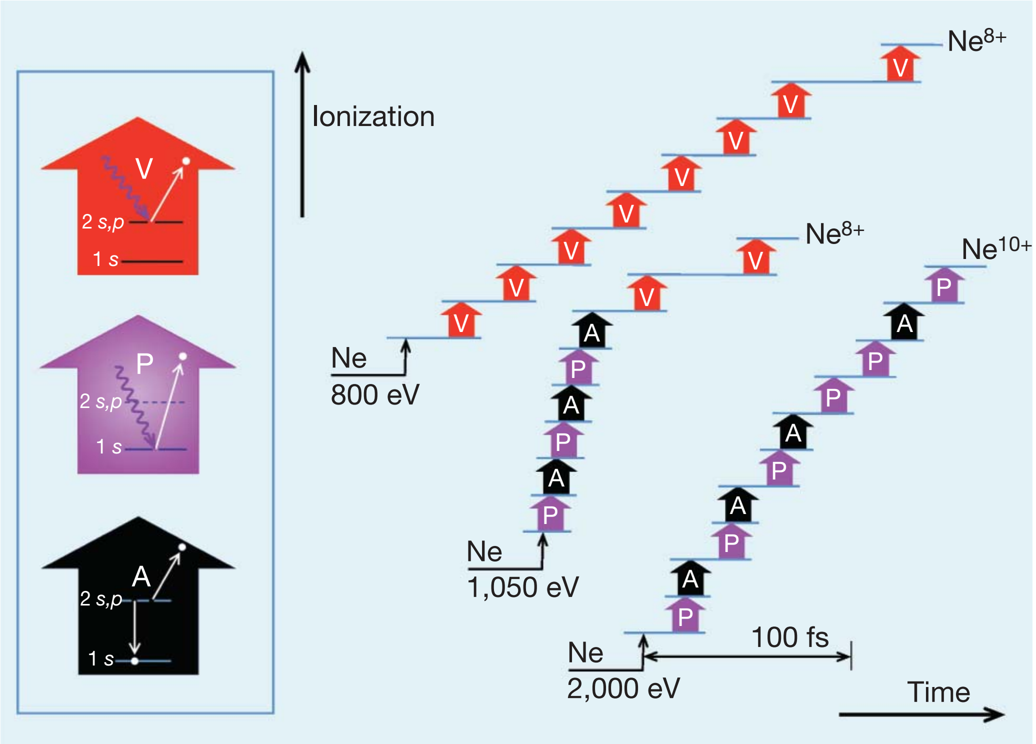
Electronic damage during FEL pulses



Picture taken from *Nature* **466**, 35 (2010)

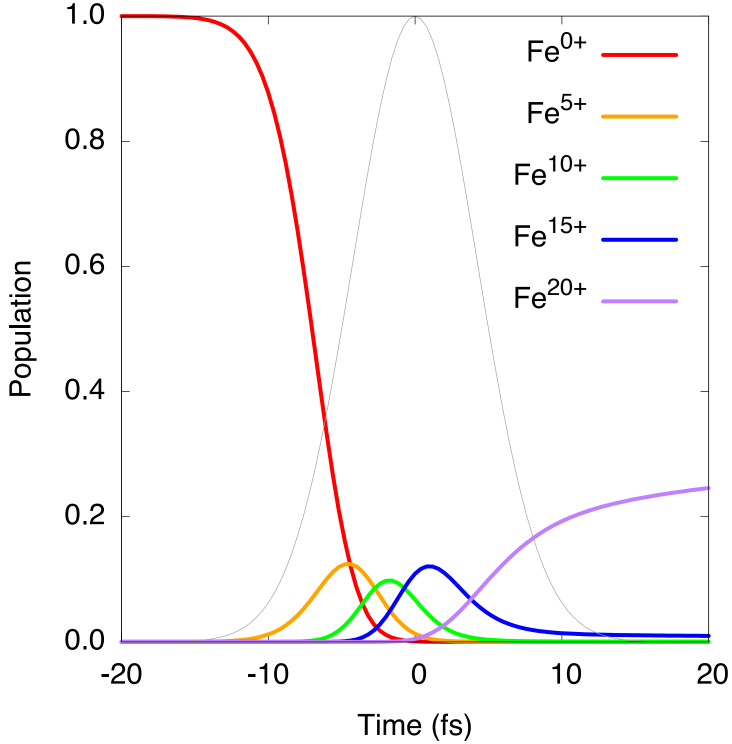


Young *et al.*, *Nature* **466**, 56 (2010)

- *Diffraction-during-ionization*: electronic radiation damage is unavoidable.
- Good agreement between theoretical model and LCLS experiments

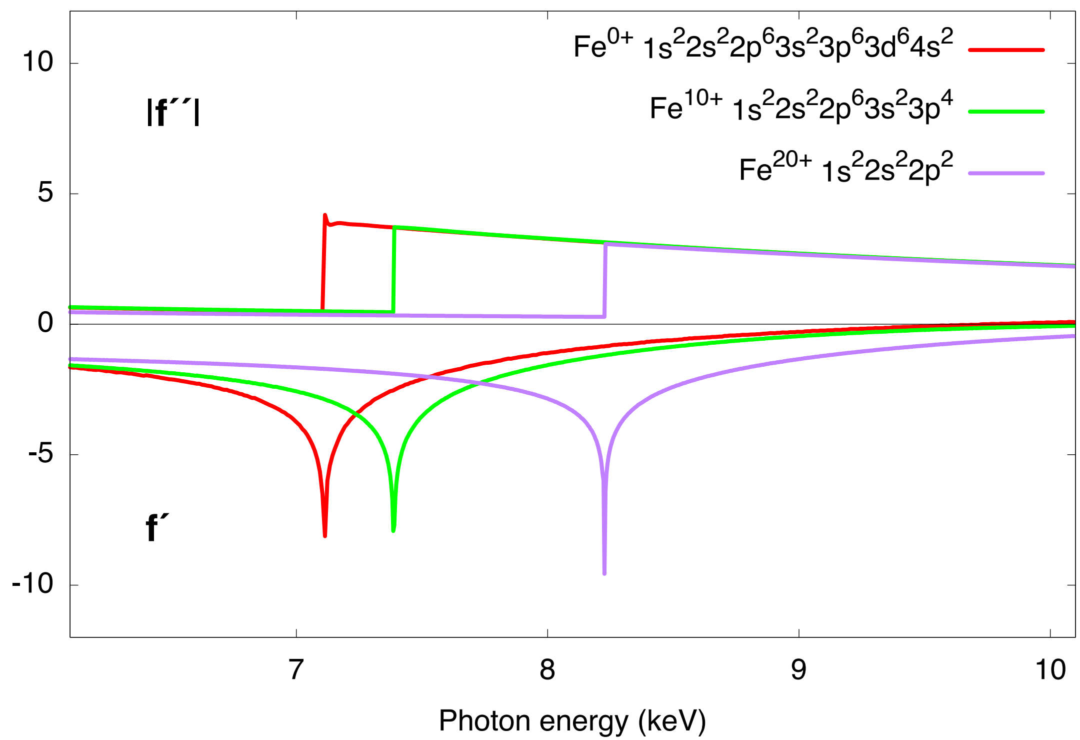
Electronic damage to heavy atoms

Electronic damage dynamics of Fe during an intense x-ray 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* (in press)

Speculation of MAD at FEL

- Heavy atoms as anomalous scatters will be more ionized than other atoms during intense x-ray pulses.
- Anomalous scattering will be changed when heavy atoms are ionized.
- Stochastic electronic damage to heavy atoms would destroy coherent scattering signals in nanocrystals...
- MAD would not be applicable for phasing at high x-ray intensity...?

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

Scattering intensity including elec. damage

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

$$I = (I_1, I_2, \cdots I_{N_H})$$

$$P_I(t) = \prod_{j=1}^{N_H} P_{I_j}(t)$$

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

- 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* (in press)

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Generalized Karle-Hendrickson equation

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

3 unknowns at every single **Q**: $\left|F_P^0\right|, \; \left|F_H^0\right|, \Delta\phi^0 (= \phi_P^0 - \phi_H^0)$

$$a(\omega) = \frac{1}{\{f_H^0\}^2} \sum_{I_H} \bar{P}_{I_H} \left|f_{I_H}(\omega)\right|^2 \qquad \tilde{a}(\omega) = \frac{1}{\{f_H^0\}^2} \int_{-\infty}^{\infty} dt\, g(t) \left|\tilde{f}_H(\omega, t)\right|^2$$

$$b(\omega) = \frac{2}{f_H^0} \sum_{I_H} \bar{P}_{I_H} \left\{ f_{I_H}^0 + f_{I_H}'(\omega) \right\} \qquad c(\omega) = \frac{2}{f_H^0} \sum_{I_H} \bar{P}_{I_H} f_{I_H}''(\omega)$$

How to obtain those MAD coefficients including elec. damage dynamics?

Son, Chapman & Santra, *PRL* (in press)

XATOM: x-ray and atomic physics toolkit

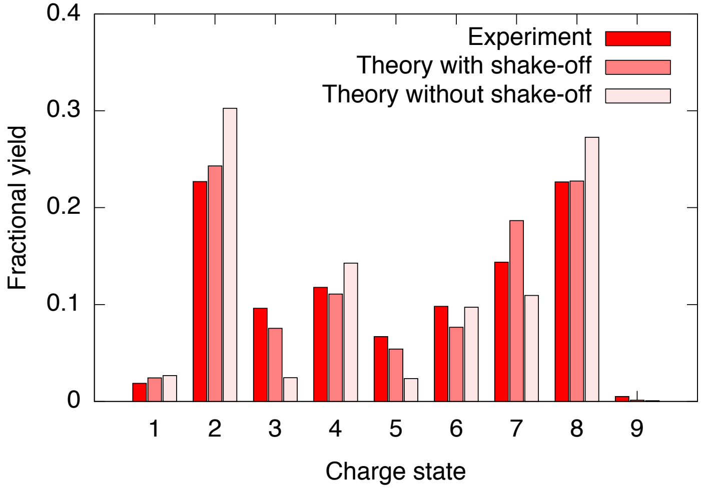
- X-ray–induced atomic processes for any element and any configuration
  - photoionization cross section $$\sigma_{\mathrm{P}}(i,\omega) = \frac{4}{3}\alpha\pi^2\omega N_i \sum_{l_j=|l_i-1|}^{l_i+1} \frac{l_>}{2l_i+1} \left| \int_0^\infty P_{n_i l_i}(r) P_{\varepsilon l_j}(r)\, r\, dr \right|^2$$
  - Auger / Coster-Kronig decay rate $$\Gamma_{\mathrm{A}}(i,jj') = \pi \frac{N_i^{\mathrm{H}} N_{jj'}}{2l_i+1} \sum_{L=|l_j-l_{j'}|}^{l_j+l_{j'}} \sum_{S=0}^{1} \sum_{l_{i'}} (2L+1)(2S+1)|M_{LS}(j,j',i,i')|^2$$
  - fluorescence rate $$\Gamma_{\mathrm{F}}(i,j) = \frac{4}{3}\alpha^3 (I_i - I_j)^3 \frac{N_i^{\mathrm{H}} N_j}{4l_j+2} \cdot \frac{l_>}{2l_i+1} \left| \int_0^\infty P_{n_i l_i}(r) P_{n_j l_j}(r)\, r\, dr \right|^2$$
  - coherent x-ray scattering form factor $$f^0(\mathbf{Q}) = \int \rho(\mathbf{r})\, e^{i\mathbf{Q}\cdot\mathbf{r}}\, d^3r$$
  - shake-off branching ratio $$p_{\mathrm{SO}}(i;I,I') = 1 - \left| \int_0^\infty P_{n_i l_i}(r;I) P_{n_i l_i}(r;I')\, dr \right|^2$$
  - **dispersion correction for coherent x-ray scattering form factor**
- Rate equation model to simulate electronic damage dynamics

$$\frac{d}{dt}P_I(t) = \sum_{I' \neq I}^{\text{all config.}} \left[\Gamma_{I'\to I} P_{I'}(t) - \Gamma_{I\to I'} P_I(t)\right]$$

Son, Young & Santra, *PRA* **83**, 033402 (2011)

XATOM: examples of FEL sciences

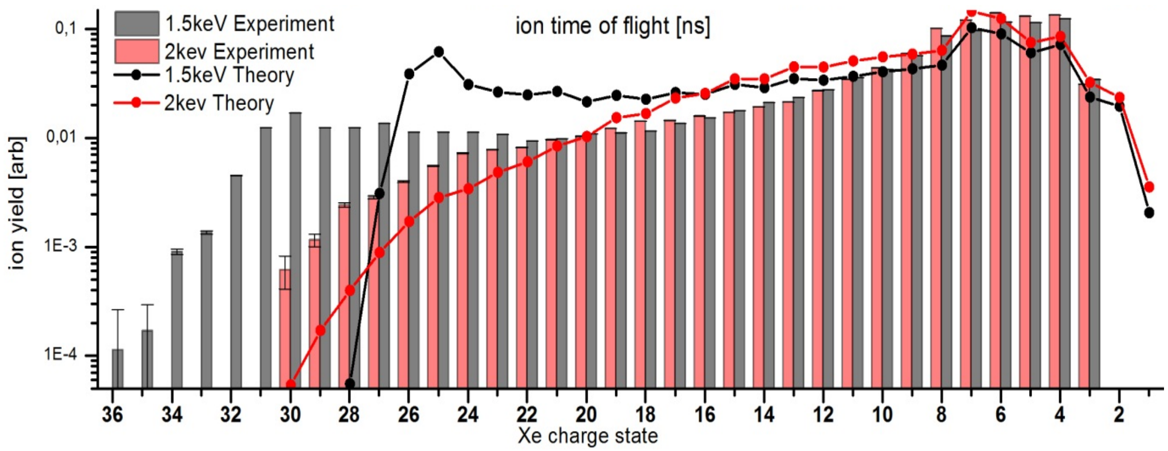
Ne $1s^2 2s^2 2p^6$
N of config. = 63
@ 1110 eV (1.27 mJ)



Doumy *et al.*, *PRL* **106**, 083002 (2011)

Collaboration with Ohio State Univ. and Argonne National Lab.

Xe $1s^2 2s^2 2p^6 3s^2 3p^6 3d^{10} 4s^2 4p^6 4d^{10} 5s^2 5p^6$
N of config. = 1,120,581
@ 1500 / 2000 eV (2.5 mJ)

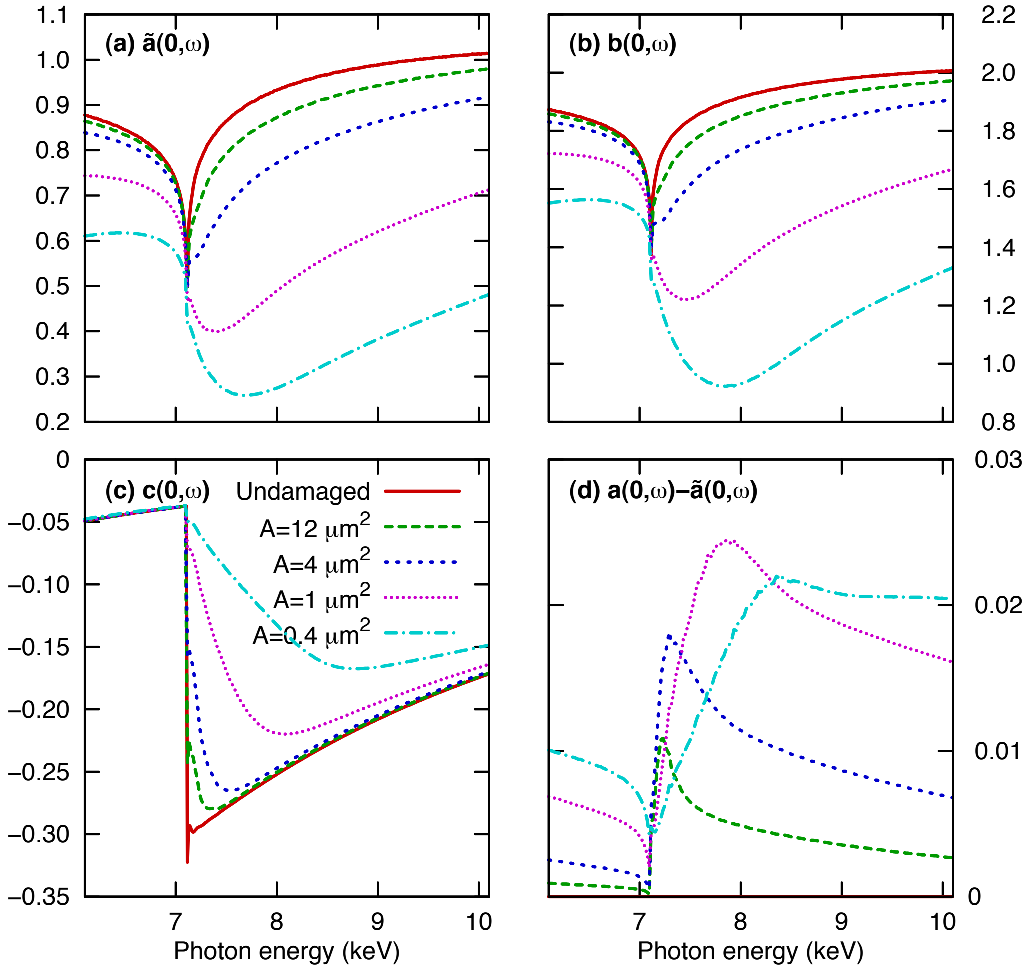


Rudek *et al.* (to be submitted)

Collaboration with Max Planck Advanced Study Group at CFEL

Calculations of MAD coefficients

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



$$
\begin{aligned}
&\left|F_P^0\right|^2 + \left|F_H^0\right|^2 \tilde{a}(\omega) \\
&\quad + \left|F_P^0\right|\left|F_H^0\right| b(\omega)\cos\Delta\phi^0 \\
&\quad + \left|F_P^0\right|\left|F_H^0\right| c(\omega)\sin\Delta\phi^0 \\
&\quad + N_H \left|f_H^0\right|^2 \left\{a(\omega) - \tilde{a}(\omega)\right\}
\end{aligned}
$$

$$a(\omega) = \frac{1}{\{f_H^0\}^2} \sum_{I_H} \bar{P}_{I_H} \left|f_{I_H}(\omega)\right|^2$$

$$\tilde{a}(\omega) = \frac{1}{\{f_H^0\}^2} \int_{-\infty}^{\infty} dt\, g(t) \left|\tilde{f}_H(\omega, t)\right|^2$$

$$b(\omega) = \frac{2}{f_H^0} \sum_{I_H} \bar{P}_{I_H} \left\{f_{I_H}^0 + f'_{I_H}(\omega)\right\}$$

$$c(\omega) = \frac{2}{f_H^0} \sum_{I_H} \bar{P}_{I_H} f''_{I_H}(\omega)$$

Son, Chapman & Santra, *PRL* (in press)

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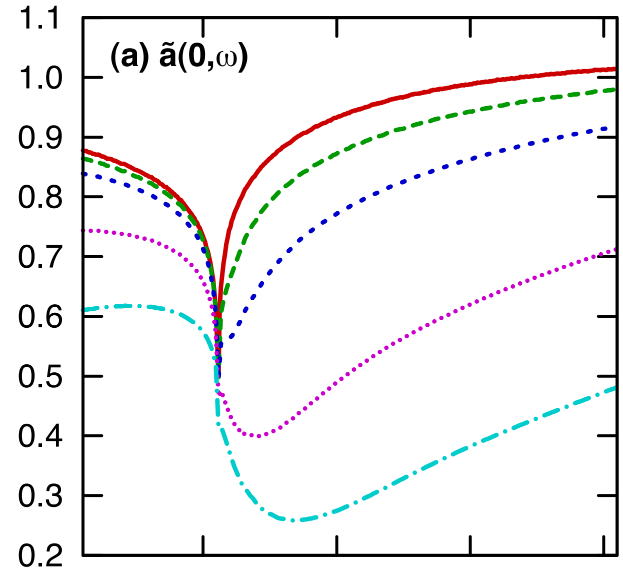
MAD phasing at high x-ray intensity

- Bleaching effect: MAD coefficients $\tilde{a}$ and b are dramatically bleached out and their minimum is deepened and broadened.
- The contrast in $\tilde{a}$ and b becomes enhanced; the contrast in c is reduced but not completely eliminated. $\rightarrow$ MAD can be done.
- Broadening of the edge
  $\rightarrow$ less precision of ω
- Bleaching effect provides an alternative phasing method similar to SIR (single isomorphic replacement) or RIP (radiation-damage induced phasing).



Son, Chapman & Santra, *PRL* (in press)

MAD phasing for nanocrystals

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

$$|F_H^0|^2 \tilde{a}(\omega) = \int_{-\infty}^{\infty} dt\, g(t) \left| \tilde{f}_H(\omega, t) \sum_{j=1}^{N_H} e^{i\mathbf{Q}\cdot\mathbf{R}_j} \right|^2$$

dynamical form factor:

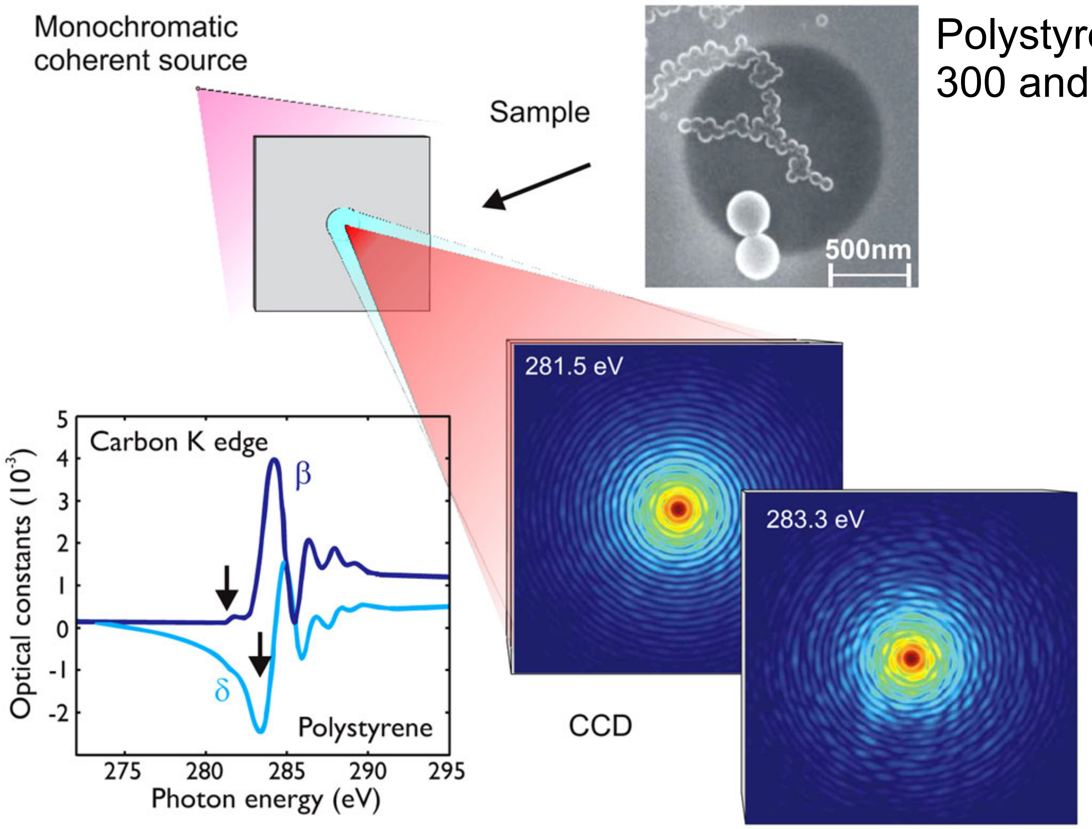
$$\tilde{f}_H(\omega, t) = \sum_{I_H} P_{I_H}(t) f_{I_H}(\omega)$$

- $\left|F_H^0\right|^2 \tilde{a}(\omega)$ implies that all heavy atoms are described by the same dynamical form factor → *Bragg peaks*
- $N_H \left|f_H^0\right|^2 \{a(\omega) - \tilde{a}(\omega)\}$ represents fluctuations from all different configurations induced by electronic damage → *diffuse background*

Son, Chapman & Santra, *PRL* (in press)

MAD with light atoms

- Extension of MAD to non-periodic nano-structures
- MAD near the carbon *K*-shell edge

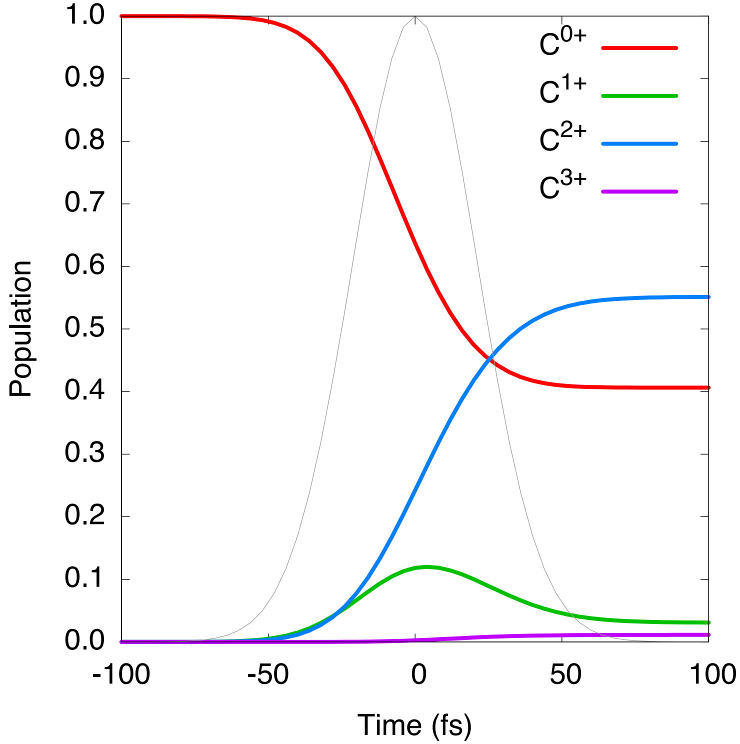


Polystyrene spheres, 300 and 90 nm in size

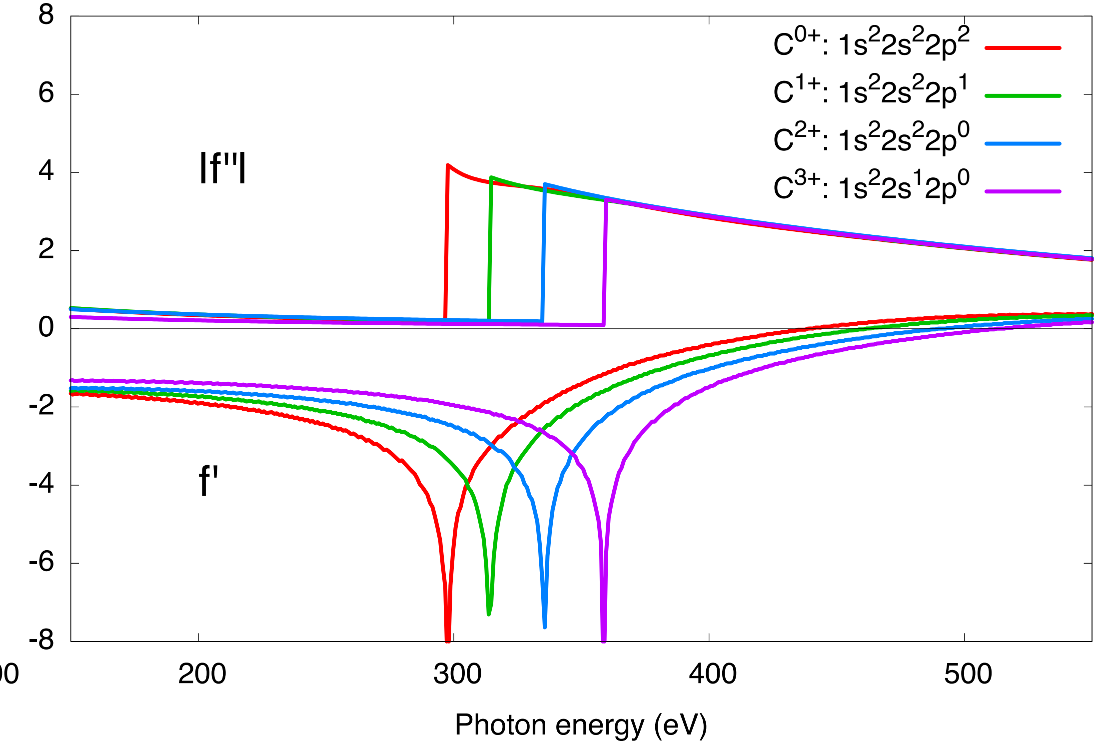
Scherz *et al.*, *PRL* **101**, 076101 (2008)

MAD at FLASH

Electronic damage dynamics of C during an intense x-ray pulse



Dispersion corrections of atomic form factors of C and its ions



300 eV, 1×10^{10} photons/μm^2
50 fs FWHM

Conclusion

- MAD phasing method in extreme conditions of ionizing radiations
- Combination of detailed electronic response at the atomic level and molecular imaging during intense x-ray pulses
- Existence of a generalized Karle-Hendrickson equation for the MAD method at high intensity
- Bleaching effect on the scattering strength to be beneficial to the phasing method
- A new opportunity for solving the phase problem in single-shot imaging of single molecules, nano-sized crystals, and nano-sized objects with FELs

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Zoltan Jurek
Nikita Medvedev
Robert Thiele

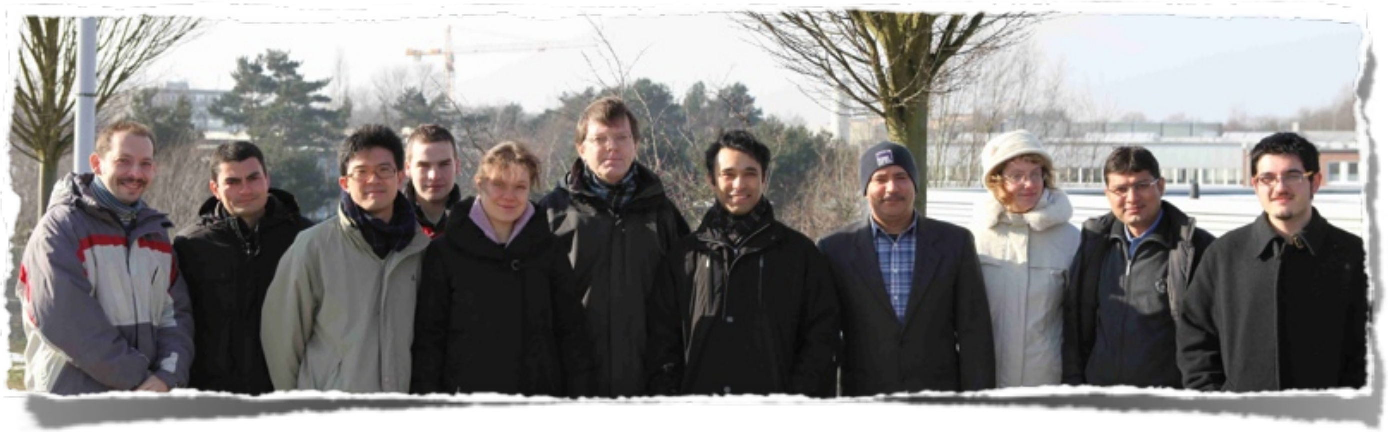

photo taken in early 2011

> **CFEL Coherent Imaging Division at DESY**

Henry N. Chapman, Thomas White, Andrew Aquila

Take-home message

FEL goes MAD.