Happy phasing with electronic radiation damage at high x-ray intensity

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X-ray Radiation Damage to Biological Crystalline Samples
DESY, Hamburg, Germany / April 10–12, 2014

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

Collaboration

CFEL Theory Division

Robin Santra

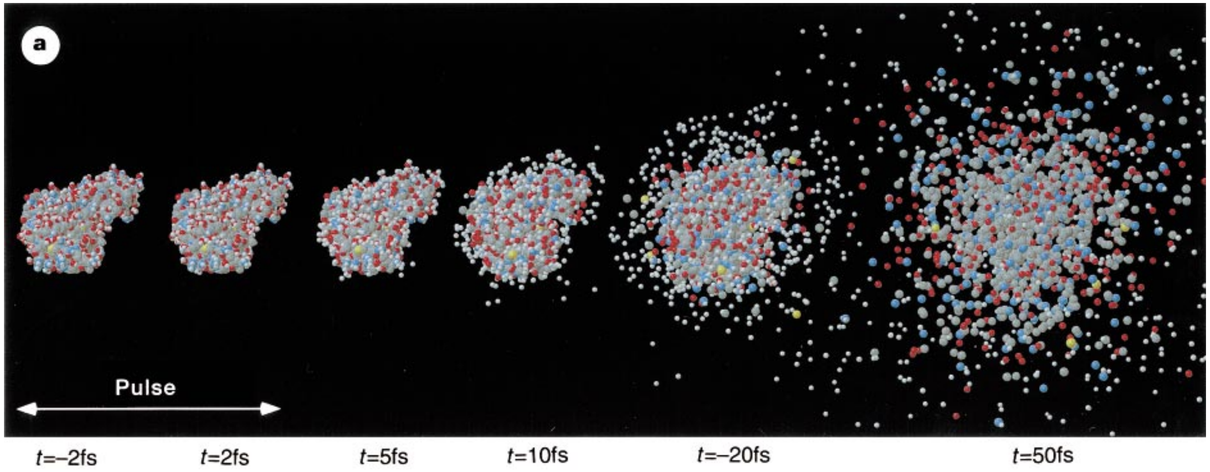
CFEL Coherent Imaging Division

Henry Chapman

Lorenzo Galli

Radiation damage by XFEL

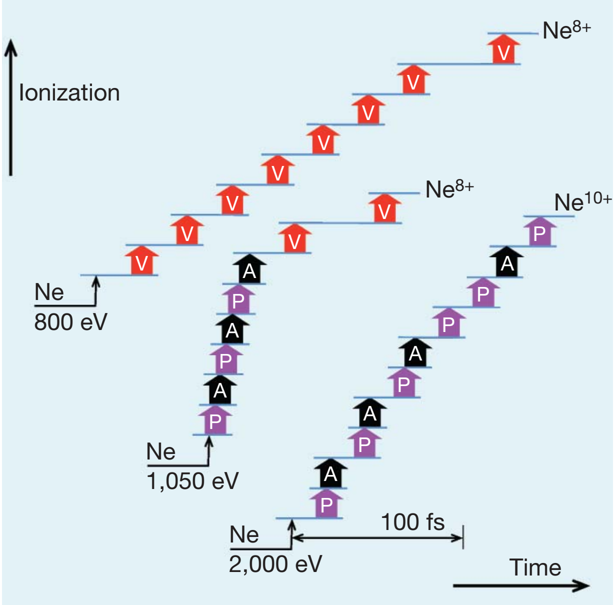
Coulomb explosion (nuclear damage)



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

Diffraction before destruction

Electronic damage



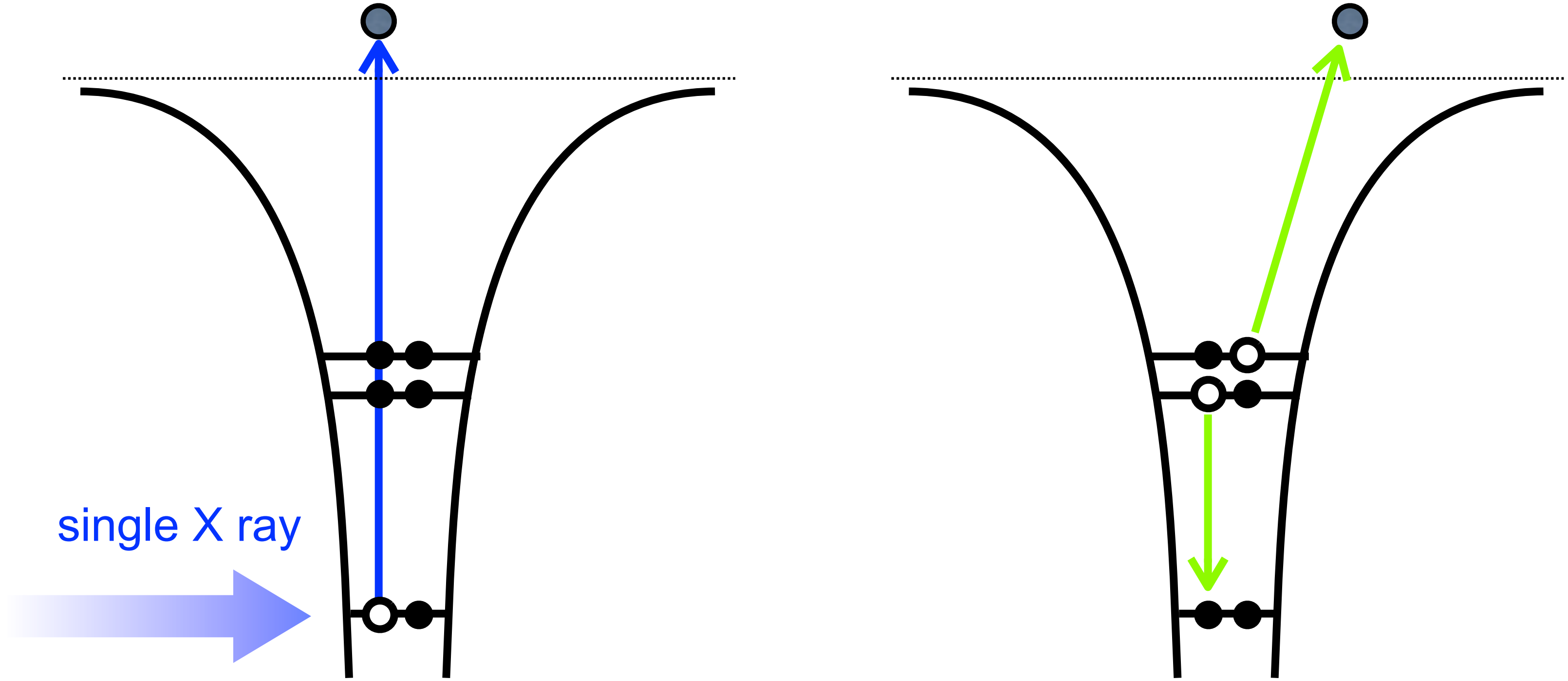
Young *et al.*, *Nature* **466**, 56 (2010).

Diffraction during ionization

Electronic radiation damage

- Unavoidable at high x-ray intensity (time scale: ~subfemtoseconds)
- Can we reduce electronic radiation damage?
  - frustrated ionization: *higher* intensity, *less* ionization
  - seeded XFEL pulse: *narrower* bandwidth, *less* ionization
- Can we take benefits from electronic radiation damage?
  - understanding of ionization dynamics mechanism
  - turn x-ray ionization into an advantage for phasing

Photoabsorption by X-rays



photoionization

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

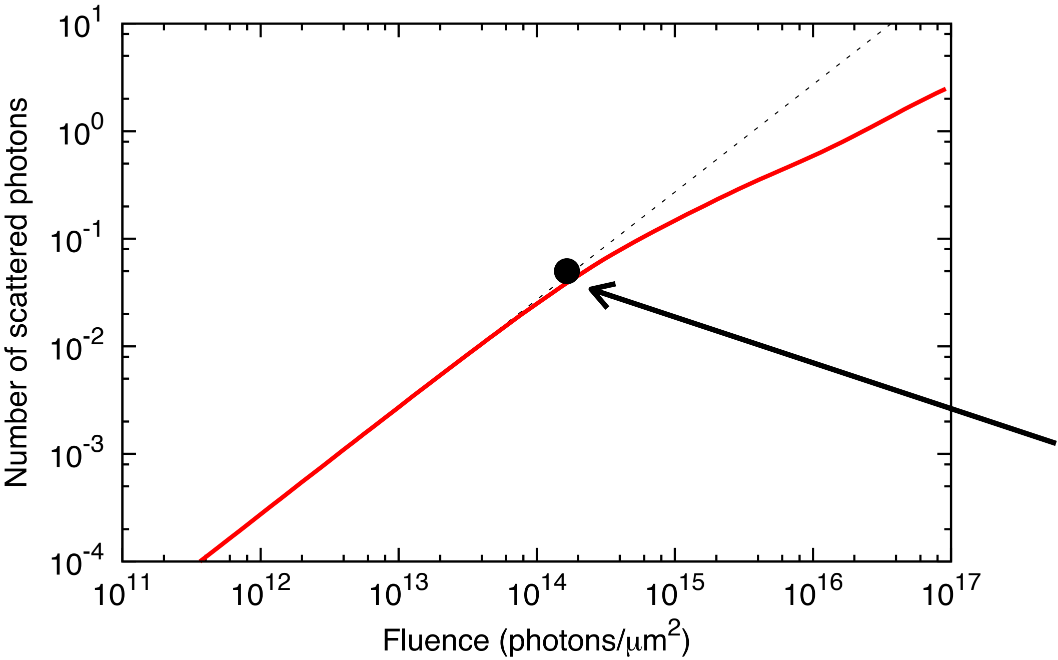
Auger decay

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

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

Beyond saturation in high-intensity regime

- Fluence (photons/unit area) to saturate one-photon absorption



probability = $\sigma_{abs} \times F$

$\sigma_{abs} \times F_{sat} = 1$

C @ 8 keV

$\sigma_{abs} = 0.084$ kbarns

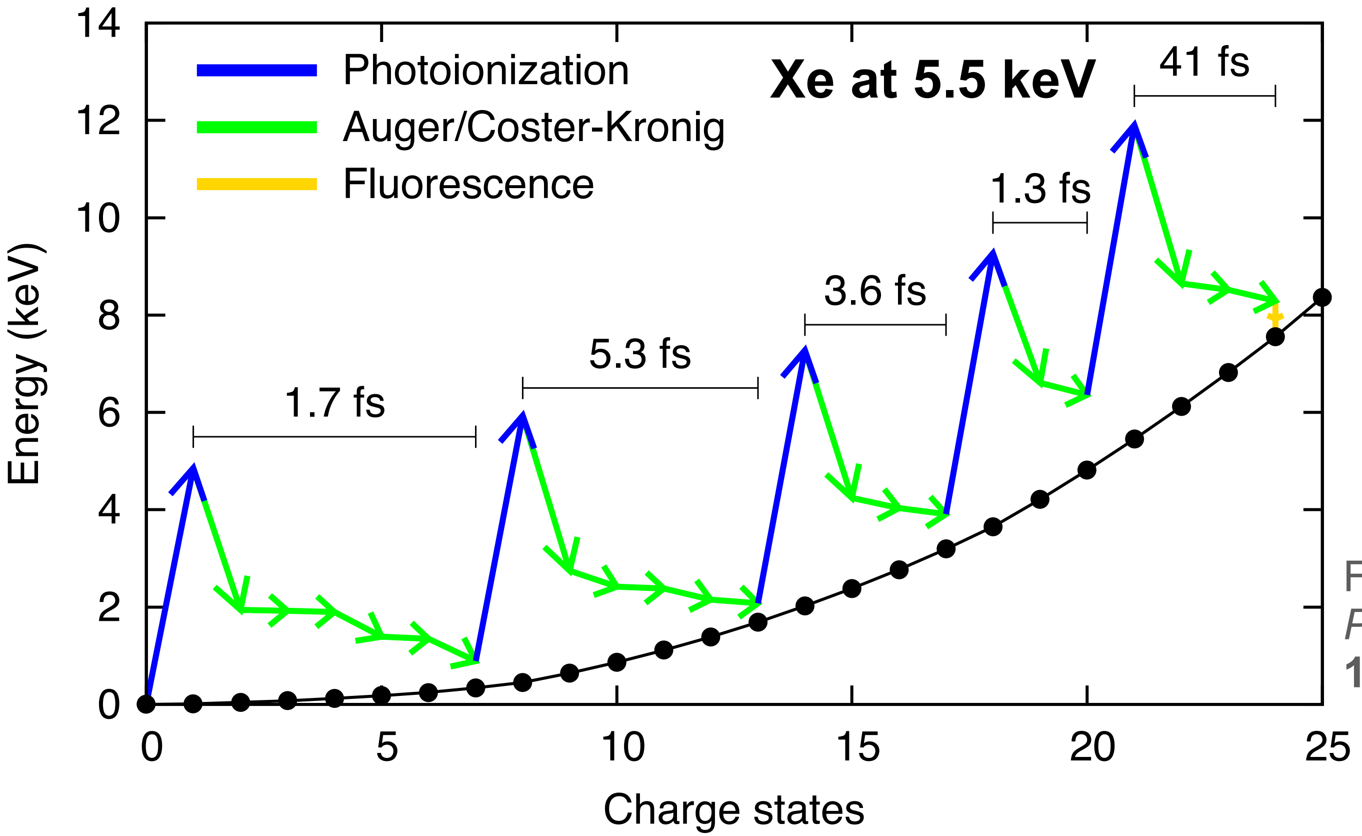
⬇

$F_{sat} = 1.2\times10^{14}$ ph/μm^2

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

- High x-ray intensity beyond one-photon absorption saturation
  - Synchrotron (10^4~10^6 ph/μm^2) ➔ at most one photon absorbed
  - XFEL (10^{10} ph/μm^2 or higher) ➔ at least one photon absorbed

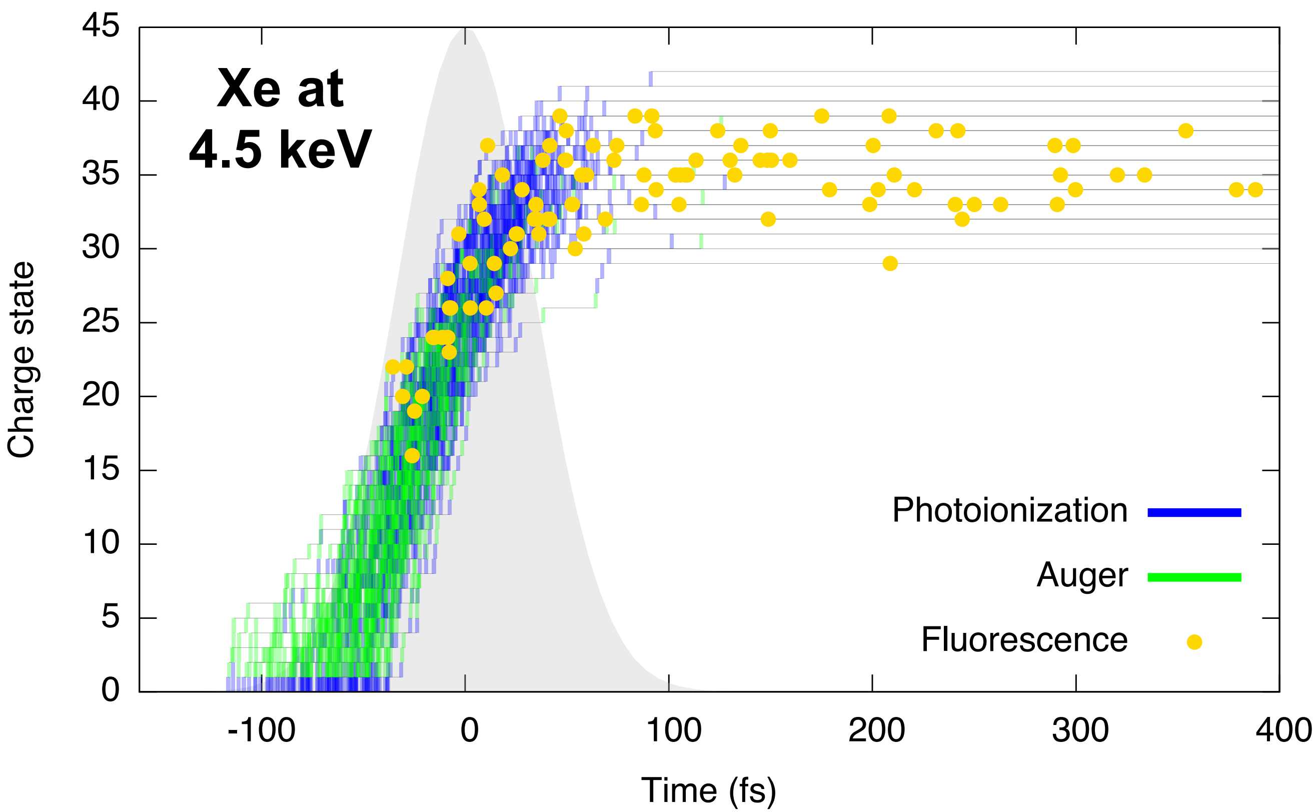
Sequential multiphoton multiple ionization



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

- described by sequences of photoionization, Auger, and fluorescence
- heavy atoms at higher photon energies ➔ relevant for phasing

Complex inner-shell ionization dynamics

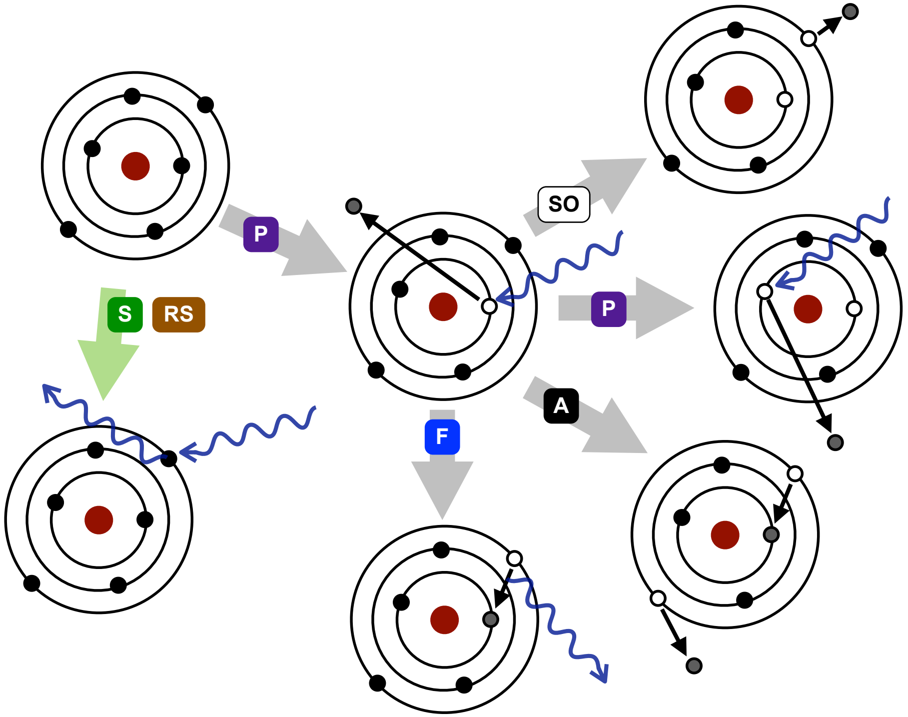


Son & Santra,
PRA **85**,
063415 (2012).

- more than one million electronic states calculated
- more than 40 million x-ray-induced processes calculated
- conventional quantum chemistry codes not applicable

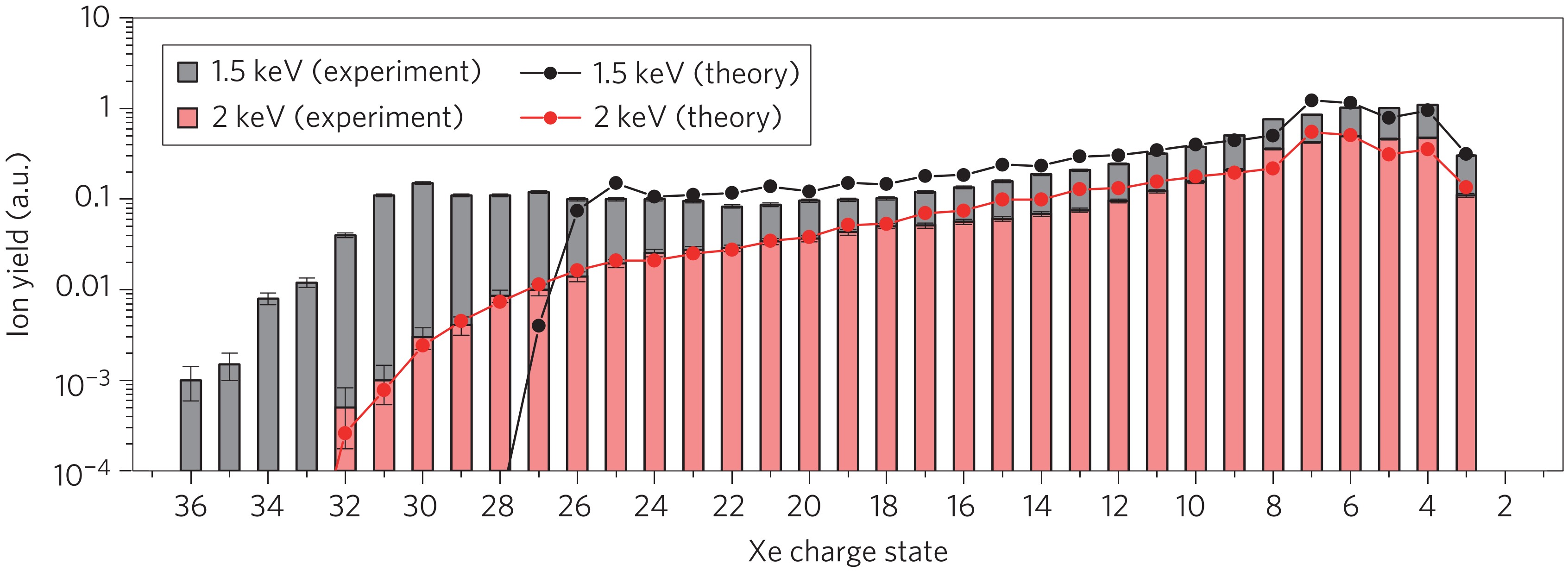
XATOM: all about x-ray atomic physics

- Computer program suite to describe dynamical behaviors of atoms interacting with XFEL pulses
- Use the Hartree-Fock-Slater model
- Calculate all cross sections and rates of x-ray-induced processes for any given element / any given charge state / any given electronic configuration
- Solve coupled rate equations to simulate ionization dynamics
- Calculate ion / electron / photon spectra



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

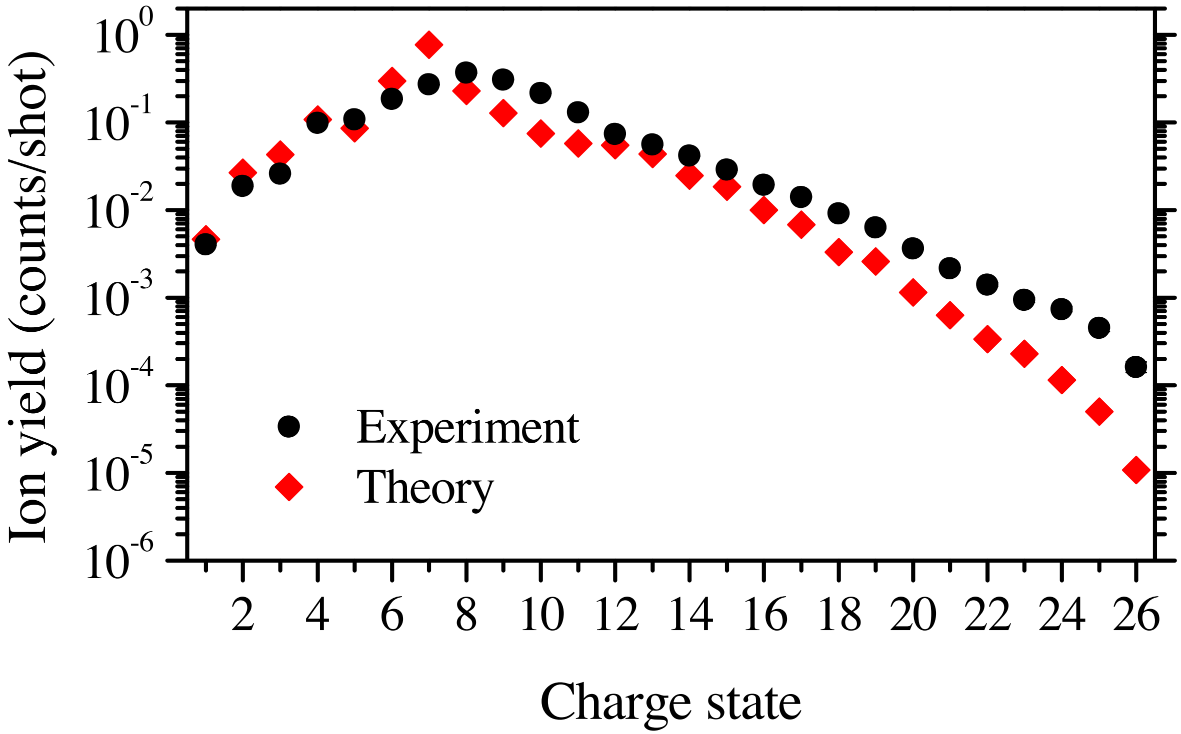
Xe at LCLS



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

- 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
- Resonance-enabled ionization: can be suppressed by narrow bandwidths

Xe at SACLA



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

- At 5.5 keV: deep inner-shell (*L*-shell) ionization dynamics
- Good agreement between experiment and theory
- Theoretical challenges: >20-million config. with >2-billion processes

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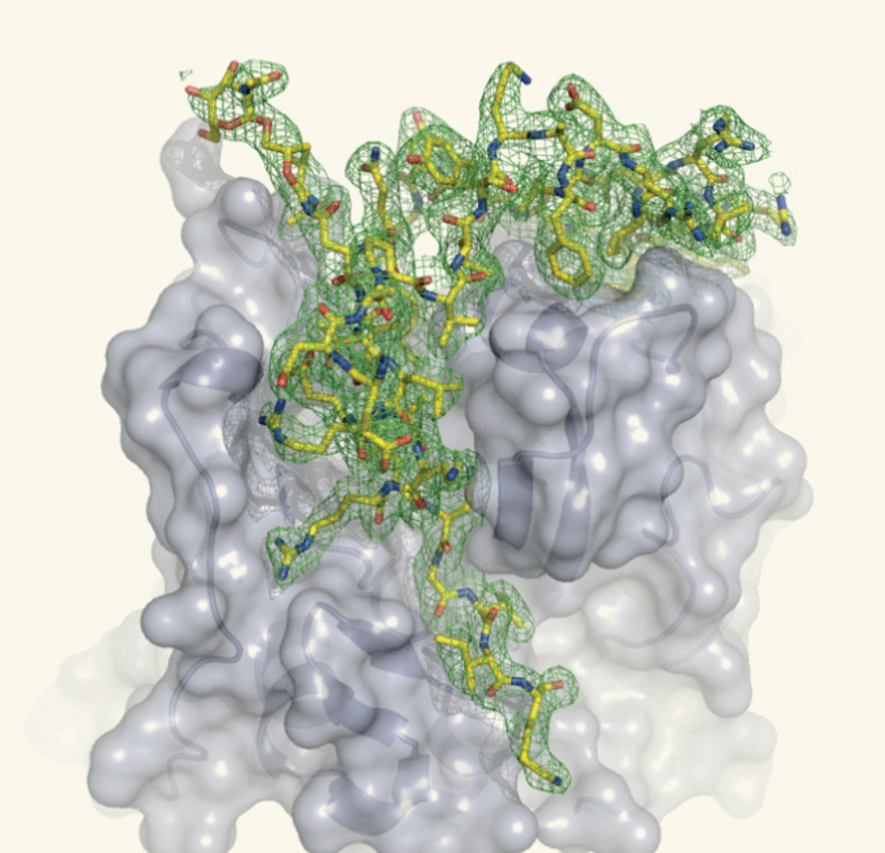
Phasing for XFEL experiments

- Mainly solved by molecular replacement
  e.g.) Redecke *et al.*, *Science* **339**, 227 (2013).
- SAD in the intermediate intensity regime (< the saturation fluence)
  Barends *et al.*, *Nature* **505**, 244 (2014).
- Need for *ab initio* phasing method at high x-ray intensity



Cathepsin B: The first new protein structure determined by using XFEL

Picture taken from *Nature* **505**, 620 (2014).

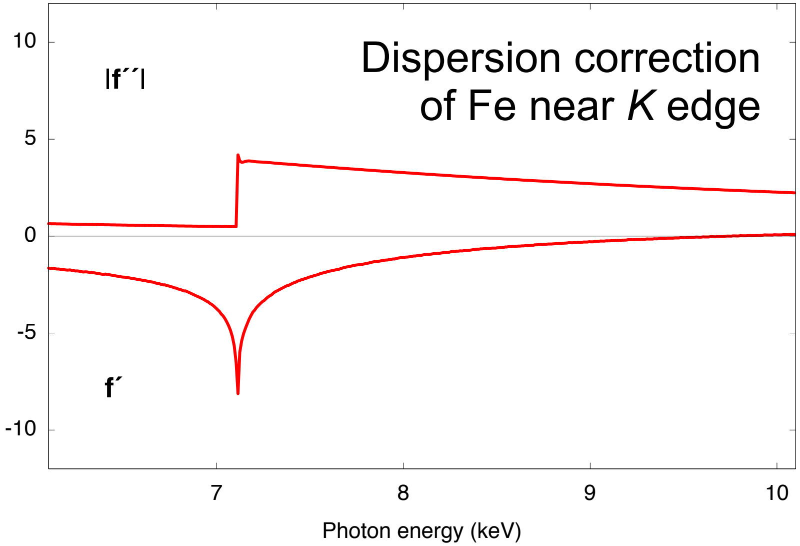
Multiwavelength Anomalous Diffraction

- 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.

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



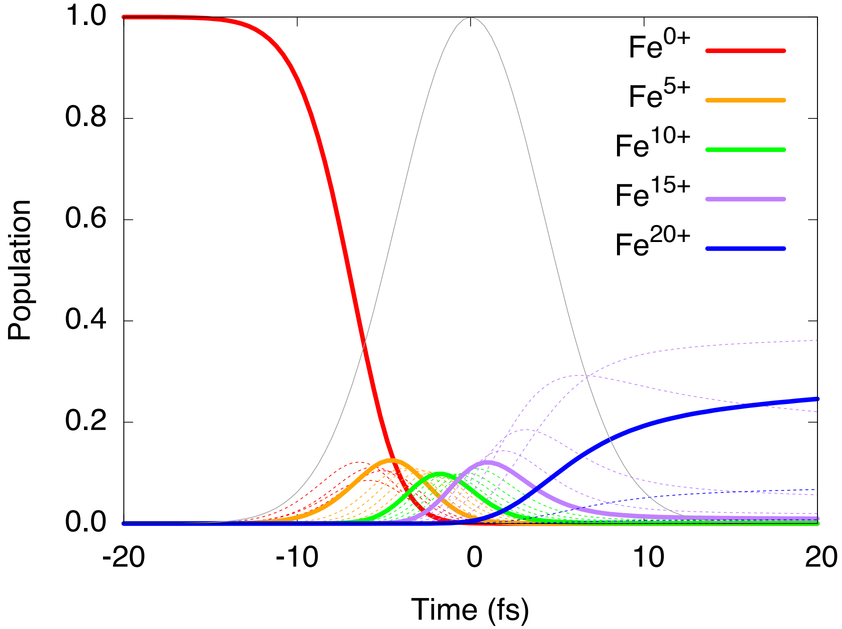
Karle-Hendrickson equation:

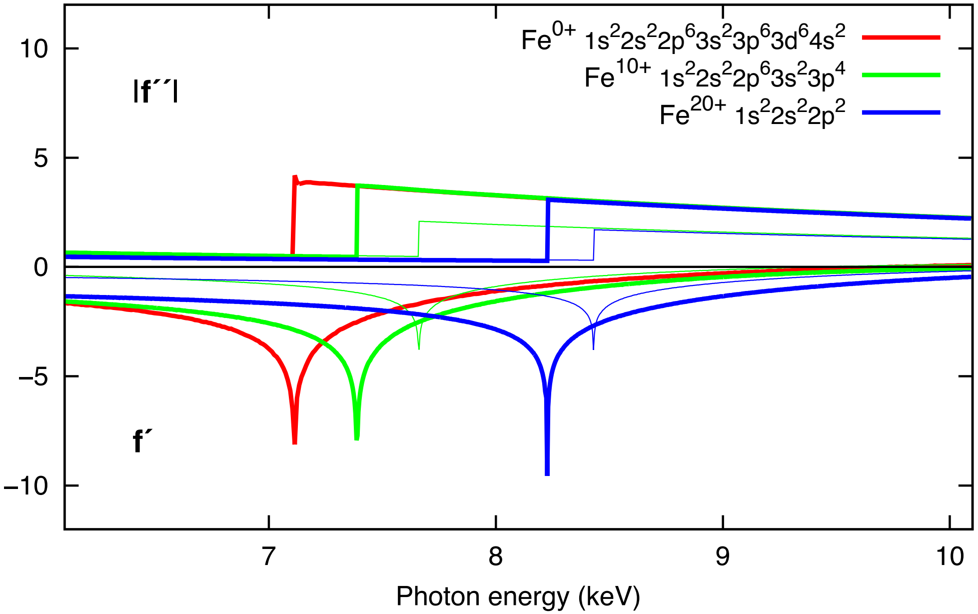
$$\begin{aligned}|F_T(\omega)|^2 &= \left|F_T^0\right|^2 + \left|F_A^0\right|^2 a(\omega) \\ &+ \left|F_T^0\right| \left|F_A^0\right| b(\omega) \cos\Delta\phi^0 \\ &+ \left|F_T^0\right| \left|F_A^0\right| c(\omega) \sin\Delta\phi^0\end{aligned}$$

Review: Hendrickson, *Science* **254**, 51 (1991).

Dynamical behavior of heavy atoms

- Saturation fluence for Fe at the edge ~ 2.4×10^{11} ph/μm^2
- Extensive electronic rearrangements
- Dramatic change of anomalous scattering for high charge states





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

Scattering intensity including ionization

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

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

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

- All changes among N_H heavy atoms in a crystal are included.
- *P*: protein, *H*: heavy atoms; only heavy atoms scatter anomalously and undergo ionization 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).

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Generalized Karle-Hendrickson equation

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

- MAD coefficients: $a(\mathbf{Q},\mathcal{F},\omega)$, $b(\mathbf{Q},\mathcal{F},\omega)$, $c(\mathbf{Q},\mathcal{F},\omega)$, and $\tilde{a}(\mathbf{Q},\mathcal{F},\omega)$

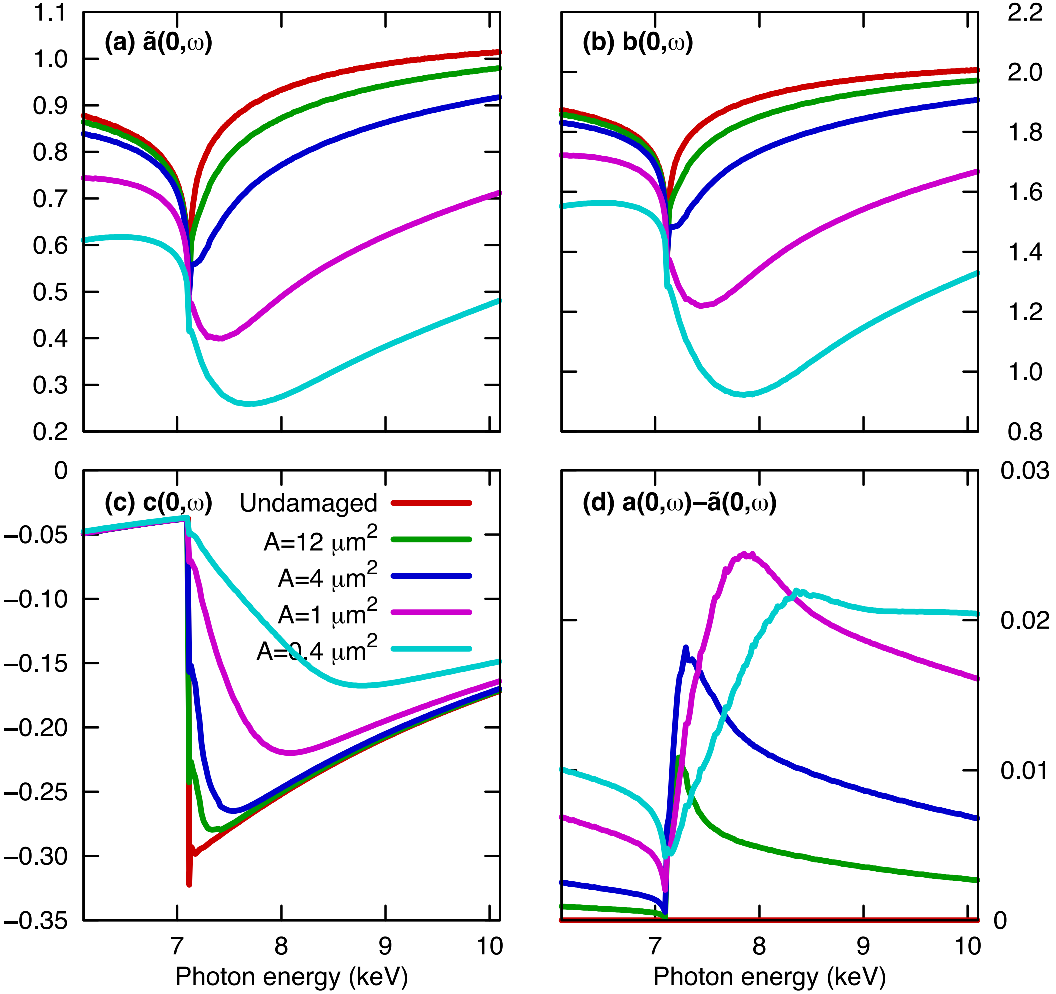
  → measured or calculated including electronic damage dynamics

- 3 unknowns: $\left|F_P^0(\mathbf{Q})\right|$, $\left|F_H^0(\mathbf{Q})\right|$, $\Delta\phi^0(\mathbf{Q})$ $\left[= \phi_P^0(\mathbf{Q}) - \phi_H^0(\mathbf{Q})\right]$

  → solvable with measurements at 3 different wavelengths.

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

MAD coefficients



- Needs time-dependent populations and form factors for all possible electronic configurations
- calculated by XATOM

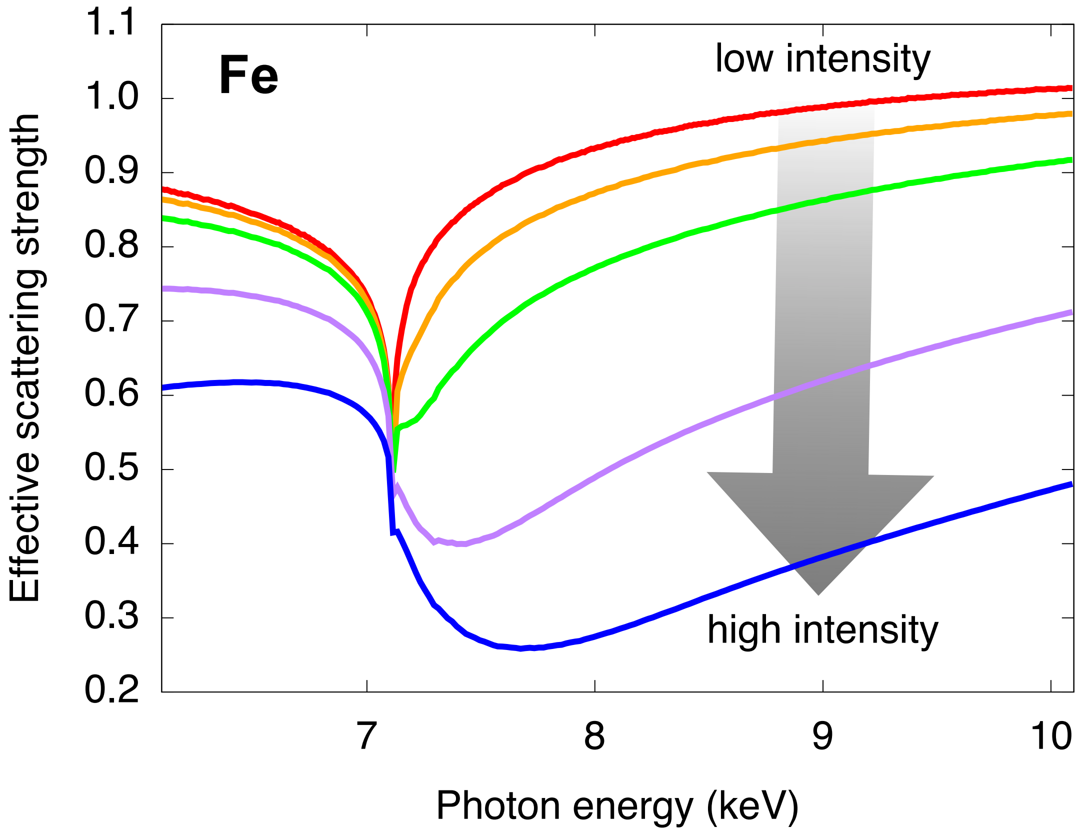
$$a(\omega) = \frac{1}{\{f_H^0\}^2} \sum_{I_H} \bar{P}_{I_H} \left|f_{I_H}(\omega)\right|^2$$

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

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

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

High-intensity MAD



- **MAD works**: enhanced contrast at different wavelengths
- bleaching effect: minimum deepened and edge broadened ➔ easy to choose wavelengths
- potential new phasing methods

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

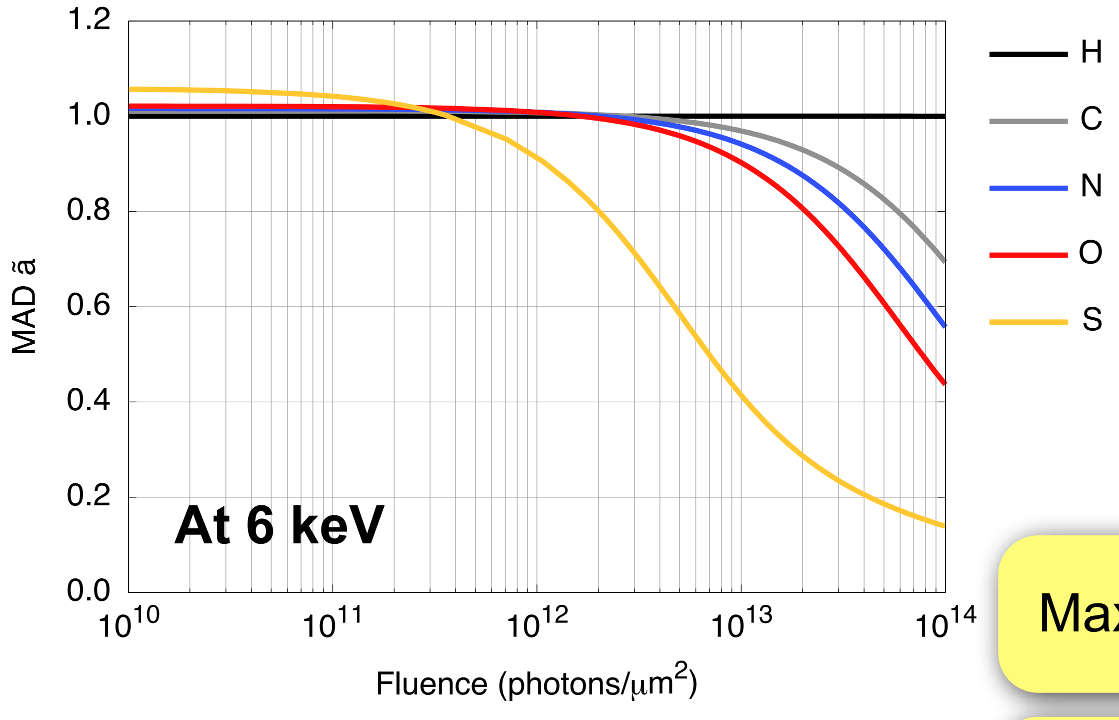
Brand-new phasing method

- **MAD** (multi-wavelength anomalous diffraction): $\Delta F_{\Delta\lambda}$
- **SAD** (single-wavelength anomalous diffraction): $\Delta F_{\pm}$
- **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

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

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

HIP: high-intensity phasing



Max Nanao's talk

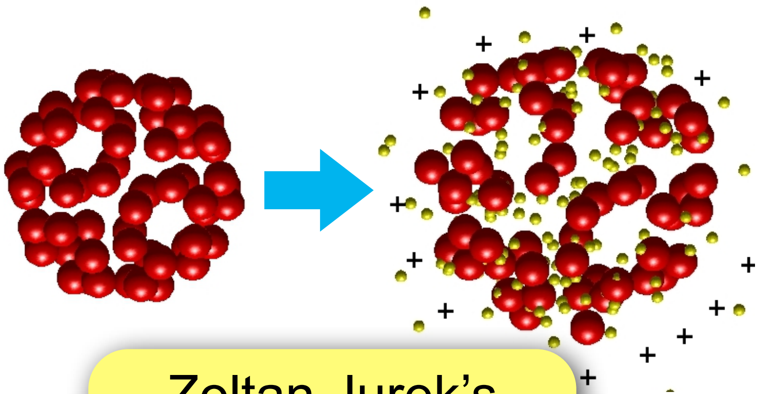
Lorenzo Galli's poster

- HIP: exclusively achievable with intense x-ray pulses
- Non-linear response / far from the edge
- Approach 1: selective ionization for heavy atoms; RIP scheme applied
- Approach 2: GKH equation applied; a multi-fluence version of MAD

Outlook: new developments

XMDYN

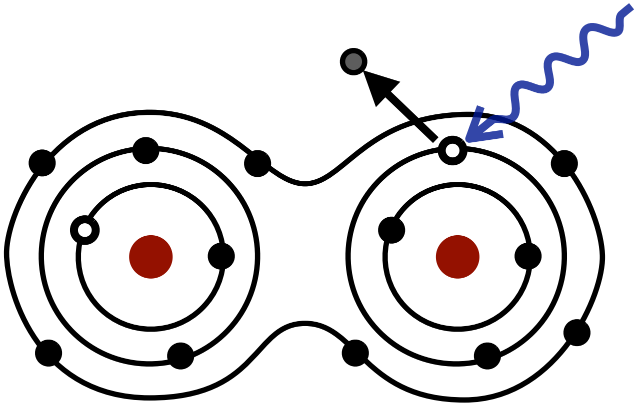
- atomic processes by XATOM
- molecular dynamics by XMDYN
- C_{60} at LCLS
- Ar cluster at SACLA



Zoltan Jurek's poster

XMOLECULE

- detailed description on molecular environment
- molecular Auger effect and charge redistribution



Conclusion

- Electronic radiation damage: multiphoton multiple ionization dynamics via sequences of one-photon processes
- XATOM provides dynamical behavior of individual atoms; tested by LCLS and SACLA experiments
- High-intensity MAD in extreme conditions of ionizing radiations
- HIP: brand-new phasing only achievable at high x-ray intensity
  - Multi-fluence AD / RIP mimicking SIR
- Novel phasing at high x-ray intensity: new opportunities for solving the phase problem in macromolecular crystallography with XFELs