Phasing with electronic radiation damage at high x-ray intensity

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

DESY

Collaboration

CFEL-DESY Theory Division

Robin Santra

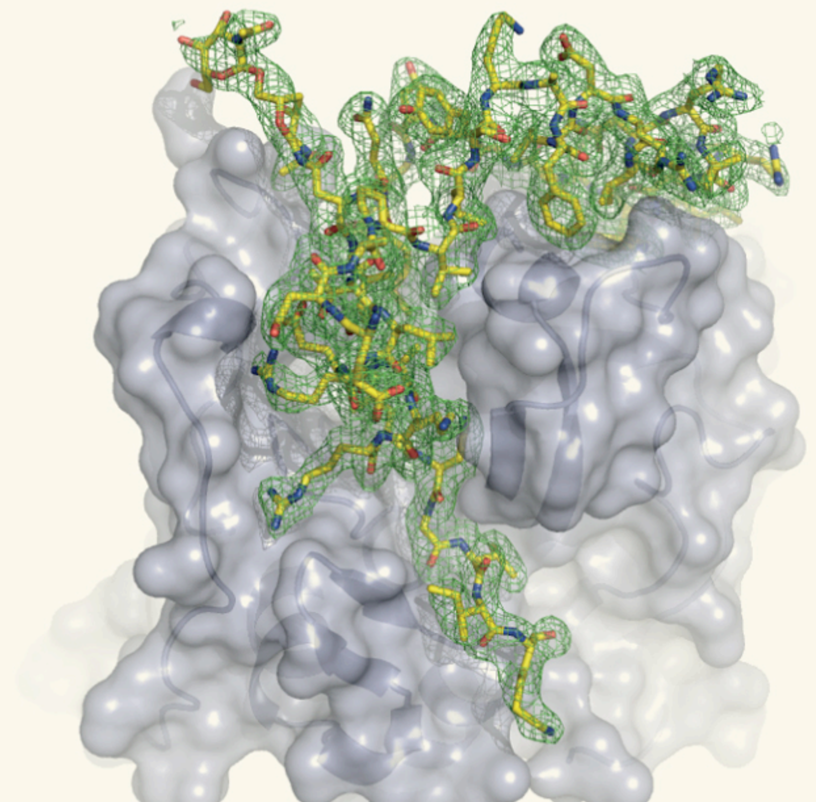
CFEL Coherent Imaging Division

Henry Chapman

Lorenzo Galli

Phasing for XFEL experiments

- Phase problem: a fundamental obstacle in obtaining a structure from x-ray diffraction
- Mainly solved by molecular replacement
  e.g.) Redecke *et al.*, *Science* **339**, 227 (2013).
- SAD in the intermediate intensity regime
  Barends *et al.*, *Nature* **505**, 244 (2014).
- Need for *ab initio* phasing method at high x-ray intensity



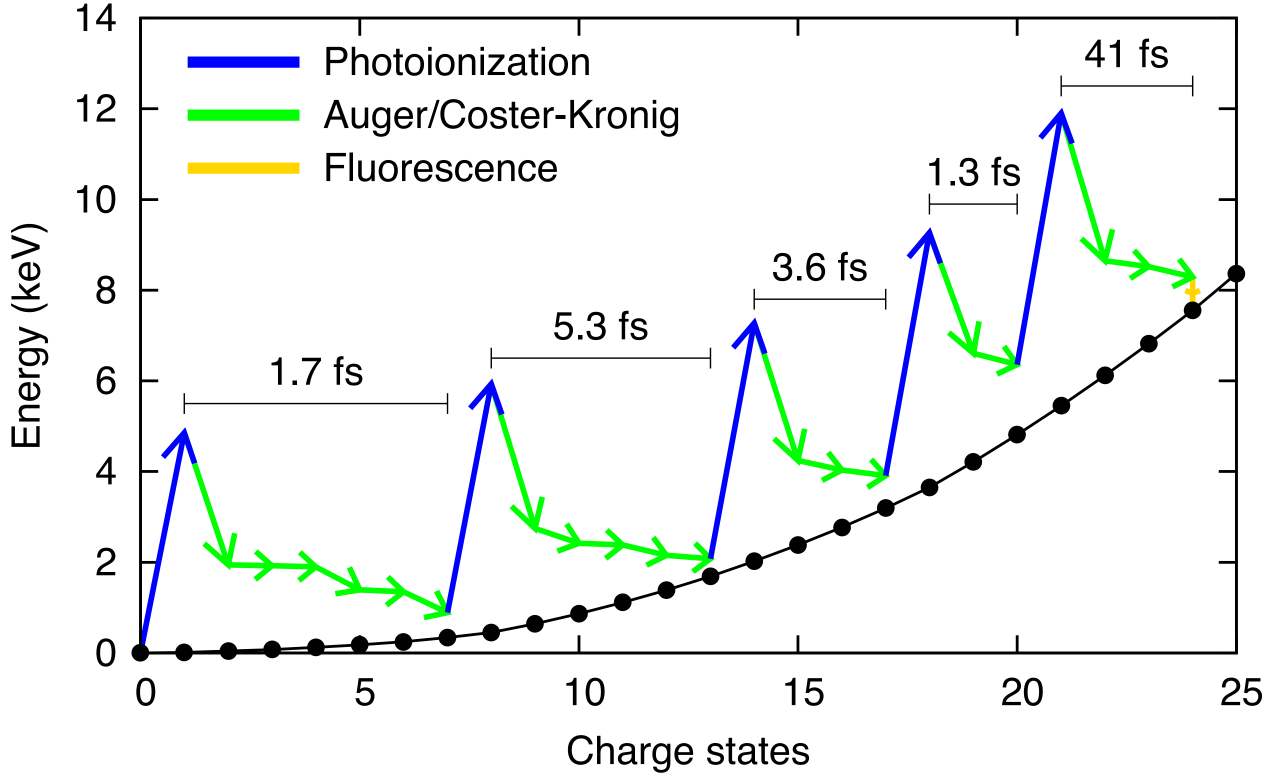
Cathepsin B: The first new protein structure determined by using XFEL

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

Electronic radiation damage

- Unavoidable at high x-ray intensity (time scale: ~femtoseconds)
- Can we reduce electronic radiation damage?
  - *much shorter* pulse duration, *less* ionization (frustrated ionization)
  - *narrower* bandwidth, *less* ionization (resonance-enabled ionization)
- Can we take benefits from electronic radiation damage?
  - understand ionization dynamics mechanism
  - turn x-ray multiple ionization into an advantage for phasing

Sequential multiphoton multiple ionization



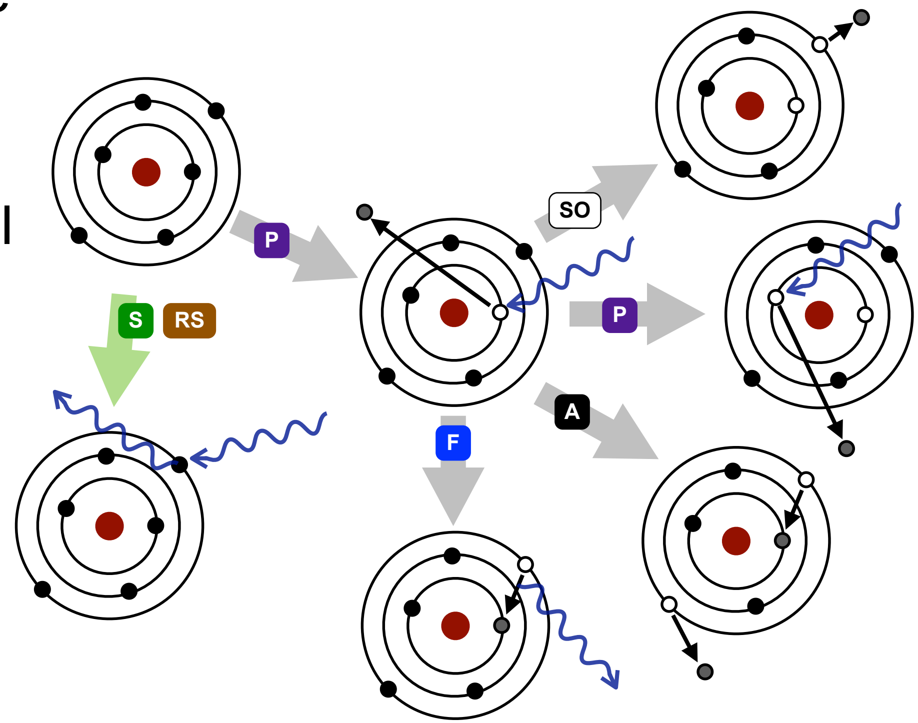
Xe @ 5.5 keV

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

- described by sequences of photoionization, Auger, and fluorescence
- complex inner-shell ionization dynamics (>2B x-ray-induced processes)

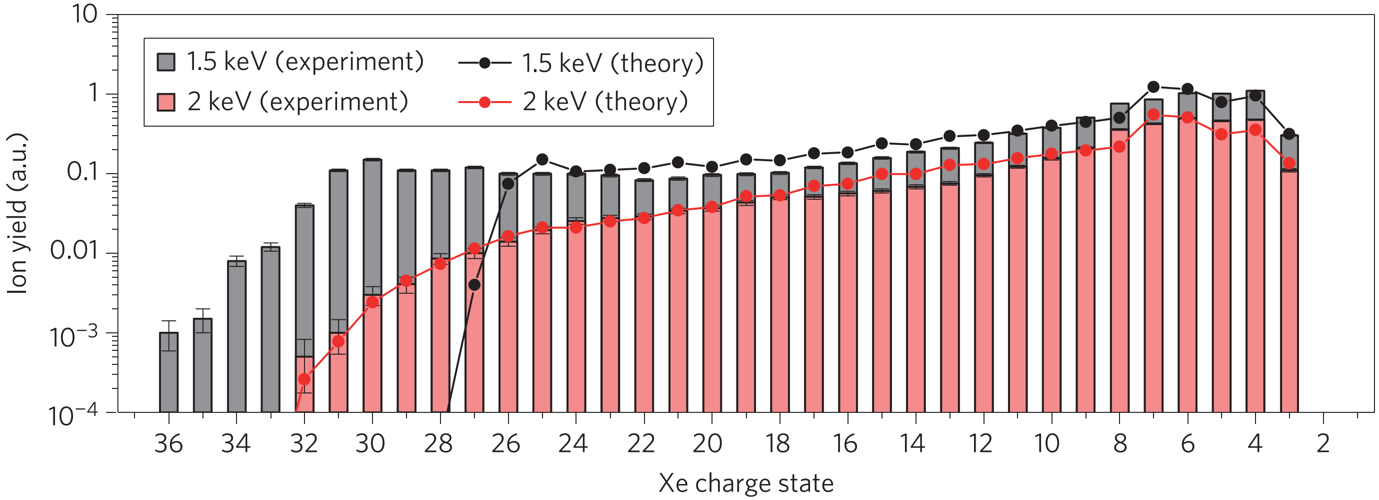
XATOM: all about x-ray atomic physics

- Computer program suite to describe dynamical behaviors of atoms interacting with XFEL pulses
- Uses the Hartree-Fock-Slater model
- Calculates all cross sections and rates of x-ray-induced processes for any given element
- Solves coupled rate equations to simulate ionization dynamics
- Calculates ion / electron / photon spectra, directly comparable with XFEL experiments



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

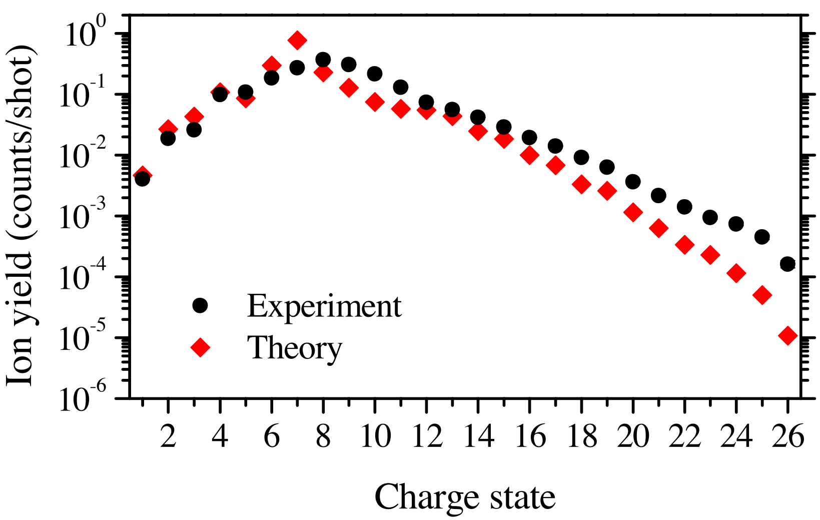
Charge-state distribution: EXP vs. theory



Xe at LCLS

- 1.5 keV: ~Xe^{36+}
- 2.0 keV: ~Xe^{32+}

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



Xe at SACLA

- 5.5 keV: ~Xe^{26+}

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

heavy atoms at higher photon energies

relevant for phasing

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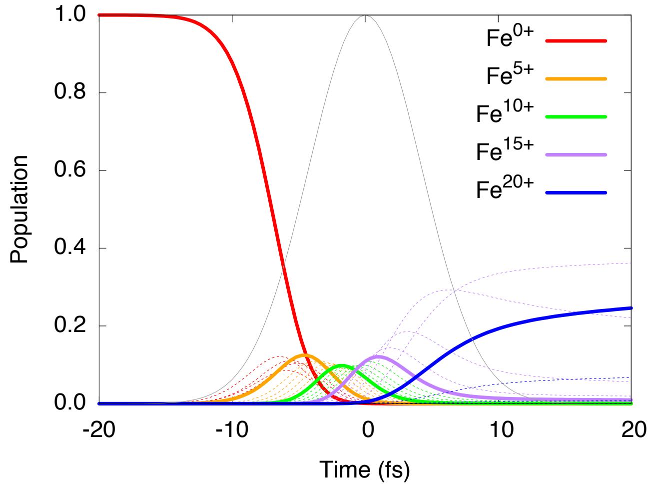
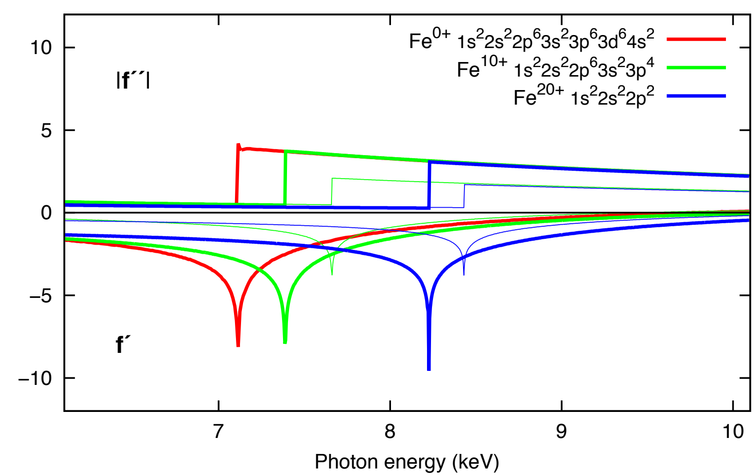
MAD with XFEL

- MAD (multiwavelength anomalous diffraction): employing the dispersion correction of x-ray scattering from heavy atoms
- Can we use MAD with XFEL?
  - Unavoidable electronic radiation damage, especially to heavy atoms
  - Dramatic change of anomalous scattering for high charge states
  - Stochastic ionization nature destroying coherent signals
- Need to understand dynamic behaviors of individual atoms





Generalized Karle-Hendrickson equation

Scattering intensity including ionization dynamics of heavy atoms

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

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 coeff: measured or calculated / **3 unknowns**: solvable with 3 measurements

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

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MAD coeff. including ionization dynamics

- Time-dependent form factor: dynamically synchronized for all heavy atoms ➔ contributing coherent signals

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

- Relative effective scattering strength

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

- XATOM describes dynamical behaviors $P_{I_H}(\mathcal{F},\omega,t)$ and computes $f_{I_H}(\omega)$ for every single I_H

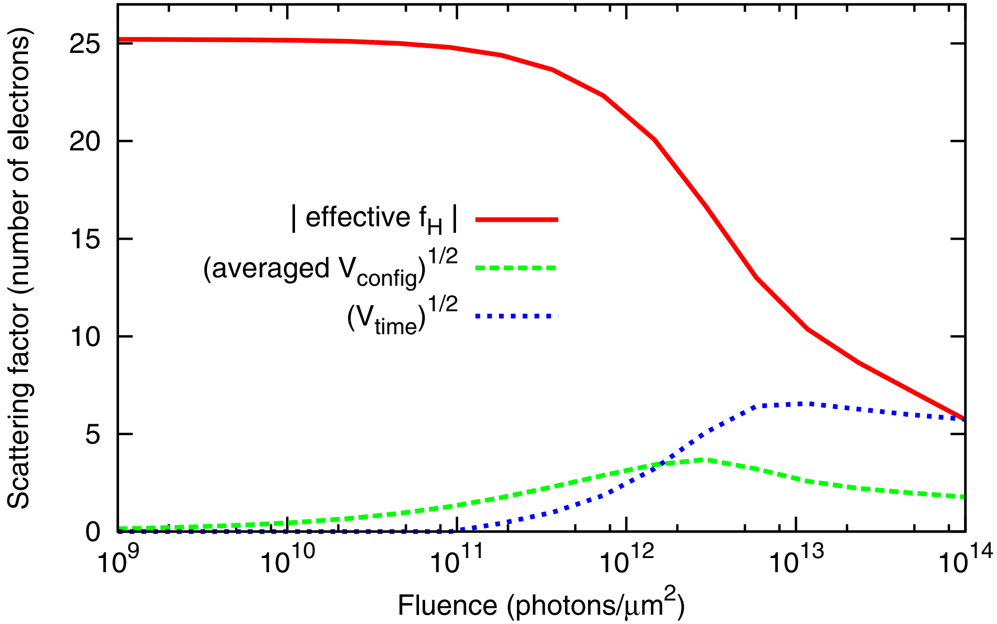
Fluctuation effect on scattering strength

Generalized KH equation: not only for phasing but also for refinement

$$\frac{dI}{d\Omega} = \mathcal{F}C(\Omega)\left[\left|F_P^0 + \bar{f}_H \sum_{j=1}^{N_H} e^{i\mathbf{Q}\cdot\mathbf{R}_j}\right|^2 + N_H \bar{V}_{\mathrm{config}} + \left|\sum_{j=1}^{N_H} e^{i\mathbf{Q}\cdot\mathbf{R}_j}\right|^2 V_{\mathrm{time}}\right]$$

conventional crystallographic software

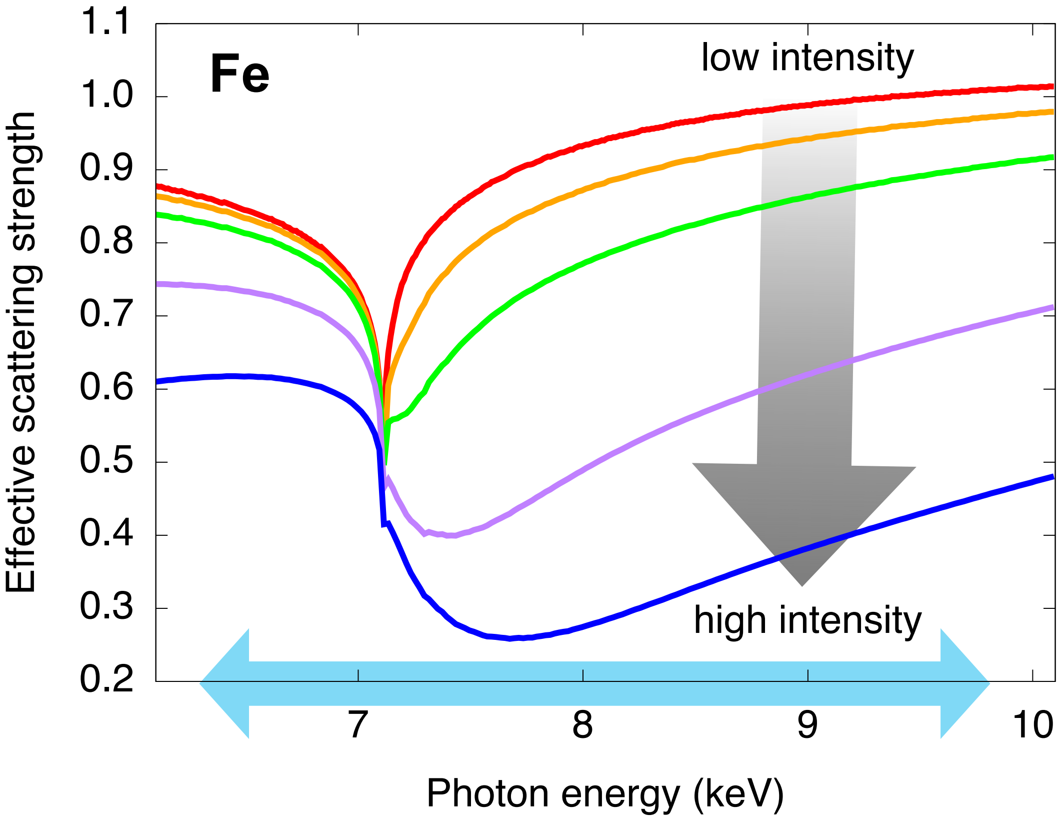
full expression from generalized KH equation



Fe @ 8.1 keV

Son, Chapman & Santra, *J. Phys. B* **46**, 164015 (2013).

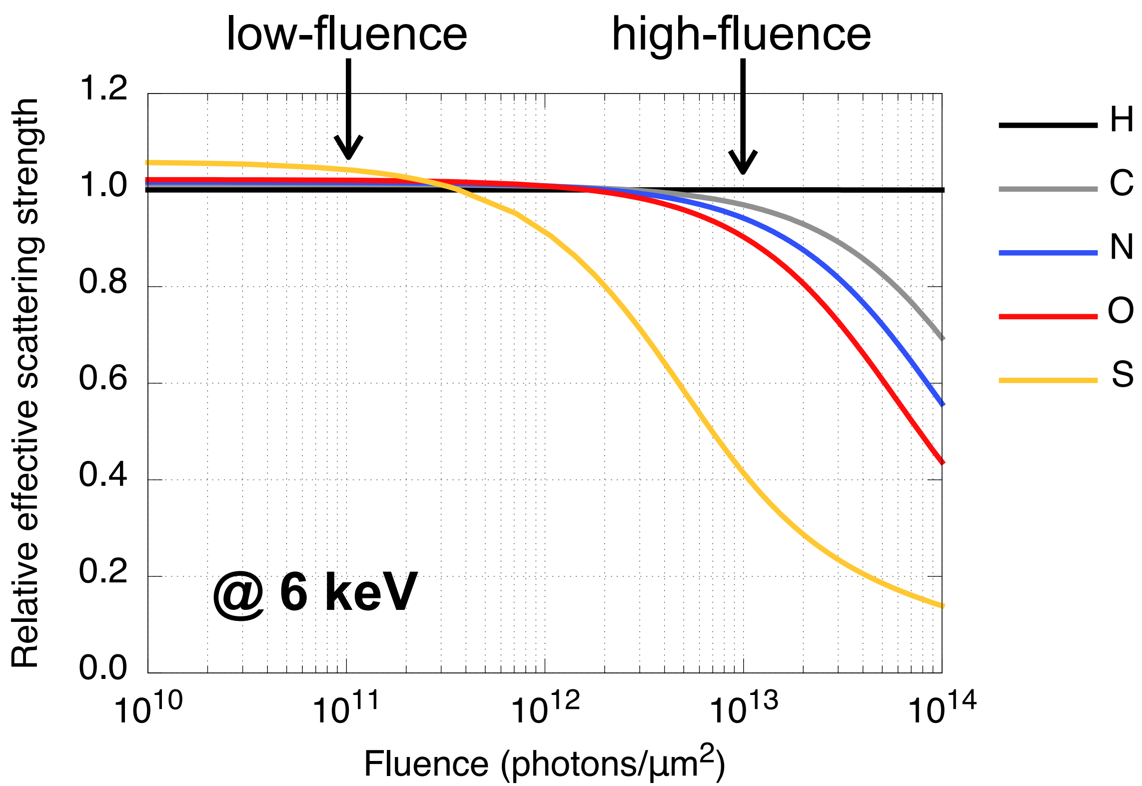
MAD at high x-ray intensity

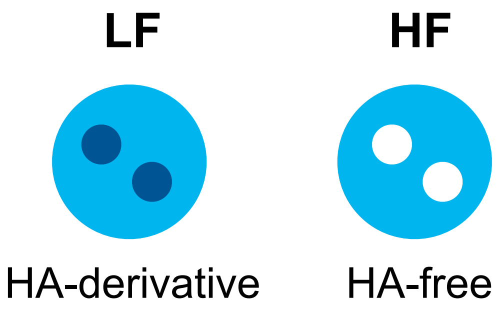


- calculated by XATOM
- different ionization mechanism before and after the edge
- contrast at different wavelengths
- contrast at different fluences, too
- easier to vary fluence than wavelength

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

Towards high-intensity phasing (HIP)

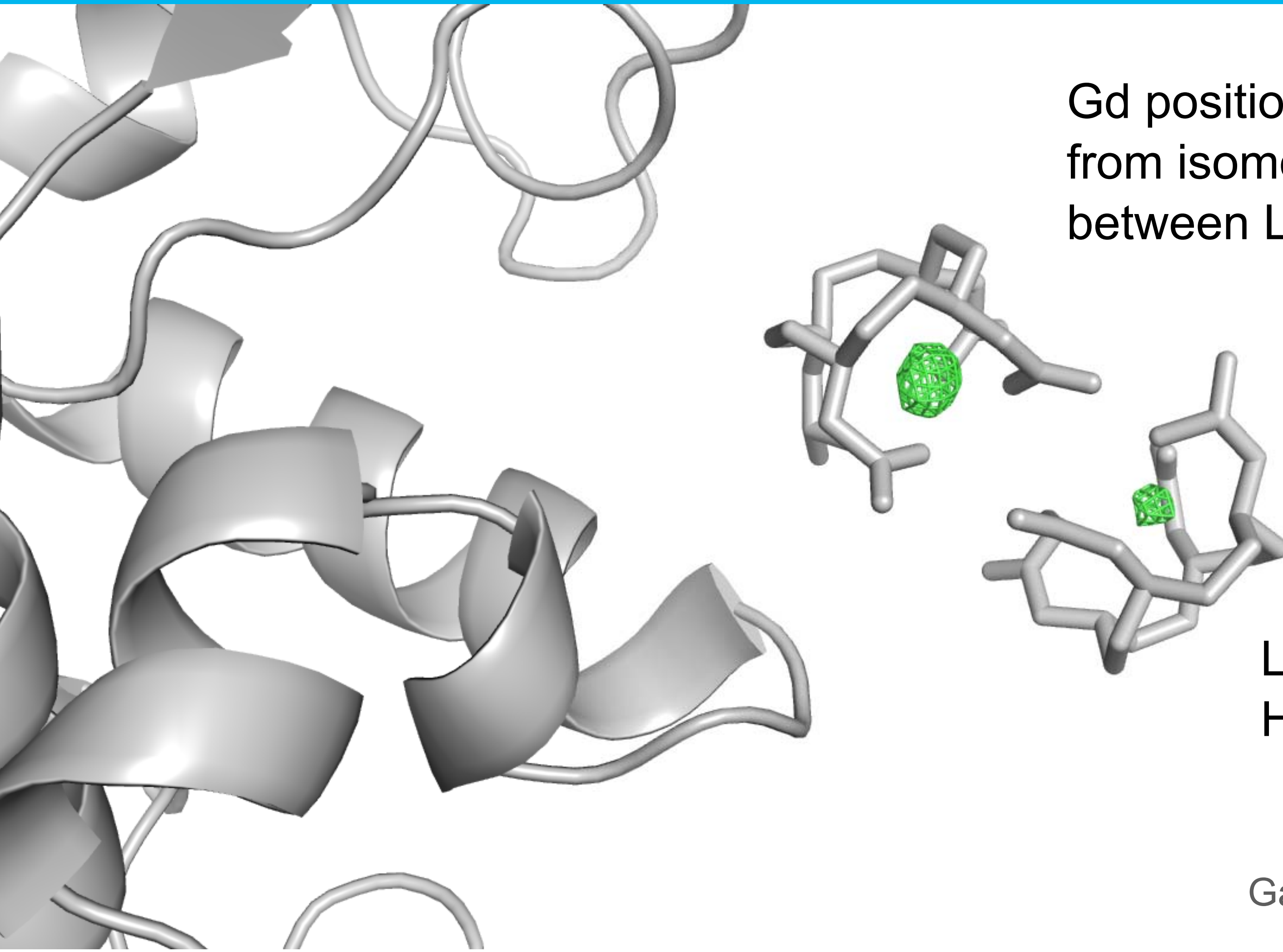




Galli *et al.*, *J. Synch. Rad.* (2015, in press).

- exploit electronic radiation damage to S atoms ($\sigma_S > \sigma_{\text{light atoms}}$)
- simulated datasets of Cathepsin B including ionization for all atoms
- phased by the RIP workflow (High-intensity RIP)

Case study: Gd-derivatized lysozyme



Gd positions are identified from isomorphous difference between LF and HF.

LF: Gd-derivative
HF: mimic native

Galli *et al.*, (submitted).

Gd is really heavy

- Gd-lysozyme diffraction measured at LCLS CXI (8.5 keV)
- Gd: 64 electrons
- XATOM calculation
  - ionization dynamics: $P_{I_H}(t)$ for every I_H (N of I_H > 400M)
  - anomalous scattering calculation: $f_q(\omega)$ for every q (N of q = 64)

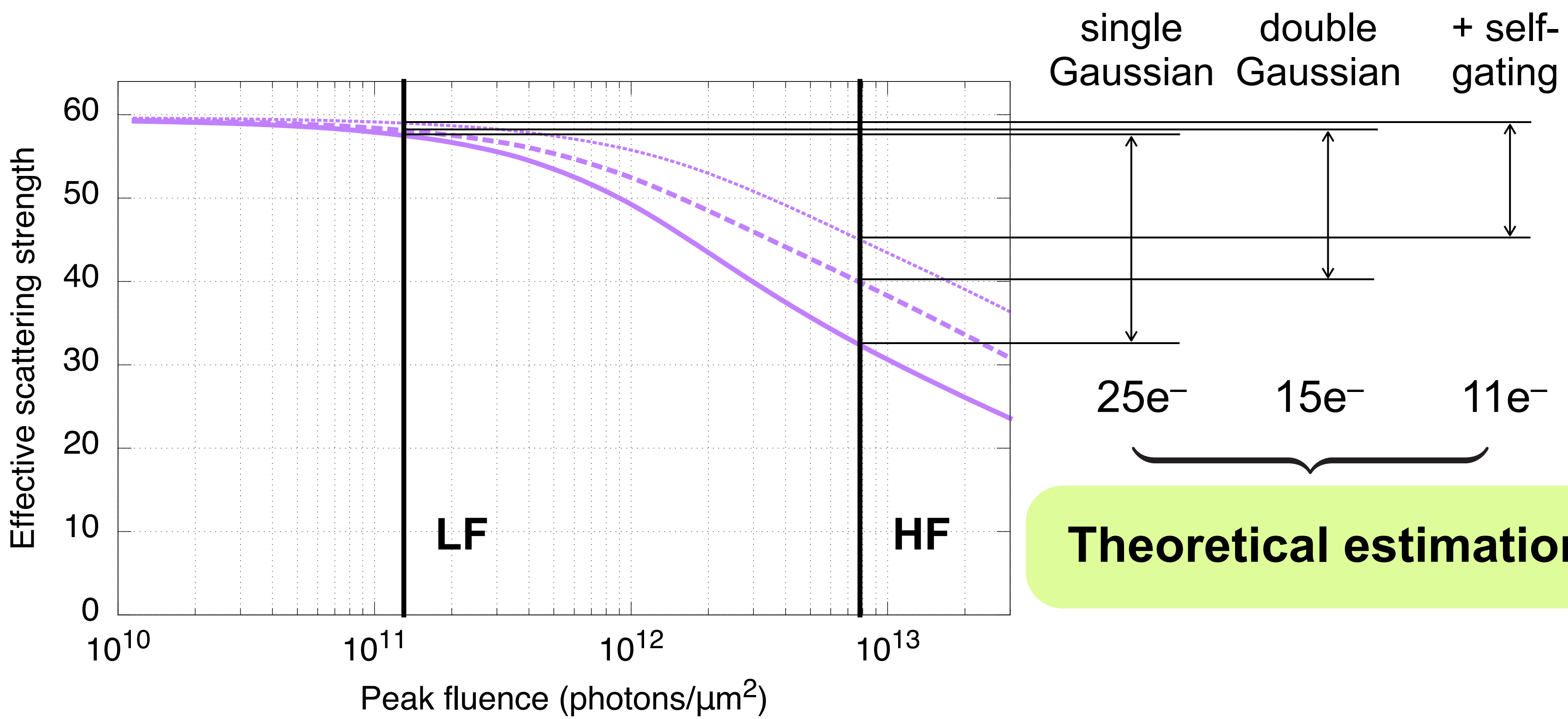
$$\tilde{f}(\mathbf{Q}, \mathcal{F}, \omega, t) = \sum_q P_q(\mathcal{F}, \omega, t) \left[f_q^0(\mathbf{Q}) + f_q'(\omega) + i f_q''(\omega) \right]$$

- Effective scattering strength for Gd

$$f_{\mathrm{eff}} = \sqrt{\frac{\int d^3x \int dt \mathcal{F}(\mathbf{x}) g(t) |\tilde{f}(\mathbf{Q}, \mathcal{F}, \omega, t)|^2}{\int d^3x \int dt \mathcal{F}(\mathbf{x}) g(t)}}$$

$\mathcal{F}(\mathbf{x})$: spatial profile, $g(t)$: temporal profile of the x-ray beam

Scattering strength differences



Theoretical estimation

Experimental analysis

- From the difference density map: 8.8~12e⁻
- From anomalous refinement (f' and f''): 5e⁻

List of speculations

- based on an atomic model
  - relativistic treatment for heavy atoms
  - molecular environment
  - local plasma environment / collisional ionization
- **calibration of x-ray beam parameters**
- **self-gating of the Bragg peaks**
- **ionization-induced fluctuation at high x-ray intensity**
- crystal size
- scaling procedure

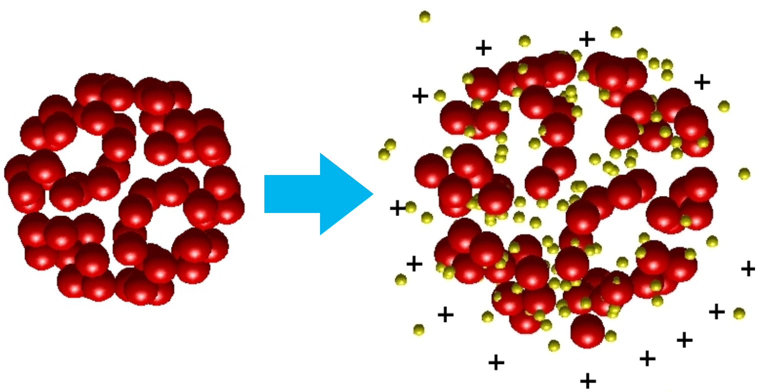
Theoretical estimation: 11~25e$^-$

Experimental analysis: 5~12e$^-$

Galli *et al.*, (submitted).

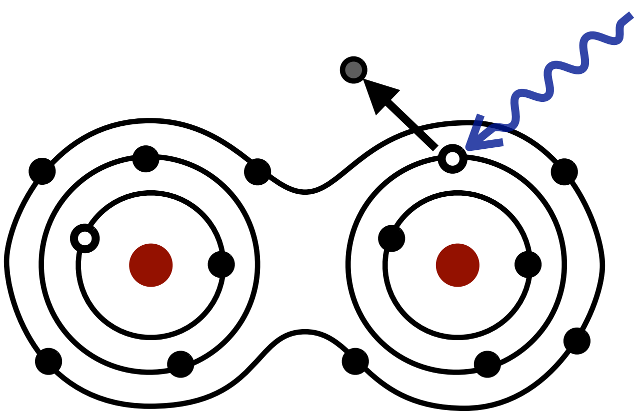
Outlook: new developments

- **XMDYN (Zoltan Jurek)**
  - atomic processes by XATOM
  - molecular dynamics by XMDYN
  - C_{60} at LCLS
  - Ar cluster at SACLA



Murphy *et al.*, *Nature Commun.* **5**, 4281 (2014).

- **XMOLECULE (Yajiang Hao, Ludger Inhester, Kota Hanasaki)**
  - detailed description on molecular environment
  - molecular Auger effect and charge redistribution



Conclusion

- Electronic radiation damage: unavoidable at high x-ray intensity
- XATOM describes multiphoton multiple ionization dynamics of individual atoms; tested by LCLS and SACLA experiments
- Generalized Karle-Hendrickson equation: a key formula for phasing at high x-ray intensity
- High-Intensity Phasing (HIP): new opportunities for solving the phase problem in nanocrystallography with XFELs

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UXSS 2015

June 22–25, 2015
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http://conferences.cfel.de/uxss_2015/ (will open in February)

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