Multiwavelength anomalous diffraction at high x-ray intensity

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Abstract

The **multiwavelength anomalous diffraction (MAD)** method is widely used in x-ray crystallography with synchrotron radiation to determine phase information by employing dispersion corrections from heavy atoms on coherent x-ray scattering. **X-ray free-electron lasers (XFELs)** show promise for revealing the structure of single molecules or nanocrystals within femtoseconds, but the phase problem remains largely unsolved. Because of the extremely high fluence of XFELs, samples experience severe and unavoidable electronic radiation damage, especially to heavy atoms, which hinders direct implementation of the MAD method with XFELs. We propose a generalized version of the MAD phasing method at high x-ray intensity. We demonstrate the existence of a **Karle–Hendrickson-type equation** for the MAD method in the high-intensity regime and calculate relevant coefficients with electronic damage dynamics and accompanying changes of the dispersion correction. Here we present the **XATOM** toolkit to simulate detailed electronic damage dynamics and discuss how the proposed method is applicable to the **phase problem in femtosecond x-ray nanocrystallography**.

Introduction

Multiwavelength anomalous diffraction (MAD)

> The phase problem is a fundamental obstacle in constructing an electronic density map from x-ray diffraction. Since we can measure only scattering intensity, we may lose phases that contain more important information for the structural determination.

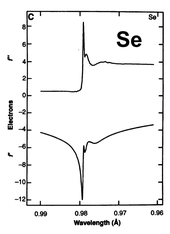
$$F^0(\mathbf{Q}) = \int d^3r\ \rho(\mathbf{r})\ e^{i\mathbf{Q}\cdot\mathbf{r}} = \left|F^0(\mathbf{Q})\right|\ e^{i\phi^0(\mathbf{Q})}$$

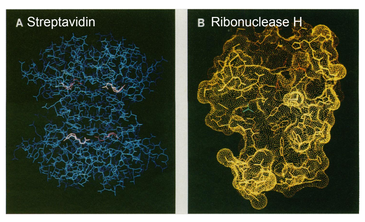
> The anomalous scattering at different wavelengths provides a simple way (MAD phasing with the Karle-Hendrickson equation) to solve the phase problem.

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

> Advantages of MAD: (a) algebraically solvable, (b) different datasets obtained by physical changes (wavelength), (c) no atomic replacement in sample preparation, (d) no chemical rearrangement during x-ray pulses, (e) no need for iterative phase retrieval algorithm, and (f) no need for previously known crystal structures.

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





Figures from Hendrickson, *Science* **254**, 51 (1991).

Ultrafast x-ray scattering

> Another bottleneck of x-ray crystallography is the need for large-scale high-quality crystals, which are very difficult to be grown or are simply not available in many cases of interest.

> The unprecedented high x-ray fluence from XFELs provides a sufficiently large number of photons to enable structure determination from diffraction measurements of streams of single molecules and nanocrystals.

> Due to an extremely high fluence that is ~100 times larger than the conventional damage limit, samples are subject to severe radiation damage.

> The ultrashort x-ray pulses generated by XFELs enable us to carry out "diffraction-before-destruction" within femtosecond timescales to suppress nuclear motion.

> Electronic radiation damage is unavoidable, which is characterized by multiphoton multiple ionization via a sequence of one-photon inner-shell ionizations and relaxations.

> The phase problem remains largely unsolved.

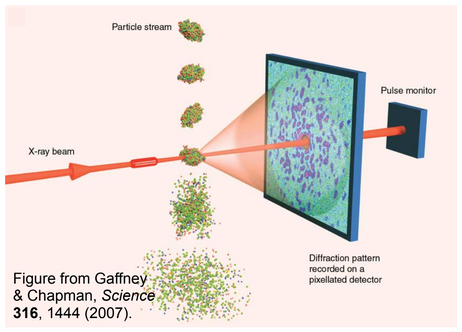


Figure from Gaffney & Chapman, *Science* **316**, 1444 (2007).

Prior speculations regarding MAD at XFEL

> Heavy atoms as anomalous scatters will be more ionized than other atoms during intense x-ray pulses, because the photoabsorption cross section of the heavy atom is much higher than that of the light atom and for heavy atoms a vacancy in deep inner shells causes several relaxation steps in the cascade through the subshells, resulting in further electron ejections.

> Anomalous scattering will be dramatically changed when heavy atoms are highly ionized.

> Stochastic electronic damage to heavy atoms would destroy coherent scattering signals in nanocrystals...

> MAD would not be an applicable route for phasing in the presence of severe radiation damage...

> 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.

> Our proposed method can overcome both major bottlenecks in x-ray crystallography:

phase problem → MAD,

growing high-quality crystals → XFEL.

XATOM toolkit

Theory

We implement an integrated toolkit, XATOM, to treat x-ray-induced processes based on nonrelativistic quantum electrodynamics and perturbation theory within the Hartree–Fock–Slater model.

Physical processes

> Photoionization

> Auger (Coster–Kronig) decay

> Fluorescence

> Shake-off

> Elastic x-ray scattering

> Resonant elastic x-ray scattering (dispersion correction)

The toolkit can compute photoionization cross sections, Auger / fluorescence rates, shake-off branching ratios, and atomic form factors for a given electronic configuration of any atomic species.

Damage dynamics

To simulate electronic damage dynamics in intense x-ray pulses, we use the rate equation approach with photoionization cross sections, Auger rates, and fluorescence rates, for all possible *n*-hole electronic configurations for all possible +*n* charge states.

Applications

> Ionization, relaxation, and scattering dynamics at high intensity

> Nonlinear x-ray absorption processes

> Charge distribution analysis of noble gases in XFELs

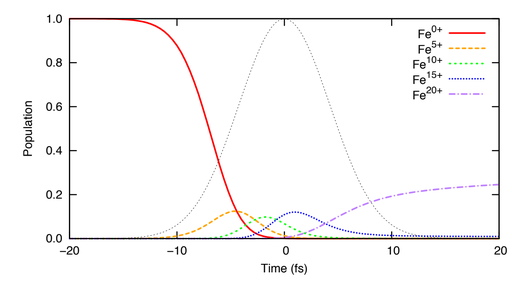
> Photoelectron / Auger / fluorescence spectra

> Multi-wavelength anomalous diffraction at high intensity

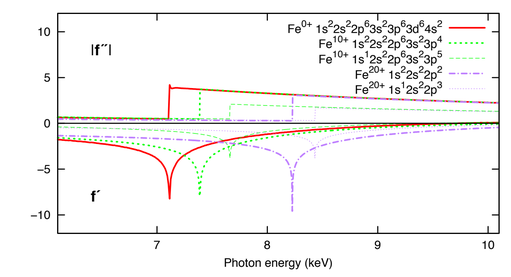
Electronic damage to heavy atoms

The ground-state configuration for neutral Fe: $1s^2 2s^2 2p^6 3s^2 3p^6 3d^6 4s^2$

For electronic damage dynamics of a Fe atom, 27,783 coupled rate equations are solved.



Population dynamics of Fe charge states during an XFEL pulse of 8 keV, 5×10[12] photons/μm², 10 fs FWHM



Dispersion corrections of atomic form factors of Fe and its ions

Generalized Karle-Hendrickson equation

The scattering intensity (per unit solid angle) is given by

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

$$I = (I_1, I_2, \cdots I_{N_H}), \quad P_I(t) = \prod_{j=1}^{N_H} P_{I_j}(t), \quad f_{I_j}(\mathbf{Q},\omega) = f_{I_j}^0(\mathbf{Q}) + f_{I_j}'(\omega) + if_{I_j}''(\omega)$$

We made the following assumptions:

> 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.

We demonstrate the existence of a Karle-Hendrickson-type equation in the high-intensity regime.

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

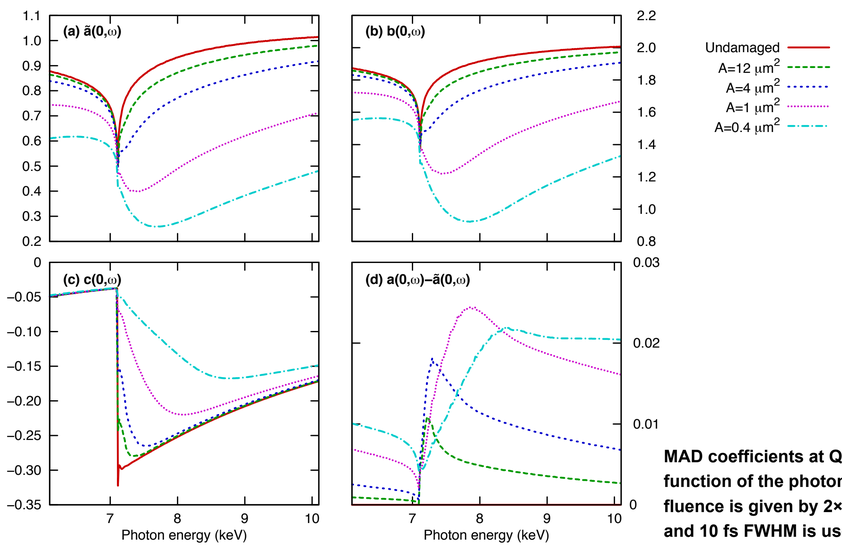
$$a(\mathbf{Q},\omega) = \frac{1}{\{f_H^0(\mathbf{Q})\}^2}\sum_{I_H}\bar{P}_{I_H}\left|f_{I_H}(\mathbf{Q},\omega)\right|^2, \qquad \tilde{a}(\mathbf{Q},\omega) = \frac{1}{\{f_H^0(\mathbf{Q})\}^2}\int_{-\infty}^{\infty} dt\, g(t)\left|\sum_{I_H} P_{I_H}(t) f_{I_H}(\mathbf{Q},\omega)\right|^2$$

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

> MAD coefficients: $a(\mathbf{Q},\omega)$, $b(\mathbf{Q},\omega)$, $c(\mathbf{Q},\omega)$, and $\tilde{a}(\mathbf{Q},\omega)$ → calculated with detailed electronic damage dynamics by XATOM.

> 3 unknowns at a given $\mathbf{Q}$: $\left|F_P^0(\mathbf{Q})\right|$, $\left|F_H^0(\mathbf{Q})\right|$, and $\phi_P^0(\mathbf{Q}) - \phi_H^0(\mathbf{Q})$ → solvable with measurements at 3 different wavelengths.

MAD coefficients at high x-ray intensity



MAD coefficients at Q=0 for Fe as a function of the photon energy. The fluence is given by 2×10[12] photons/*A* and 10 fs FWHM is used.

> With three or more different wavelengths, the unknowns can be solved by the least-squares method.

> *L*-shell ionization dynamics dominates below the edge, whereas *K*-shell ionization dynamics dominates after the edge.

> 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.

> Broadening of the edge at high intensity makes precision of the photon energy less important in experiments.

> It provides an alternative phasing method similar to single isomorphic replacement (SIR) or radiation-damage induced phasing (RIP).

> In our model, resonant absorption processes and shakeup or shakeoff processes are not included.

Femtosecond x-ray nanocrystallography

Experimental implementation

> The pulse shape and the fluence at a given position **x** in the x-ray beam may differ from shot to shot.

> Ensemble average: we numerically confirmed the following relation to within 3%.

$$\left\langle \frac{dI[\mathcal{F}(\mathbf{x})g(t)]}{d\Omega} \right\rangle \approx \frac{dI[\langle\mathcal{F}(\mathbf{x})g(t)\rangle]}{d\Omega}$$

> The total signal can be obtained by integrating over the interaction volume:

$$\int d^3x\, \frac{dI\left[\langle\mathcal{F}(\mathbf{x})g(t)\rangle\right]}{d\Omega} n_{\mathrm{mol}}(\mathbf{x})$$

> The basic structure of the equation remains unchanged.

MAD phasing for nanocrystals

> Bragg peaks (proportional to N_H^2): the second term implies that all heavy atoms are described by the same *dynamical* form factor.

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

> Diffuse background (proportional to N_H): the last term represents fluctuations form all different configurations induced by electronic damage dynamics.

$$N_H\left|f_H^0(\mathbf{Q})\right|^2\left\{a(\mathbf{Q},\omega) - \tilde{a}(\mathbf{Q},\omega)\right\}$$

> $(a - \tilde{a})$ is an order of magnitude smaller than $\tilde{a}$ and not confined to the Bragg peaks, implying that the high x-ray intensity does not fully destroy the coherent signals.

Conclusions

> We propose the MAD phasing method in extreme conditions of ionizing radiations.

> Our analysis combines electronic response at the atomic level and molecular imaging during intense x-ray pulses.

> We demonstrate the existence of a generalized Karle-Hendrickson equation for the MAD method at high x-ray intensity.

> Our results show that the generalized version of the MAD method is still applicable to the phase problem even in the presence of severe radiation damage.

> The beaching effect on the scattering strength of heavy atoms, which unexpectedly enhances the coefficient contrast in the MAD method, can be beneficial to phasing.

> Our study opens up a new opportunity of solving the phase problem in femtosecond nanocrystallography with XFELs.

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