On dose related issues in XFELs vs. ERLs

Outline:

- Motivation
- Overview of processes involved
- “Conventional” protein damage in crystallography
- Cryoprotected X-ray microscopy

Motivation

Biological and Environmental Research Advisory Committee (BERAC) at Department of Energy (DOE) meeting on April 30 - May 1 (2003) Washington, DC aims at addressing the following question from the Director of Office of Science

http://www.science.doe.gov/ober/berac/synchrotron.html

"*What characteristics of the next generation x-ray light sources (e.g., their extremely short femtosecond time scale x-ray pulses; high average or peak brightness; coherence) are most important in enabling science, from determination of physical structures to biological functions, for the biological community in the coming 10-20 years?*"

The response suggests (see http://www.science.doe.gov/ober/berac/StructBio.pdf):

… superiority of X-FELs over ERLs in "*greater potential for* **breakdown** *science by biological community*" (page 4). The reasoning behind this view is most succinctly recapped by the following phase that "*ERLs will be far less powerful than X-FELs due to limited number of photons per ERL pulse*" (page 16).

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Recap of radiation properties

	XFEL	ERL
Photons/pulse	10^{12}	10^{6-7}
Rep. Rate [Hz]	10^{2}	10^{9}
Pulse duration [ps]	0.1	0.1 – 2
Source size [µm]	30	10

The scare of XFELs

- If focused to 10 μm spot, the peak power density is 10^{16} W/cm^2
- 200 kiloton nuclear weapon where 6% of the energy is emitted in X and γ rays over a time period of 100 ns creates peak photon density of 10^{17} W/cm^2 within the bomb casting
- $E \sim \sqrt{Z_0 I}$, $Z_0 = 377\ \Omega$, i.e. electric field ~ 10^{11} V/m
- Coulomb field acting on an outer electron 10 V/ 1 Å ~ 10^{11} V/m
- <u>NOT</u> a strong field regime: $U_p = e^2E^2(\lambda^2/16\pi^2)/mc^2$, e.g. average kinetic energy of wiggling electron is only ~ 1 μeV
- OR amplitude of the wiggling motion is $a_w = 4U_p/eE \sim 5\times10^{-7}$ Angstrom

*1 Å light oscillation takes only **0.3 attosecond***

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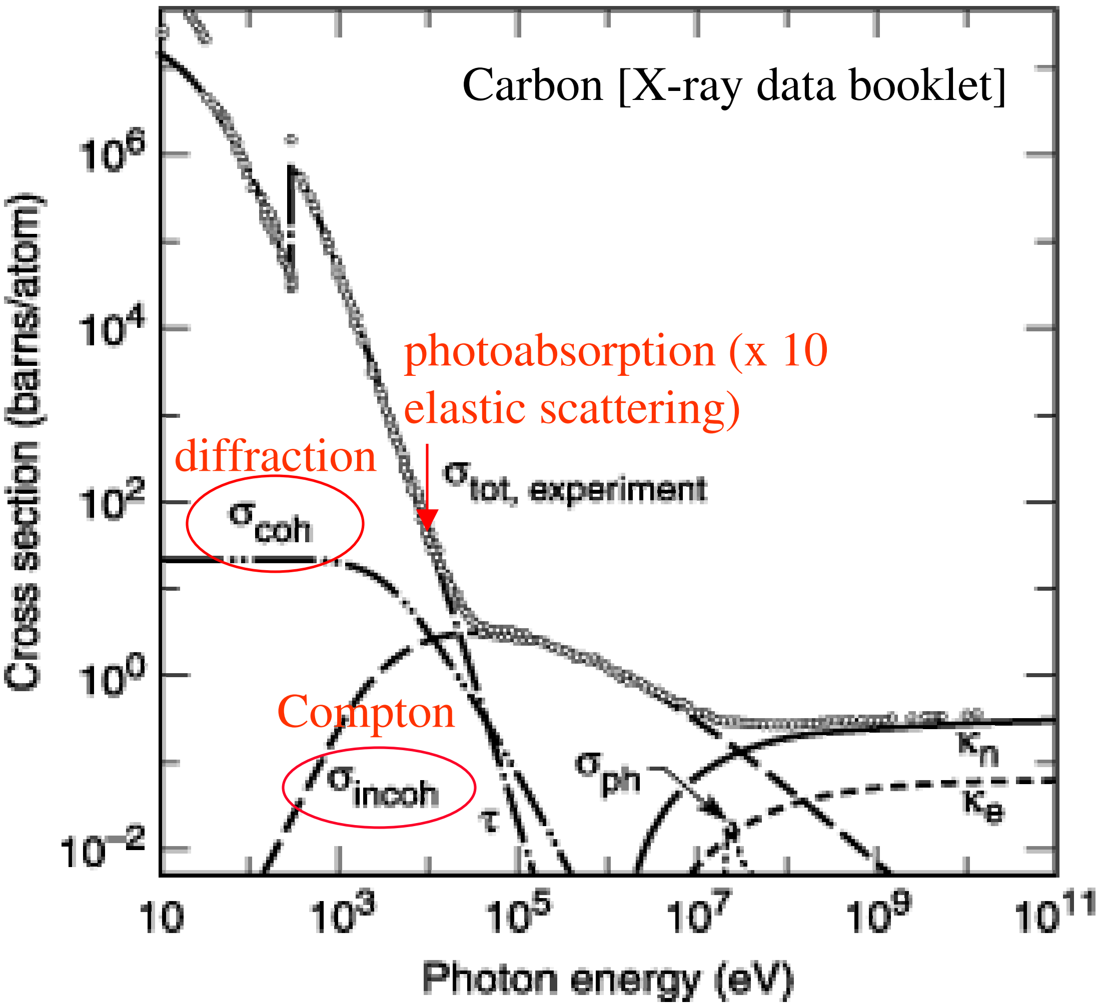
Processes involved



Carbon [X-ray data booklet]

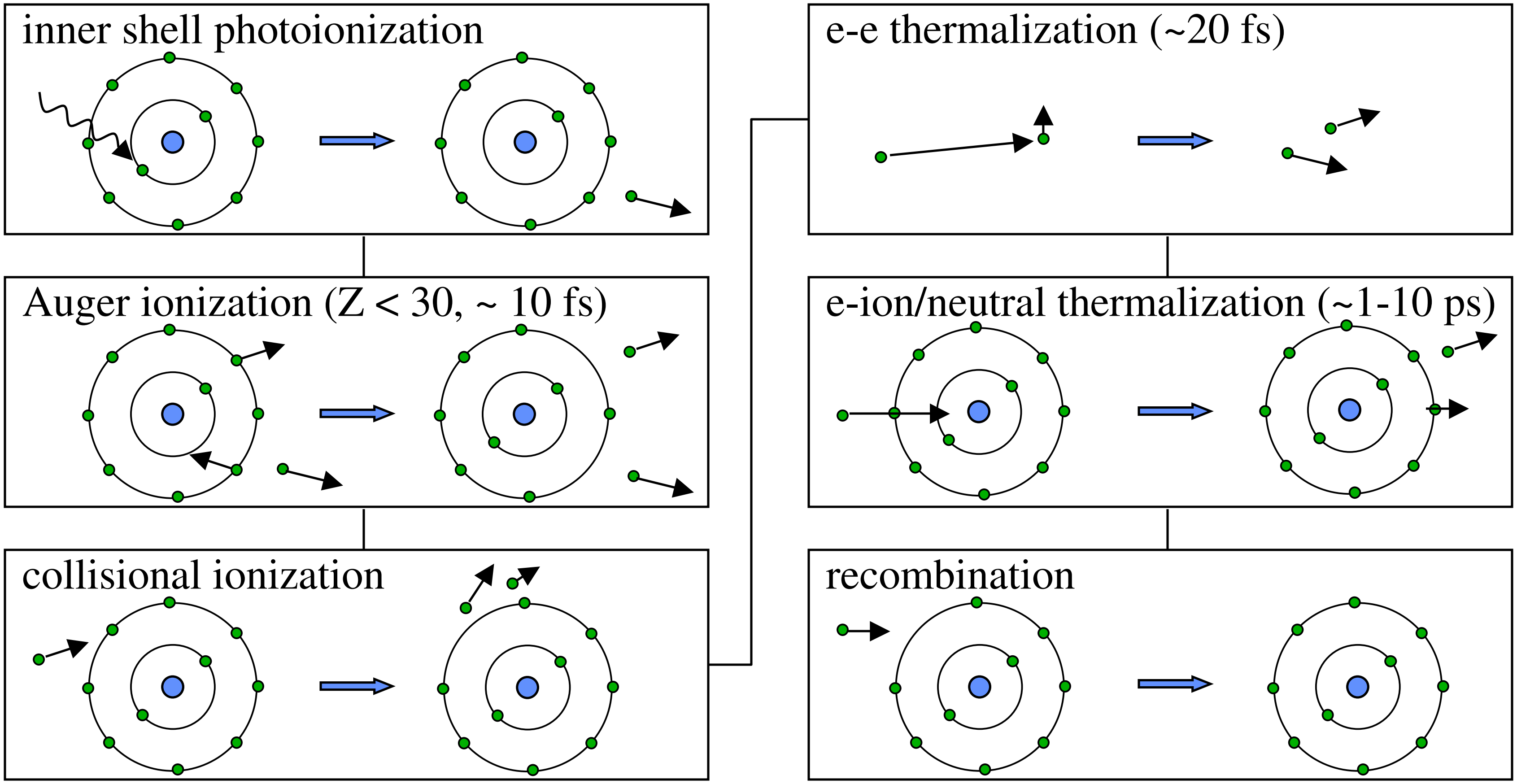
photoabsorption (x 10 elastic scattering)

diffraction

Compton

X-ray and electron processes

R.A. London et al, "Computational studies of high intensity X-ray matter interaction", Optics for Fourth Generation X-ray Sources, SPIE Proc (2001), **4500**, p. 51



inner shell photoionization

Auger ionization (Z < 30, ~ 10 fs)

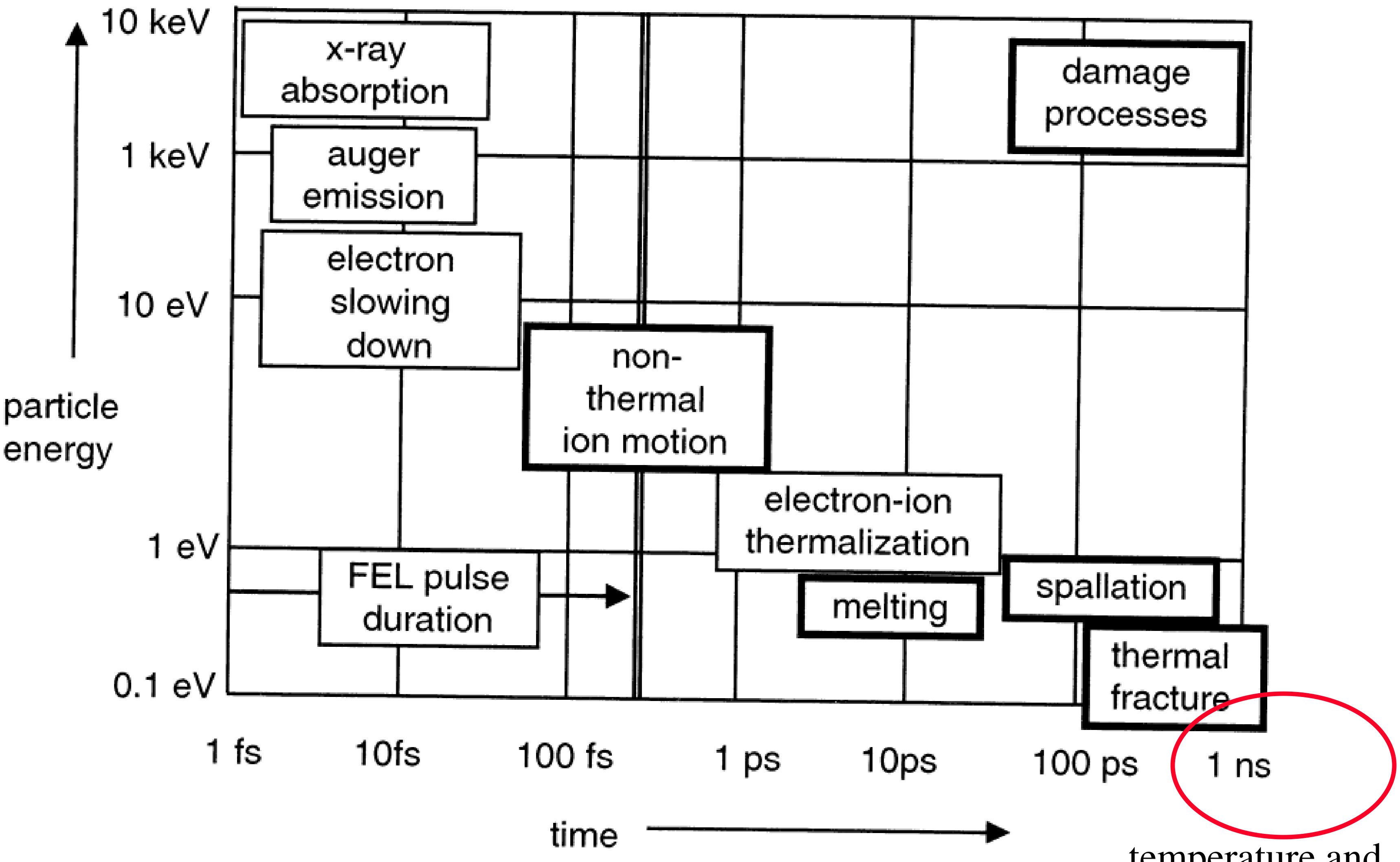
collisional ionization

e-e thermalization (~20 fs)

e-ion/neutral thermalization (~1-10 ps)

recombination

Energy-time plot for x-ray-matter interaction



temperature and density relax. time

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Fluence [J/cm^2] that matters

- for very short pulses (e.g. both XFELs and ERLs) it's fluence that matters
- XFEL: $10^{12}\times$10keV ~ 1 mJ / pulse; ERL: 10^6-$10^7\times$10keV ~ 10 nJ / pulse
- tolerable dose can be estimated as following (e.g. Si):
  - specific heat times 1700 – 300 K temperature difference
  - plus fusion heat, = 78 kJ/mole
  - normalized per atom ~ 0.8 eV/atom
- most elements have melting dose between 1/3 to 1 eV/atom
- < 0.1 eV/atom considered safe

Damage onset with instantaneous dose

0.1 eV/atom
threshold for permanent structural changes
↓
1 eV/atom
most materials are melted
↓
10 eV/atom
ablation begins
↓
higher dose eventually leads to Coulomb explosion

Tolerable spot size for melting

Use protein density 0.8 Da/Å^3

carbon photo-absorption cross-section $\sigma_a = 85$ barn/atom

dose per atom: $E_{pulse}\,\sigma_a$ / area

For tolerable dose 0.1 – 1 eV/atom

XFEL	ERL
10 – 30 µm	6* – 60 nm

For smaller spot sizes, one moves into a "single shot" regime

For high-Z materials this number is worse

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* low flux regime

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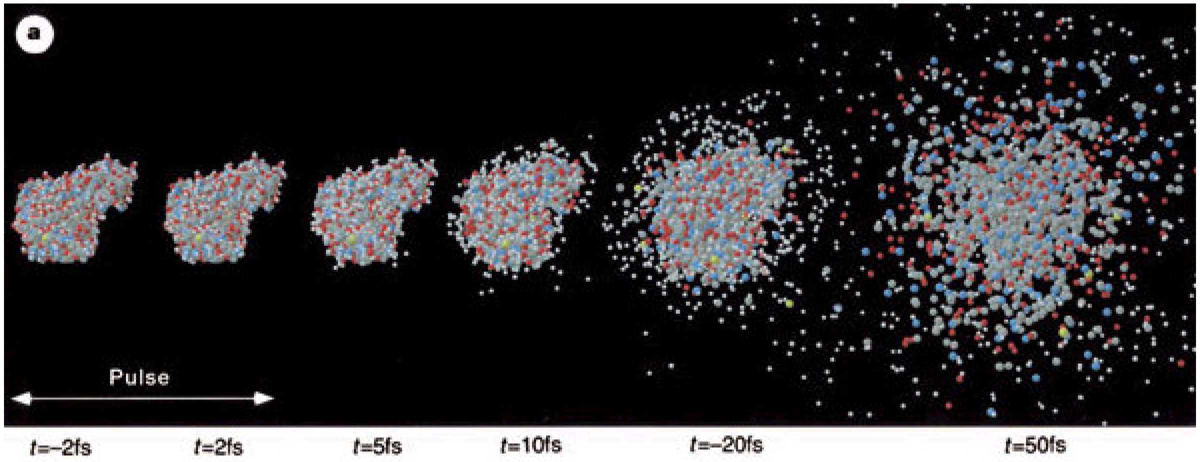
Explosive proteins

R. Neutze, et al., *Nature*, **406**, 752-757, January 17, 2000



Very briefly: calculations were done for T4 lysozyme (diameter 32 Å, N_C ~ 1000);
flux 4×10^6 X-rays/Å^2 with ~ 2000 primary ionization events;
elastically scattered ~ 200 photons.
The claim is that if pulse is sufficiently short (much shorter than the LCLS spec), $5\times5\times5$ lysozyme nanocrystal will scatter to <2Å resolution.

Conventional damage to proteins

- Primary: breaking of chemical bonds
- ~~Secondary: chemical damage by free radicals~~
- ~~Tertiary: crystal lattice destabilized in absence of further chemical damage (domino effect)~~

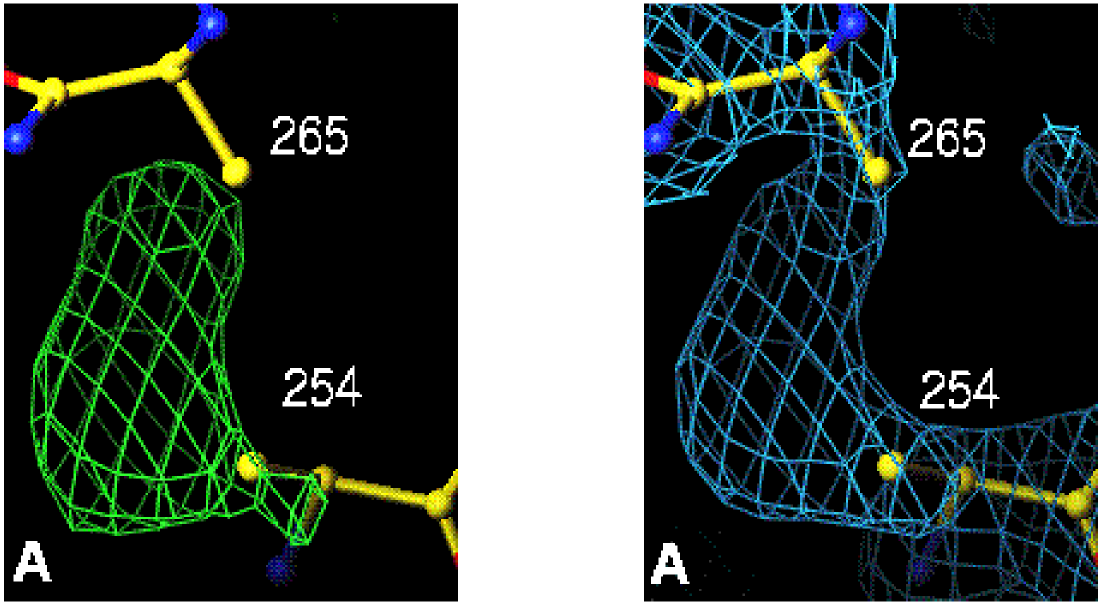
cryoprotection helps with these two (prevents mass loss)

- Primary radiation dose 10^7 Gy or ~200 X-rays/Angstrom^2 (Henderson's limit)
- It's accumulated dose that matters (unlike "fast melting")
- Despite the very different mechanisms, the damage dose is 1.4 eV/atom, very similar to the "single shot melting"
- Coulomb explosion requires much greater dose (delivered in a single pulse)

Disulphide bonds go first

M. Weik, et al., *PNAS*, Vol. 97, Issue 2, 623-628, January 18, 2000

Each frame is a complete data-set collected in about 3.5 minutes, each data-set is a 15 minutes time point. The left panel is the $3F_o$-$2F_c$ map and model of the 254-265 disulfide bridge, and the right panel is the F_o-F_c map of the same S-S bond.



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Cryoprotection prevents mass loss

T. Beetz and C. Jacobsen, J. Synchrotron Rad. (2003). **10**, 280–283

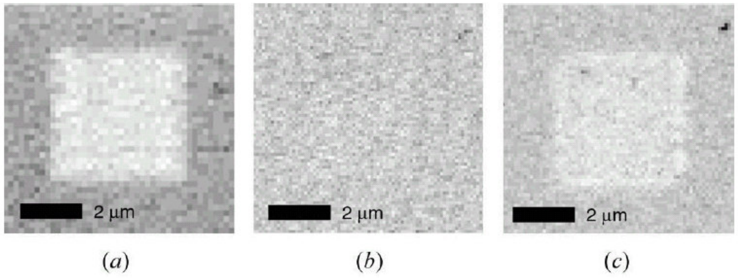

Figure 2
(*a*) Coarse area scan at room temperature of a region that was dosed at room temperature. The square in the middle indicates the mass loss of the dosed region. (*b*) Coarse area scan at liquid-nitrogen temperature of the region that was dosed at liquid-nitrogen temperature. The image shows no visible mass loss at the dosed region. (*c*) Same area as that in image (*b*) but after warming up the sample; the dosed region becomes visible.

Radiation damage for ~ 10 nm resolution in cryoprotected X-ray microscopy is estimated to be at ~10^{10} Gy (~1 keV/atom ac. dose) [J. Maser et al., J. Microscopy (2000), **197**, p. 68]

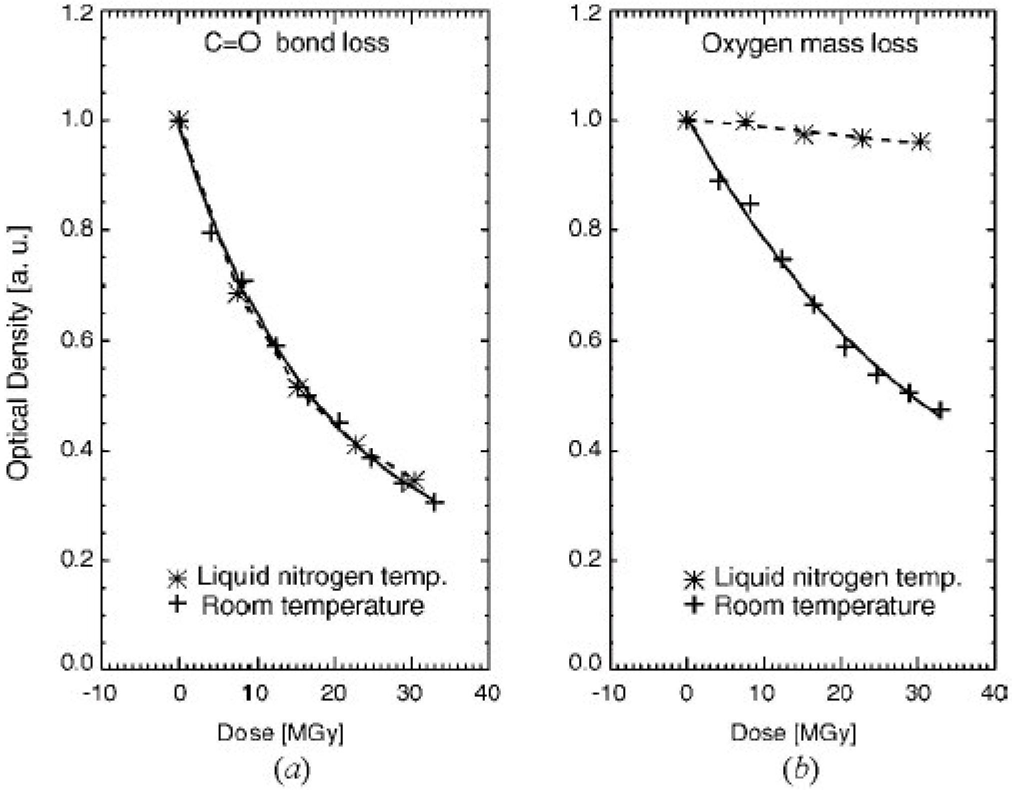

Figure 4
(*a*) Loss of C═O peak intensity and (*b*) mass loss as a function of dose at liquid-nitrogen and room temperatures. The data were fitted using equations (2) and (3), where the fitting coefficients are summarized in Table 1.

Some preliminary conclusions

- Cryoprotection is likely to be ineffective for “single shot melting”, i.e. X-ray microscopy is better off with c.w. source like an ERL
- Applications requiring multiple exposures of the same sample (e.g. tomography) with good resolution will prefer c.w. source over XFEL
- “single shot” experiments are for XFELs
- …