Hydrodynamic Model of X-ray-Irradiated Biological Molecules

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Outline

I. Background: Flash Imaging of Biological Molecules

II. Continuum Model for Radiation Damage

III. Atomic Processes During Irradiation

IV. Coulomb Explosion

V. Pulse Requirements for Biological Imaging

VI. Ideas to overcome radiation damage

VII. Conclusions
X-Ray Crystallography Has Been Very Successful for Studying Biological Molecules at Atomic Resolution

• Requires the use of *crystals* containing many identical molecules to enhance the signal and reduce the damage.

• However, it is difficult or not-yet-possible to crystallize many molecules.

• It is desirable to develop a method to obtain images from single (uncrystallized) molecules.

• The extreme brightness and short duration of X-ray Free Electron Laser (XFEL) pulses can enable atomic-resolution imaging of single bio-molecules.
With an XFEL, We Can Capture an Image Before the Molecular Structure is Altered

- Image in shorter time than it takes for the damage to manifest itself  
  (Solem, Baldwin, and Chapline, 1980)

- Use fs XFEL pulses to image single molecules (Neutze, Hajdu et al., 2000)

- Low scattering cross-section overcome by high intensity pulse
- Image many identical samples to build-up signal and get 3-D structure
- Electron density is reconstructed from diffraction intensity

Remaining Questions Include…

• What is the minimum X-ray fluence versus sample size and resolution to classify each diffraction pattern?

• How many views are needed to reconstruct the 3D structure?

• What is the maximum X-ray fluence and pulse length before the radiation damage degrades the image?

Specifically, our goal is to determine:

• Radiation damage versus beam parameters
• Radiation damage versus sample size
• How short must the pulses be?
One-Dimensional Continuum Model for Radiation Damage

- Sample is treated as a continuum of matter
- Sample has spherical symmetry
- Rate equations are used to model ionization of each atomic species (H,C,N,O,...)

Compared to molecular dynamics model (Neutze et al 2000), the hydro model does not treat atomic motions as accurately, but enables the inclusion of more complete set of physics, is much faster, and can treat larger molecules.
Overview of Physical Processes

• X-ray photo-ionization
  – Include secondary collisional ionization by escaping photo electrons

• Auger ionization

• Electrostatic trapping of electrons
  – Determine spatial distribution of trapped electrons by a balance between pressure and electrostatic forces
  – Include secondary collisional ionization

• Determine atomic motion by electrostatic forces due to net charge of ions and trapped electrons
Trapping of Electrons

Electron escapes if

\[ E_{\text{electron}} > \frac{3eQ}{2r} \text{(center)} \]
\[ E_{\text{electron}} > \frac{eQ}{r} \text{(surface)} \]

Otherwise electrons are trapped

- Positive molecule charge increases with time
- Eventually, free electrons are trapped
Atomic Damage Processes During Irradiation
Example: Carbon Irradiated with 12keV X-Ray Photons

Initial State

Ground State

Photoelectric Absorption

- Photoelectrons escape with ~12keV initially
- Some secondary ionization (low-energy e-), usually trapped

Auger Relaxation

- Dominant over fluorescence
- 260-500eV electrons usually trapped

Collisional Ionization

- Secondary ionization sustains until electron energy becomes small

Atomic processes modeled through rate equations for each atomic species
Standard Model Parameters

- Photon energy = 12 keV

- Pulse length = 20 fs, flat-top profile

- Fluence = $3 \times 10^{12}$ ph/(100 nm)$^2$
  - Necessary to achieve 2 Å resolution of 20 Å molecule
  - Flux = $1.5 \times 10^{11}$ ph/(fs–100 nm$^2$)

- Radius = 60 Å and composition $H_{51.61}C_{30.77}N_{8.16}O_{9.40}S_{0.60}$
  - Comparable to anthrax lethal factor protein
Ionization of Carbon

- Photoionization initiates cascade
- Collisional ionization very quickly dominates
- By 10 fs, carbon is stripped to C^{3+}
Ionization Increases With Flux and Molecule Radius

Onset of photoelectron trapping earlier for bigger molecules
⇒ Stronger ionization
Net Positive Charge Leads to Coulomb Explosion of the Molecule

For Comparison: Explosion without Electron Redistribution

(similar to Neutze et al., (2000))

Full model shows faster expansion of outer layers, but slower expansion of inner layers
The Trapped Electrons Shield the Core of the Molecule, Forming a 2-layer Configuration

Neutralized core experiences little atomic motion but strong secondary ionization.

Charged outer layer experiences substantial atomic motion but little secondary ionization.
Atom Motion Increases with X-ray Flux

(Molecule Radius = 50 Å)

Fraction of molecule that is displaced by more than 2Å (%)

Flux (ph/(fs–100nm^2)):
- 2.5x10^{11}
- 7.5x10^{10}
- 2.5x10^{10}
- 7.5x10^{9}

Time (fs): 0 10 20 30 40
The maximum pulse length is limited by damage and image signal

**Preliminary Results**

- Fluence set by required signal (Huldt, Szoke and Hajdu, 2003)
- Damage pushes us towards low fluence and shorter pulse.
- Signal required to classify images pushes us towards high fluence.

- Longer pulse would be allowed if:
  - information about molecule orientation were available
  - we could determine original atomic positions from partially ionized atoms
  - tamper could be used

- Resolution (Å)
- Radius of particle (Å)

Fluence set by required signal

- $10^{13}$
- $3 \times 10^{12}$
- $10^{12}$
- $3 \times 10^{11}$ photons in (0.1 µm)$^2$

- 30fs
- 20fs
- 15fs
- 4fs
- 1fs
A Molecule Tamper Might Extend the Allowable Pulse Length

- Tamper holds back motion of the inner molecule (“inertial confinement”) and provides extra electrons that neutralize the molecule.

- Extra electrons accelerate ionization processes
- Tamper will also generate noise in the image, that must be overcome.

- Movie of explosion with and without tamper!!
Fluence = $3 \times 10^{12}$
Radius = 20 Å
Tamper = 10 Å, H₂O
Pulse length = 20 fs
Conclusions

• We have developed a hydrodynamic model for short pulse x-ray imaging of biological molecules,
  – Photo-, Auger, and collisional ionization
  – Coulomb force
  – Electron spatial distribution

• Hydro model is very fast compared to molecular dynamics.

• Electron trapping and subsequent collisional ionization are very important in bounding the pulse length for atomic scale resolution to $\leq 4$ fs.

• Reconstruction from partially ionized atoms or information about molecule orientation may allow longer pulses.

• A molecular tamper may also extend the allowable pulse length,