“Making the Molecular Movie”: Quest for the Structure-Function Correlation in Biology

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Mother Nature and the Big Bang of Chemistry
The “Molecular Dance”: Functionally Important Protein Motions

What is the mechanism of correlated atomic displacements?
Structure - Function Correlation ⇒ resolve atomic motions on timescales faster than the onset of diffusive motions…..observe force correlations
Making the “Molecular Movie” ...First Frames


⇒ Resolved atom pair correlations on timescales faster than diffusion
4th Generation Light Sources

<10^{-14} second flashes of coherent x-ray pulses to catch molecular structures on the fly.....approx 100 fs time resolution wrt structural dynamics

SLAC, DESY, Spring-8


http://www.xfel.eu/XFE
Lpresse/en/hintergrund
/flash/index.html

http://www.xfel.spring8.or.jp/
Molecular Structure w/o Crystals

10^6 x-rays/Å^2 required to ensure one scattered photon per atom → ionizes molecule

→ Need to repeat 10^5 to 10^6 times for full reconstruction


⇒ LENSLESS IMAGING....Electrons

Alternative Choice (vide infra)...still need crystals for seeing atomic motions
## Electrons vs. X-rays

<table>
<thead>
<tr>
<th>Electrons</th>
<th>X-rays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongly scattered</td>
<td>Weakly scattered</td>
</tr>
<tr>
<td>Table top experiment</td>
<td>Synchrotron/laser based</td>
</tr>
<tr>
<td>Pumped volume better matches scattering length</td>
<td>Pulse duration independent of photon number</td>
</tr>
<tr>
<td>Energy deposited in sample per scattering event 400-1000 times less (1.5 A X-rays)</td>
<td>Potential for Laue diffraction</td>
</tr>
<tr>
<td>* Incoherent</td>
<td>* Coherent</td>
</tr>
</tbody>
</table>

* Coherent e-wavepackets possible with “atom” tips (V. Deyirmenjian, J. Sipe, R.J.D. Miller…in progress)
Single Molecule Imaging

Electrons have a major advantage over x-rays re: $10^6$ higher scattering cross section and completely different damage mechanism

⇒ Need $10^7$ electrons now...likely $10^4$ when fully optimized.....numbers are within reach

⇒ Lensless imaging with x-rays best for in vivo imaging of actual functions
Single Point Projection Sources: "Electron Lasers"

Etched tungsten tips had been proven a coherent source for electrons:

Heinz Schmid and Hans-Werner Fink

B. Cho, T. Ichimura, Shimizu, and C. Oshima
CCD

UV laser

Mesh

Phosphor screen

Electrons

Negative voltage $V_{\text{tip}}$

Javier Groshaus
Magnification x 15000

FIG 1: Collagen fibers suspended over micron sized graphite holes at different magnifications

⇒ Can go to much higher magnification via camera position .... Imaging single nanotube....Nm resolution now....vibrations are washing out fringes.......
“Movies” Require Many Molecules: Diffraction from Identically Prepared Systems

- **temporal (fs) resolution**
- **structural (atomic) resolution**
- crystalline systems (phase transitions)
- molecular systems (photoreactions)

Camera for the atomic level “movie”
Motivation and Challenges for Electron Sources

Time-resolved electron diffraction harbours great promise for resolving the fastest chemical/condensed phase processes with atomic level structural detail (i.e. make Molecular Movies) ⇒ generally irreversible processes.

• **How to get sufficient current density (100 mA/mm\(^2\) or more) to the sample for near single shot structure determinations -- must avoid space-charge effects (Coulomb repulsion) that act to broaden the electron pulse as it propagates.**

• **How to solve \(t = 0\) problem for synchronizing “film”**

• **How to characterize femtosecond electron pulses --- major problem as the pulse profile rapidly evolves in time/propagation......time resolution required is (was) beyond all current technologies.**
Progression of Ultrafast Electron Diffraction

Major Milestones re: Resolving Structural Changes
The influence of space-charge on the propagation dynamics of fs electron packets through a photoactivated electron gun (right) was investigated with:

- **Classical N-body simulation**
  - Numerical simulation of the full N-electron equations of motion using a Barnes-Hut tree algorithm.

- **Mean Field Model**
  - Approximate potential of electron packet as a disk of charge to generate the pulse length equation:

\[
\frac{d^2 l}{dt^2} = \frac{Ne^2}{m \varepsilon_o \pi r^2} \left[ 1 - \frac{l}{\sqrt{l^2 + 4r^2}} \right]
\]

l = pulse length, t = propagation time, N = number of electrons, r = electron beam radius,

Velocity (or Kinetic Energy) Chirp

- Vacuum is dispersive for electrons: 
  \[ v = \sqrt{\frac{2E_k}{m}} \]
- The spatial distribution of velocities evolves as the pulse lengthens.
- Electrons redistribute inside the packet to produce a linear velocity chirp.
- The dynamical time-scale is related to the potential energy of the initial charge distribution (pulse).

Axial velocity (Vz) vs. axial position (Z) for all electrons in the pulse at four times (T) during its propagation (N = 10 000, τ₀ = 150 fs, r(0) = 75 µm, 1.5 mrad initial beam divergence).
**Femtosecond Electron Gun**


⇒ Increased electron “brightness” for diffraction studies by 3 orders of magnitude
Electron Pulse Compression

(6000 electrons, Chirp = 200 V/ps)

⇒ Expect another factor of 1000 increased “brightness” re: re-bunching
⇒ less than 50 femtosecond time resolution
Higher electron pulse densities, shorter pulse durations

<table>
<thead>
<tr>
<th>Machine</th>
<th>$N$</th>
<th>$t_p$ (fs)</th>
<th>$L_c$ (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4th</td>
<td>~5k</td>
<td>200</td>
<td>3</td>
</tr>
<tr>
<td>5th</td>
<td>~625k</td>
<td>&lt;50</td>
<td>7-30</td>
</tr>
</tbody>
</table>

Modified from - van Oudheusden T, de Jong EF, van der Geer SB, Luiten OJ et al. JAP 102 (9) 093501, 2007
All Optical-Electron Pulse Measurement: Determination of Camera Shutter Speed

Pulse energy of approx. $1-10 \text{ mj at 800 nm}$ and $10 \mu\text{m}$ beam $\Rightarrow$ less than 100 fs resolution: Siwick et al. *Opt. Lett.* 30, 1057 (2005)….ALLS project

$$U_{\text{pond}} = \frac{(e^2 \lambda^2 I)}{(2\pi mc^3)}$$

$I$ = intensity, $\lambda$ = wavelength, $c$ = speed of light,
$e$ = electron charge, and $m$ = electron rest mass.
Sampling the Electron Pulse (I)

- We obtain time traces by scanning the delay between the electron pulse and the laser “scattering pulse”.
- Scattering reduces the number of electrons in the pulse around the laser focus resulting in a hole in the electron beam.
Electron Bunch Dependence of Pulse Duration — Enhanced Grating Scattering

⇒ Microjoule pulses/all fibre systems now possible

⇒ 30 fs response function/10 fs accuracy t=0
How does a solid melt on the ultrafast timescale?

Solid equilibrium structure
Monatomic fcc lattice, \( a = 4.05 \text{Å} \)

Liquid equilibrium structure
Radial density function shows liquid structure


http://www-solidstate.physik.uni-bremen.de/~ischnell/fcc/

Need time-resolution!
Ultrafast Solid-Liquid Phase Transition in Aluminum


150 shots, ~6000 e/pulse
New Electron Gun Design

- Irreversible reaction
- Large number of e-/pulse required
- Single-shot experiment, 3-10 acquisitions per time point
- e- pulse duration: 250 - 400 fs FWHM (depending on number of electrons)

Characterized by cross-correlation measurement


Samples: free-standing 111-oriented Au (20 nm), Si and Bi (30 nm) films

2 cm gun capable of 200 fs high bunch number pulses
Possible effects of (intense) electronic excitation on the interatomic potential:

a) none
free-electron metals, e.g., Al

b) bond softening
semiconductors, e.g., Si, InSb
Rousse et al., Nature (2001)

c) bond hardening
proposed for Au
Recoules et al., PRL (2006)

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Peierls-distorted
lattices, e.g., Bi

Solid state dynamics under strongly-driven conditions

Harb et al., PRL (2008)
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Ernstorfer et al. Science 2009: Atomic View
on the Formation of Warm Dense Matter
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Sciaini et al., Nature 2009
Electronic Acceleration of Atomic Motions

Sciaini et al, Nature 2009
Ultrafast melting of Bismuth

A7 structure: rhombohedral distortion of cubic lattice (Peierls-Jones effect) → electronic excitation launches large-amplitude optical phonon along the direction of the Peierls distortion

Strong electronic excitation softens the $A_{1g}$ mode and triggers the transverse $E_g$ mode (Hase et al., PRL (2002), Zijlstra et al., PRB (2006))

Formation of 3D isotropic state requires shear motion (along $E_g$). How effective is the shear under strong excitation?

Note: 111-orientation of Bi film: diffraction signal insensitive to $A_{1g}$ oscillation

from: Zijlstra et al., PRB (2006)
Bismuth

Reversible condition, over 1000 shots averaged

Deposited over C-coated mica

Deposited over NaCl

Excited carrier density < 1%

Lattice heating dynamics ~ 2.5 ps
Strongly driven nonreversible conditions, a few shots per time point
Significantly above melting
Excited carriers ~ 11%

Negative time delay

+1 ps time delay

20 shots

Scattering vector modulus (1/Å)

Radially averaged intensity [a.u.]

Liquid Bi

Crystalline Bi
Ultrafast melting of Bismuth: raw data

excitation: 180 J/m², 8 averages per time point

static diffraction
Accelerated disordering

At high excitation the potential becomes anharmonic and $A_{1g}$ and $E_g$ modes couple

Electronically accelerated atomic motions \( \Rightarrow \)

“Electron gas peddle”
Free-standing (001)-oriented Si

Silicon-on-insulator  

Release

Wet transfer

Prepared by Max Legally and coworkers:

*M. Roberts et al., Nature of Materials, 5, 388 (2006).*
Direct Observation of Key Shear Modes: Low Excitation

Kinetics of the 220 Diffraction Spot

Two oscillation modes at periods of 7.6 and 11.4 ps

⇒ Direct view of Collective Modes — Step Towards Proteins
Summary

The “Camera for the Molecular Movie” is now in-hand

First Atomic View of Melting...one of the simplest everyday occurrences of structural changes.....to Plasma Formation

⇒ Dynamics correlate to e-phonon coupling/band str.

“Molecular Movies” Filmed on Location at U of Toronto with electron “back lighting” — single shot capabilities (collaborations welcome) ....and soon SLAC, DESY, SPRING-8 with x-rays.

⇒ Sending Probes into Transition States (Atomic Terra Incognito) to beam back pictures of atoms and turn notions into indelible facts of Nature