EE213. Microscopic Nanocharacterization of Materials

Three Dimensional Imaging/Characterization

Holography
Tomography

March 1, final paper rough outline due. COB
Final Paper

1. Paper: due last day of class

2. Topic should be about a particular microcharacterization technique and comparison with at least one other method. From topics covered in course outline.

3. You must discuss the spatial resolution characteristics and limits.

4. Abstract or summary of each paper listed as references.

5. Discuss typical application use, briefly.
EE213. Final Topics

Ryan Gardner  Photoelectron microscopy

M. Ahsan Habib  NSOM

Bingzhang Lu  Atomic Force Microscopy

Evan Petersen  Confocal, 2 photon and wide field microscopy

Renee Sully  SIMS

Bin Yao  ?
HOLOGRAPHY principle

From Wikipedia
Photographed Images at 2 different angles from a hologram of a mouse
electron holography — another characterization tool.

1940's

original idea by Gabor in the 1940's / 1949
1947. 182. 454-467

idea was to invert the aberrations of
electron microscope lenses —

Nobel Prize in
the '70s / 1971

demonstrated with lasers in the late '60's — (Leith & Upatnieks,)
JOSA. 52. 1123-30

and with electrons in the '80's —

basically creating an interference pattern that
has info on amplitude and phase of scattered wave
— a single image only contains the amplitude info since it is 

\[ I(x, y) = |Ae^{i\phi}|^2 \]

holography was an alternative to aberration correction
AND it allowed one to create a 3D image \[ \text{since they change the "phase" of an electron wave.} \]
exception of Rothamsted Experimental Station and a few centres in the United States, there existed no other laboratory where experiences in so many aspects of plant virus study could be obtained, applications from foreign workers for this training being very frequent. Unfortunately, these activities had to be severely curtailed owing to the lack of laboratory accommodation. Nevertheless, it may be mentioned that students have come to take either research degrees or courses of instruction in plant virus work from Argentina, Australia, Belgium, Brazil, Canada, China, Czechoslovakia, Denmark, Gold Coast, India, New Zealand, Poland, Portugal, South Africa, Sweden and the United States, and visitors have come from all over the world.

In looking back over two decades, it becomes evident how, with increasing knowledge and new technical discoveries, the trend of virus research has changed. In the beginning, most of the emphasis was placed on the disease, and symptomatology was all-important, although the study of the relationships between the virus and the insect vectors was already being undertaken. The isolation of tobacco mosaic virus by Stanley in 1935, however, was the key which opened the door to the study of the virus itself, quite apart from the disease it may cause. A brief review of some of the main contributions by the Cambridge workers illustrates this change of emphasis in virus research. For the first few years, attention was directed almost entirely towards potato virus diseases, and from this work three items of interest may be noted. The first of these was the isolation of the insect vector of potato leaf-roll, which was later also found to carry another potato virus. This was the aphid, Myzus persicae, and it was almost the first introduction to public notice of the aphid which, since that time, has become of paramount importance in the field of plant viruses and seems to be the most efficient vector of these agents in the world. It is now known to transmit more than twenty distinct viruses. The next addition to our knowledge of potato viruses was the discovery of the paracrinkle virus in potatoes of the variety King Edward; this is one of the unsolved puzzles of the virus world, since it is present in all plants of this potato variety, but no method is known by which it can spread in nature. The case of paracrinkle is often quoted as evidence of the heterogeneity of viruses by those who hold this view. The third item was the analysis, for the first time, of a plant virus complex by differential methods of transmission, and the isolation of the two potato viruses now universally known as X and Y.

In 1931 the virus of tomato spotted wilt was discovered for the first time in Europe; it was found in an ornamental plant sent to Cambridge from Cardiff. Before this it had not been seen outside Australia. Since then the distribution of the virus has become world-wide, and in Great Britain it is one of the major problems of the tomato grower with 'mixed houses'.

The viruses of tomato bushy stunt and tobacco necrosis, both described for the first time in Cambridge, have proved of great scientific interest. The virus of tobacco bushy stunt, about which more is known than of most viruses, was the first to be isolated in a three-dimensional crystalline form, and this was accomplished by Bawden and Pirie, after the former had left Cambridge. Shortly after this, the virus of tobacco necrosis was isolated as thin crystalline plates. About this time, also, the comparatively new technique of plant virus serology was applied to the study of potato virus X.

In 1938 a new virus complex affecting the tobacco plant, known as 'rossette', was investigated, the chief point of interest being the apparent relationship between the two component viruses. This is suggested by the fact that, while both viruses are aphid-transmitted if they are together in the plant, one of the two cannot be picked up by the insect if the other virus is not present.

During the period 1940–45, several new viruses have been described, those of Arabidopsis halleri and oregano, tobacco broken ringspot, tomato black ring and of two new potato diseases, vein collapse and vein yellow, which were found in some South American potatoes. Of these new viruses, those of Arabidopsis halleri and broken ringspot are of special interest, since they appeared in plants inside the experimental glasshouses with no apparent explanation of their origin.

During the last two years an extremely interesting and important new virus has been discovered and studied. Known as turnip yellow mosaic virus, it has been isolated in two different crystalline forms and, like other plant viruses studied so far, it is a nucleo-protein. In addition to the active virus, infected plants also contain a protein which is apparently the virus protein but lacks the nucleic acid. This protein has also been crystallized, and studies of the biochemical and biophysical properties of these two proteins are now in progress. The virus is also of interest in having an entirely new kind of insect vector, one with biting mouthparts, namely, a flea-beetle. This is the first record, both of transmission of a virus by this insect and of the insect transmission of a crystalline plant virus.

Using a microscope studies in conjunction with Dr. V. E. Coullet of the Cavendish Laboratory, and with Dr. R. G. W. Wyckoff in the United States, have also been made [see p. 769 of this issue of Nature]. An interesting outcome of this work is that the structure of the crystals of tobacco necrosis virus and turnip yellow mosaic virus has been demonstrated by this means.

A NEW MICROSCOPIC PRINCIPLE

By Dr. D. GABOR

Research Laboratory, British Thomson-Houston Co., Ltd., Rugby

It is known that the spherical aberration of electron lenses sets a limit to the resolving power of electron microscopes at about 5 A. Suggestions for the correction of objectives have been made; but these are difficult in themselves, and the prospects of improvement are further aggravated by the fact that the resolution limit is proportional to the fourth root of the spherical aberration. Thus an improvement of the resolution by one decimal would require a correction of the objective to four decimals, a practically hopeless task.

The new microscopic principle described below offers a way around this difficulty, as it allows one to dispose altogether with electron objectives. Micrographs are obtained in a two-step process, by electronic analysis, followed by optical synthesis, as in Sir Lawrence Bragg’s X-ray microscope. But
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THE PRINCIPLE OF WAVE-FRONT RECONSTRUCTION

Consider a coherent monochromatic wave with a complex amplitude $U$ striking a photographic plate. We write $U = A e^{i\psi}$, where $A$ and $\psi$ are real. $U$ may be decomposed into a 'background wave' $U_0 = A_0 e^{i\psi_0}$, and a remainder $U_1 = A_1 e^{i\psi_1}$ which is due to the disturbance created by the object and may be called the secondary wave. Thus the complex amplitude at the photographic plate is

$$U = U_0 + U_1 = A_0 e^{i\psi_0} + A_1 e^{i\psi_1} = e^{i\psi_0} (A_0 + A_1 e^{i(\psi_1 - \psi_0)})$$

(1)

and its absolute value $A = \left[ A_0^2 + A_1^2 + 2 A_0 A_1 \cos (\psi_1 - \psi_0) \right]^{1/2}$.

From Gabor, 1949
Figure 1. Principle of electron microscopy by reconstructed wavefronts.

From Gabor, 1949.
HOLOGRAPHY principle

From Wikipedia
Figure 6. Taking a hologram. The object under investigation covers only half of the object plane, whereas the other half serves as a reference area. The reference wave as well as the object wave are imaged by the objective lens. Due to the wave transfer function, the object wave is changed so that the aberrated image wave is formed. The biprism deflects both parts of the wave towards each other, yielding the hologram in the overlapping region.
Figure 16. Dopant profiling. The alignment of the dopants with respect to the gate electrode is increasingly critical with increasing integration density. Holographic phase images allow the mapping of potential distribution arising due to doping. The dark and bright seam (arrows) shows the potential distribution with opposite sign in p-doped and n-doped MOSFETs, respectively.
Fig. 9. Magnetic lines inside and outside a recorded magnetic tape. Detailed magnetic lines observed under various conditions, such as tape material and spacing and gap of head, provide information about how higher density recording can be attained.

From Tonomura,
Fig. 6. Hexagonal cobalt particle. (a) Schematic. (b) Electron micrograph. (c) Interference micrograph (phase amplification × 2). Phase contours in interference micrograph (c) indicate magnetic lines in $h/2e$ flux units. Magnetic lines are circular inside the particle.

From Tonomura,
Electron Holography: mapping electric fields

Figure 8
Observation of a field-emitting carbon nanotube. \( a, b, \) and \( c \) show electron holograms at bias voltages \( V_B = 0 \) V, 70 V, and 120 V, respectively. \( d, e, \) and \( f \) show reconstructed phase images corresponding to \( a, b, \) and \( c, \) respectively. The phase contours correspond to a spacing of \( 2\pi \) radians. The phase gradient in \( f \) corresponds to an electric-field strength of \( \sim 1.2 \) V nm\(^{-1} \) at the tip of the nanotube (from Reference 89).
tomography / 3D imaging.

Holography was one method of getting "3D".

tomography uses method of reconstructed 2D projections.

i.e., one reads a series of "projection" images taken from different directions.

One does this in either Fourier space or Real space.

1st paper that performed this "reconstruction" in 1968

used Fourier proj. reconst.

- This works best for periodic objects.

Another method that is widely used, particularly for objects that may not have periodicity (or symmetry)
is the "back projection" method.

Based on the Radon transformation (rather than Fourier).

Johann Radon (1917).

Translated in 1986 "→ 官"


Radon transform → sinogram
Tomography

Tomography used in all radiation characterization methods.

Example:

X-ray absorption microscopy.

\[ I_{\text{in}} \xrightarrow{\text{beam}} I_{\text{out}} \]

\[ I(t) = e^{-\int_0^t (\mu \rho) \, dt} \]

\[ \text{the line integral of absorption over the thickness of the sample} \]

\[ \Rightarrow \text{you get a "projected" density map through the sample for each "view"} \]
The Radon transform

\[ f(x,y) \]

Fig. 1. The Radon transform \( R \) can be visualised as the integration through a body \( D \) in real space \( f(x,y) \) along all possible line integrals \( L \), with its normal at an angle \( \theta \) to the horizontal.
Rodan transform / \( Rf(l, \theta) = \int f(x,y) \, ds \)

integul "projeclion"

1. take series of projections thru object at diff \( \theta \) (for various \( l \)).

then "back-project" (inverse transform) to reconstuct orignal

note that the more projections you use, the closer you get to orignal object. // (same is true for Fourier space projections)

This means we need many "images" to reconstuct 3d object but once you have the 3d, you can then go back an look at any slice //

"good reviews!"

"bird!"

R. McIntosh, D. Nicoastro and D. Mastronarde.

How Back Projection Works (simplified)

take a 2x2 pixel tomogram

\[
\begin{array}{cc}
? & ? \\
? & ? \\
\end{array}
\]

+ rows

↑ columns

take two tilt projections / at 90° to each other

we measure \( \int f(x)dx \) across the rows or columns

example:

\[
\begin{array}{cc}
1 & 2 \\
3 & 4 \\
\end{array}
\]

\[\int f(x)dx = 1+2 = 3\]

\[\int f(x)dx = 2+4 = 6\]

so we can measure the "sum" of intensities
across each "tilt" direction - in this case, over the rows or columns.

the trick is to find out how these intensities are distributed.
**Back Projection**

Row sums → we measure this

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>?</td>
<td>?</td>
<td>11</td>
</tr>
</tbody>
</table>

Column sums: 8 10

Row sums: 3.5 3.5 | 3.5 + 3.5 = 7 ("I")
| 5.5 5.5 | 5.5 + 5.5 = 11 ("II")

Note: Column sums may not be original measured sums.

**Step 1. Back Project**
- Guess intensities equally distributed
- Do it for the rows

: 1st guess: Initial row sum | \( \frac{7}{2} = 3.5 \)
# pixels summed | \( \frac{11}{2} = 5.5 \)

**Step 2. Back Project**
- Do the same for column sums.

1st Initial column sum | \( \frac{8}{2} = 4 \)
# pixels summed | \( \frac{10}{2} = 5 \)

Add to 1st guess.
Back Projection (mt)

Step 2. (mt)

\[
\begin{array}{ccc}
5.5 & 3.5 & ("I") \\
4.0 & 4.0 & ("II") \\
\end{array}
\]

(row sum)

Original values

(column sum) (8) (10)

Original values

Step 3. Add up each row, column

Subtract that from original (measured) sums.

\[
\begin{array}{ccc}
7.5 & 8.5 & 7-16 = -9 \\
9.5 & 10.5 & 11-20 = -9 \\
\end{array}
\]

(row sum (new))

Original values

(column sum) (8) (10)

Step 4. Divide row row sum by # pixels

\[10, -9/2 = -4.5\]

And add this to our "guess"

\[
\begin{array}{ccc}
7.5 & 8.5 & \\
-4.5 & -4.5 & \\
9.5 & 14.5 & -4.5 \\
\end{array}
\]

(column sum)

Row sum

\[
\begin{array}{cc}
3 & 4 \\
5 & 6 \\
\end{array}
\]

Next guess

At the elements
**Back Projection:**

**Step 5:** Now add densities of each column and subtract from original column sum (8, 10)

<table>
<thead>
<tr>
<th>3</th>
<th>4</th>
<th>3</th>
<th>4</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

**New Column Sum:** 8, 10

**Step 6:** Add the new column sum divided by # pixels to the row sum

\[
\frac{0}{2} = 0 \text{ etc.}
\]

**Row Sum:**

<table>
<thead>
<tr>
<th>3</th>
<th>4</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

**Column Sum:**

| 8 | 10 |

- The rows match the original.
- The iteration stops.
- Reconstruction is complete!

---

In a typical EM or optical tomogram, there could be 50-100 projections each with 14-1 M pixels or more.

\[\text{\therefore a tomogram would contain } > 10^8 \text{ pixels!}\]
Tomography

Tomography used in all radiation characterization methods.

Example:
X-ray absorption microscopy.

\[
\frac{I_{in}}{I(t)} = e^{-\int_0^t (\mu p) dt}
\]

the line integral of absorption over the thickness of the sample

\[\therefore \text{you get a "projected" density map through the sample for each "view".}\]
Figure 1. Principles of ET. (a) A biological specimen, in this case a bacteriophage contained in an EM sample holder, can be imaged from several orientations by tilting the holder in the microscope. (b) Process of computed back-projection, in which each tilted view is used to contribute to a reconstruction of the original structure. (c) Example of a 2D image (the face of Goethe), representing a slice cut from a 3D object in a plane perpendicular to the tilt axis. (d) Projection of the 2D object as a 1D distribution of densities reflecting the summation of all of the brightness in the picture along a set of vertical lines. (e) Reconstruction of Goethe's face achieved by back-projecting 90 of the 1D projections taken at 2° intervals between +90° and −90° from the horizontal. The ripples in the image represent the resolution limitation caused by having only 90 images. Twice the number of images taken at half the tilt increment would reduce the size of the ripples by approximately twofold. (f) A further limitation on resolution is imposed by reconstructing the image from a more restricted range of tilted views taken between +60° and −60° from the horizontal. Because a wedge of data is missing, the reconstruction quality is anisotropically degraded. The vertical detail is still sharp (note the clarity of the shoulders, the nose and the ear); by contrast, the horizontal detail is poorly defined (note the virtual absence of a mouth). This kind of anisotropy is characteristic of single-axis tomograms constructed from data collected from a limited range of tilt.
Goethe Projections

R. McIntosh, et al. 2005
- Demonstration of the FBP algorithm:
Fig. 8. (a) A montage in which each image is a voxel projection of the 3D reconstruction of an MCM41-Pd₆Ru₆ catalyst viewed at angles shown in the figure. The 3D structure of the mesopores is well resolved. The nanoparticles are coloured red to improve clarity.
MC41-Pd₆Ru₆ catalyst (HAADF signal)

Midgley and Weyland. 2003
Some references

Tomography:


Holography:
Leith and Upatnicks. JOSA. 52.pp 1123-1130.


What are the Limits in Determining Three Dimensional Structure By Electron Microscopy?
Radiation damage due to the large number of exposures needed
"damage" due to electron collisions. //

1. "elastic"

pure kinematics

\[ \frac{E}{E_0} = K = \left[ \frac{x \cos \theta + \sqrt{1 - x^2 \sin^2 \theta}}{1 + x} \right]^2 \]

\[ X = \frac{M_0}{M} = \frac{M_e}{A_{mp}} \]

when \( M_0 = M_e \), \( M = A_{mp} \) then \( X = \frac{1}{1837A} = \frac{M_e}{A_{mp}} \)

so since \( X \ll 1 \) we get

\[ \frac{E}{E_0} = 1 - \frac{(1 - \cos \theta)}{918A} \]

or \[ \Delta E (\text{to atom}) = \frac{1 - \cos \theta}{E_0} \]

Max energy transferred to atom is:

\[ \Delta E_{\text{max}} = \frac{2E_0}{918A} = 4 \frac{m_e}{A_{mp}} \cdot E_0 \]

\[ E_{\text{max}} = \frac{2m_e E_0 (E_0^2 + 2m_e^2)}{A_{mp} m_e^2} \]

relativistically

NOTE: Energy transferred to atom depends upon the eluc energy (linearly non-relativistically)

Kilowin ~ 50-60 keV
5% at 50 keV
20% at 100 keV
the recoil energy to the atom is in general:

$$E_{\text{recoil}} = E_{\text{max}} \left[ \sin \left( \frac{\theta}{2} \right) \right]^2$$

...the mutual scatt & which results in atomic displacement of the atom is:

$$\sin \left( \frac{\theta_c}{2} \right) = \sqrt{\frac{E_{\text{disp}}}{E_{\text{max}}}}$$

...energy to displace atom

\[ \text{if } E_{\text{recoil}} > E_{\text{disp}} \text{ the atom gets displaced} \]

we can get the "cross section" for displacement:

$$\sigma_{\text{disp}} = \int_{\theta_c}^{\pi} \frac{d\sigma_{\text{disp}}}{d\theta} \sin \theta \, d\theta$$

$$P_{\text{disp}} = \frac{\sigma_{\text{disp}}}{\pi R^2}$$

Huckman

and going back, we can get the threshold energy for an inc. electron to displace an atom bound by $E_D$:

$$E_{\text{threshold}} = m_e c^2 \left[ \left( 1 + \frac{A m_p E_{\text{disp}}}{2 m_e m_e c^2} \right)^{1/2} - 1 \right]$$

rel, correct

Look at plots as to what this means for KO damage by electrons / steep threshold then relatively instant with energy $E_D$
Fig. 1.2 A. The maximum energy which can be transferred by an incident electron of kinetic energy $E_0$, in an elastic nuclear collision with an atom of mass $A$. $E_{\text{max}} = \frac{2(m/m_A)}{E_0(E_0 + 2mc^2)/mc^2}$, where $m$ is the electron rest mass, $m_p$ is the proton rest mass and $c$ is the velocity of light ($M_A = m_p \cdot A$). B. The threshold energy of the incident electron, $E_t$, necessary just to produce a displacement of an atom of mass $A$ in an elastic nuclear collision. The term $E_t$ is that energy such that the maximum transferable energy shown in Fig. 1.2A is equal to the displacement energy, $E_d$. The arrows indicate the threshold energies for various atoms assuming $E_d = 1 \text{ eV}$. 
Fig. 1.2 (Continued)
Figure 1. Dependence of sputtering threshold on the atomic number (Hobbs 1987).
there is other types of "damage" due to "inelastic events"

ie., ionization events, where we lose electrons
from the atoms thereby breaking & altering bonds.

2. "inelastic"

in this case, if there is an energy loss (in the e-e collision)

> 1/2 band energy, we can break a bond.

this tends to be more prominent for low Z materials,

but probability decreases as energy goes up
since \( \sin \theta \propto \frac{1}{E_0} \) near, \( E_0 \)

in fact when \( E_0 < E_{thres} \),

for 110 displacement
rel. scatt is dominant
mechanism for damage.

---

ASIDE/

when discussing damage by charged
particles we talk about a "dose"

which is a "charge density" in charge/unit area.

ie., \( J \tau = \Phi \)

current density \( \overarc{\text{time}} \)

\[ 1 \text{\,uA/cm}^2 = 625 \text{elec/}\text{A}^2 \]
\[ E_{\text{Auger}} \approx E_K - E_{L_2} - E_{L_3} \]

- \text{fills open state}

- violent rearrangement of electron cloud can transfer energy to atom \rightarrow \text{gets displaced}

- KO time negative
example, Rohrlich and Carlson, 1954) is within a few percent of that given in Eq. (1.18). So it makes little difference with regard to the energy dependence of damage whether one compares experiments with stopping power calculations or the inelastic scattering cross sections.

![Graph showing relative damage dose vs. energy dependency of electron beam damage.](image)

\[ \delta = \frac{1}{\sqrt{1-\beta^2}}, \quad \beta = \frac{N}{C} \]

Isaacson, 1970
before looking at different "forms" of damage. Let us signals needed to collect information

\[ S = N \sum_i Y \phi \]  
signal rate

want for time \( T \), then

\[ S_T = N (J \gamma) \gamma \phi \]
the "dose" \( D \)

\[ D = \frac{S_T}{N \phi \gamma} \]  
contribution to signal event "detected"

\[ \text{dose delivered is} \]

\[ D_{\text{min}} = \frac{(S_T)_{\text{min}}}{N \phi \gamma} < D_{\text{damage}} \]
if we want to "destroy" the object

the fewer atoms/molecules detected,
the higher the dose needed to detect them!"
Table 1
Electron beam irradiation damage \(^\text{a})\): \(E_0 = 100\) keV, room temperature

<table>
<thead>
<tr>
<th>Observation</th>
<th>Dose (electrons/(\AA^2))</th>
<th>Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffraction</td>
<td>(&lt; 1)</td>
<td>Nitrocellulose</td>
</tr>
<tr>
<td></td>
<td>(1 - 10)</td>
<td>Aliphatics</td>
</tr>
<tr>
<td></td>
<td>(10^2 - 10^4)</td>
<td>Aromatics</td>
</tr>
<tr>
<td></td>
<td>(1 - 10^6)</td>
<td>Metal halides</td>
</tr>
<tr>
<td>Mass loss</td>
<td>(1 - 10^3)</td>
<td>Organics</td>
</tr>
<tr>
<td></td>
<td>(1 - 10^6)</td>
<td>Metal halides</td>
</tr>
<tr>
<td></td>
<td>(10 - 10^6)</td>
<td>Fluorine desorption</td>
</tr>
<tr>
<td></td>
<td>(10^2 - 10^9)</td>
<td>Oxygen desorption</td>
</tr>
<tr>
<td>EELS change</td>
<td>(10^{-1})</td>
<td>PMMA</td>
</tr>
<tr>
<td></td>
<td>(= 10)</td>
<td>Aliphatics</td>
</tr>
<tr>
<td></td>
<td>(1 - 10^3)</td>
<td>Metal halides</td>
</tr>
<tr>
<td></td>
<td>(10^3 - 10^{10})</td>
<td>Oxides</td>
</tr>
</tbody>
</table>

\(^a\) Data from this table come from the reviews in refs. [2,3], as well as from other articles in the literature (e.g., refs. [4,6,10,11,13,18]). The doses have been scaled to correspond to an incident electron energy of 100 keV. I have not listed dose rate or ambient conditions, since in most cases these were not reported.
Look at a typical organic material damage. L-hist/amin acid.
- x-ray intensity/Dy = 11 / 0.5 eV/Å
- mass / Dy e = 5 eV / Å²
- energy loss (amorphous) Dy e = 23 eV / Å² (25 keV)

whereas for non-organic materials
the doses may be many orders of magnitude greater.

eg atom imaging conditions could result in
J ≈ \frac{1}{2} \times 10^{-8} \text{amps/Å² sec}
\sim 3 \times 10^3 \text{elec/sec Å²} \rightarrow
with 4 μs/pxel \rightarrow 1200 \text{elec/Å²/pixel}
and still see no "evidence" of damage.

never there may be dose-rate effects; i.e. not total dose
but rate is more important! — see example LiF

sometimes damage correlated with
"imaging" damage (which can result in "equiv to" patterned
or direct nucleation)

damage is very material dependent —
if KO damage is a problem \Rightarrow image at Inner Inc. energies
1st let's look at the "does" for damage
2nd let's see how to reduce that effect.

1. different "types" of beam induced damage.
   - loss of crystallinity (my range order)
   - loss of mass (i.e., sputtering by KO receptor)
   - local structural disorder

Each one has a different characteristic
or rather how the damage proceeds with increasing dose
- in a single hit model (i.e., one event damages)
  the damage is an exponential decay with dose
  \[ I(t) = \frac{I_0}{D/D_0} e^{-D/D_0} \]
where \( D = Jt \)

- if more than one event is required to damage,
  there would be a "latent" dose

- an interesting sometimes one refers to "end pt" dose, \( D_{ept} \)
  where \( D_{ept} \) would be \( (2-5)\times D_{ave} \)
  the main pt is \( D_{ept} > D_{ave} > D_{distant} \)

- D's can vary by orders of magnitude
Fig. 1. An example of a grating structure directly etched into lithium fluoride by a 100 keV electron beam using a dose of $10^{-2}$ C/cm$^2$. The dose rate was about $5 \times 10^5$ A/cm$^2$, the sample was at 30°C and the vacuum in the sample chamber was $8 \times 10^{-10}$ Torr. The grating periodicity is 3.7 nm. Such a structure cannot be produced with dose rates less than $10^4$ A/cm$^2$. 
reduction of damage

1. spatial averaging methods
   - i.e., correlation techniques to "average" individual structures
   - xtal structures whereby you record image 3 diff. patterns
     giving you mag and phase.
     (can use many images.)

2. cryotemps.
   - slow down thermal motion / variable
   - prevent vaporization / effects
   - frozen in plane

3. "proteins" (in biological samples)

4. lower the energy of inc. beam
   - if KO is a problem
   - a balancing act between KO and injection.
GroEL / a chaperonin - found in bacteria

size - around 15 nm/

Vossmann, 2008
Single particle analysis segments and averages many particles from a sample, allowing for computer algorithms to process the individual images into a combined "representative" image. This allows for improvements in signal to noise, and can be combined with deconvolution to provide limited improvements to spatial resolution in the image.

Tomographic reconstruction

GroEL (side)

GroEL (top)

\[ \sim 15 \text{nm} \]