The Potential for *In situ* Transmission Electron Microscopy (TEM) of Electron and Ion Irradiation of Living Cells

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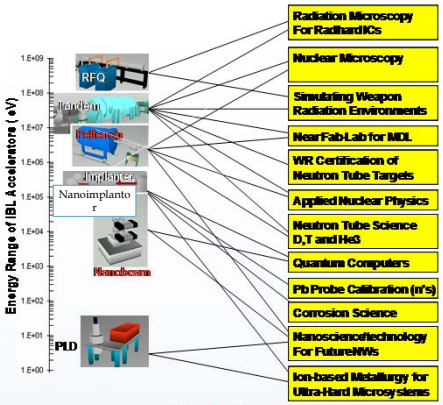
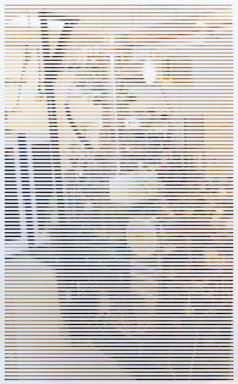
Ion Beam Lab Capabilities

Sandia's Ne Ion Beam Lab



Nanoimplantor

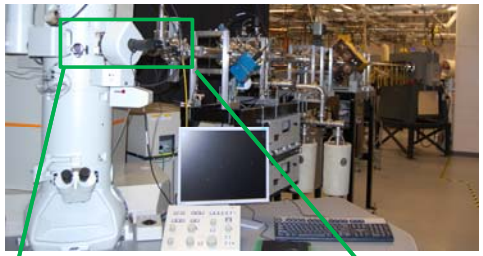


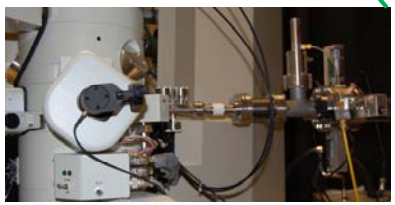
- multiple liquid metal ion source (LMIS)
- an *E* x *B* filter
- 10 nm spot size
- an ion column with a maximum accelerating voltage of 100 kV
- a high-resolution electron column

These capabilities greatly exceed the capabilities of commercially available Ga^+-based dual-beam systems in terms of irradiation doses, ion species, and nanofabrication.

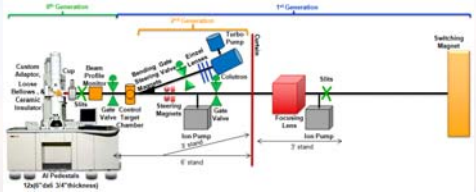
In situ TEM Ion Irradiation

In situ TEM triple beam facility





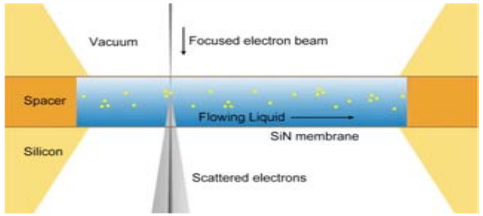
- This is only one of 11 facility world wide and only the second in the US.
- This one is better suited than the others for tomography and imaging of biological samples due to the wide polepiece gap and the single electron sensitive CCD camera.
- The facility is being developed to permit irradiation with electrons, protons, alpha particles, and a suite of heavy ions.
- The ion energy range is being developed to operate from 1 keV to 30 MeV.



- A schematic of the TEM beamline and its components
- Great care was taken in the development of the in-situ ion irradiation TEM to permit vacuum, electrical, mechanical isolation.
- The beamline is currently being developed to permit simultaneous concurrent implantation of protons, alpha particles, and heavy ions on the same location of a TEM specimen using a 6MeV Tandem and a 10 keV Colutron

In situ TEM Environmental stages

Fluid cell with microfluidic mixing and heating

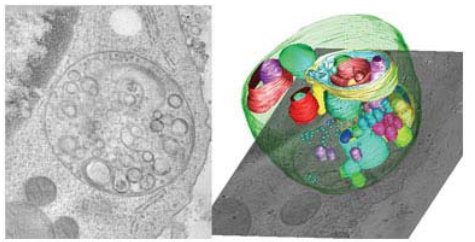


- A microfluidic stage purchased from Protochips Inc has been purchased that permits the mixing of two microfluidic channels at elevated temperatures.
- This permits real time nanoscale observations of the interaction of materials in aqueous or other solutions.

Vapor cell with up to 1 atm pressure and heating

- Permits real time observation of the interaction that occurs at a solid – vapor interface at ambient temperature through 1200 ºC
- TEM images have been collected of samples as they were exposed to room air at standard temperature and pressure.

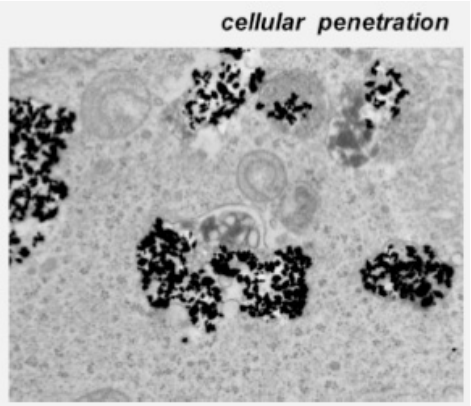
3D tomography



- Image from A.J. Koster and W.J.C. Geerts at Utrecht University
- We have the hardware and software for 3D electron tomography of similar cells. Including cells that are interacting with nanoparticles.
- We have done 3D electron tomography on nanoparticles

Potential for *in situ* research

Ex situ experiments in Literature



- Image from NanoBiotix, a commercial company that uses nanoparticles to enhance X-ray absorption by targeted tumors
- We could do similar investigations in real time

Conclusions

Fundamental Understanding of the Mechanisms Governing Nanoparticle Uptake and Irradiation Damage in Targeted Cells

- The recent capabilities developed at the Ion Beam Lab should permit the **potential for** direct real time observation at the nanoscale of:
  1. The uptake of nanoparticles by living cells as a function of cell and nanoparticle parameters.
  2. The death of the cell structure as exposed to electron and ion irradiation.
  3. 3D reconstruction of a cell during phases of both process

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