MIMMA – A MEV ION MICROSCOPE FOR BIOMEDICAL AND MATERIALS RESEARCH

Harry J. Whitlow[1], Varpu Marjomäki[2] and Leona Gilbert[2]

[1] Department of Physics University of Jyväskylä

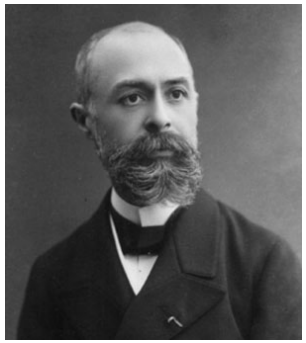
[2]Department of Environmental and Biological Sciences, University of Jyväskylä

THE IDEA

Take three Nobel prize winning discoveries and mix with some inovations from Jyväslylä.....

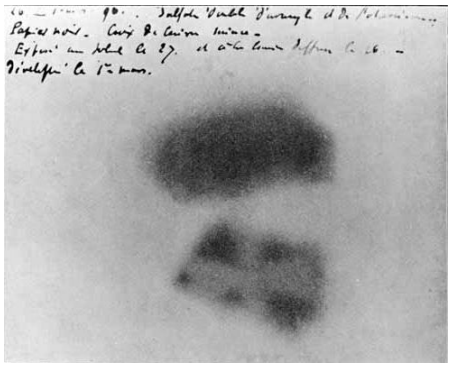
THE BASIS OF MEV ION BEAM LITHOGRAPHY

Two physics Nobel Prize winning discoveries



H. Becquerel

½ 1903 years Nobel Prize in Physics "*in recognition of the extraordinary services he has rendered by his discovery of spontaneous radioactivity*"



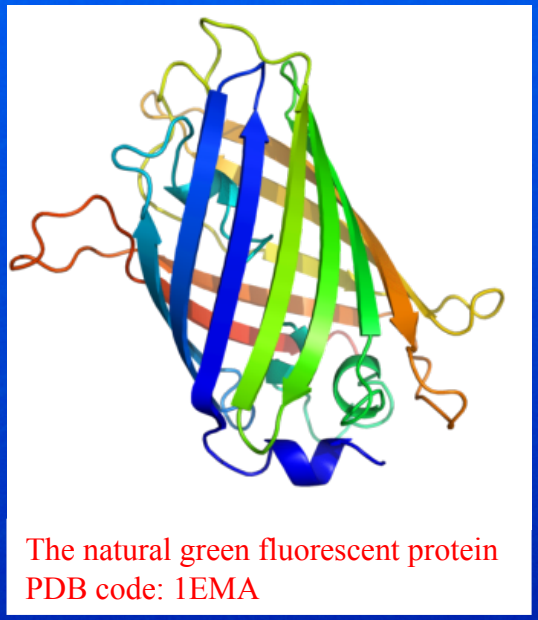
A. H. Becquerel, *Comptes Rendus* 122, (1896)420.

C.T.R Wilson

½ 1927 years Nobel Prize in Physics "*for his method of making the paths of electrically charged particles visible by condensation of vapour*"

P. Blackett (1925) Proc. Roy. Soc., A, vol. 107, Pl.6.

2008 NOBEL PRIZE IN CHEMISTRY



The natural green fluorescent protein
PDB code: 1EMA

Aequorea victoria
From Wikpedia

Osamu Shimomura , Martin Chalfie , Roger Y. Tsien "f*or the discovery and development of the green fluorescent protein, GFP*"

WHY MIMMA?

The resolution of most light microcopes is limited by the Abbe Criteria

$$h = \frac{0.61\lambda}{n \sin\theta}$$

$$h = \sim 210\ \text{nm}$$

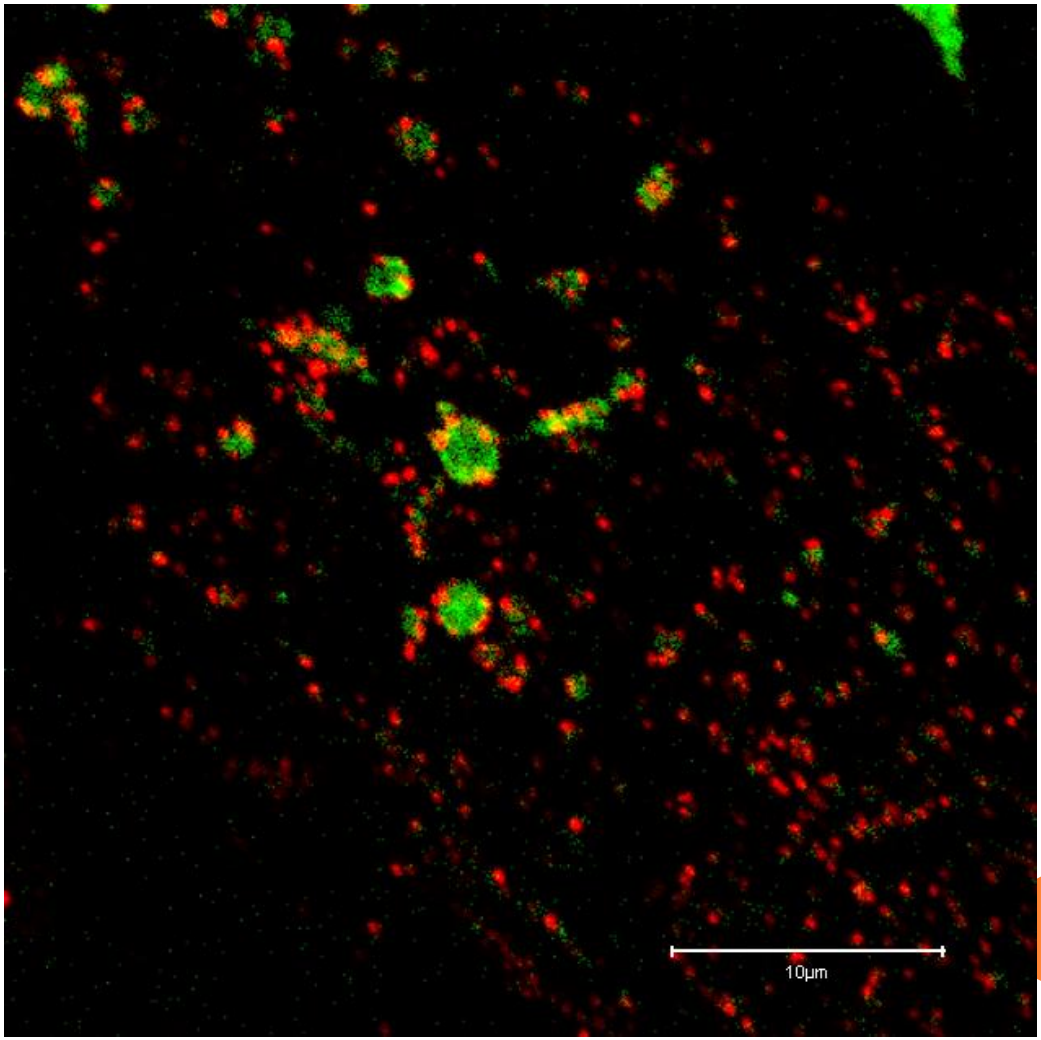
In MIMMA we use MeV ions instead of UV light to breakthrough this barrier.

This will improve the available physiological information from cells and organelles.

Courtesy of the Clendening History of Medicine Library, University of Kansas Medical Center.

FLUORESCENCE CONFOCAL MICROSCOPY

Fluorescent groups called fluorophores can be attached to antibodies that combine with a specific biomolecule. The location of these proteins in the cell can then be observed from their fluorescence under uv light

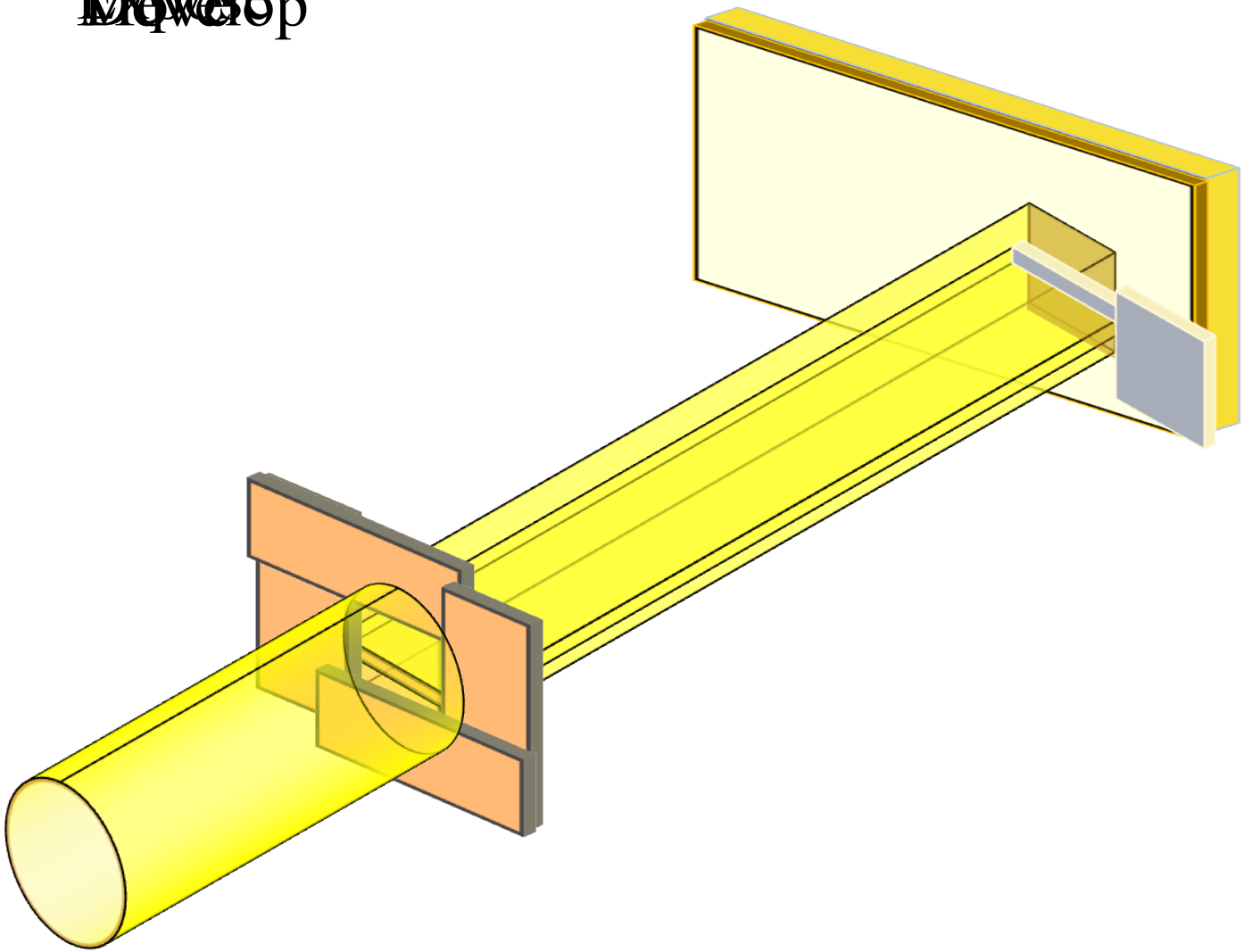


Confocal microscopy image of a human cell showing different location of two proteins in endosomes (V. Majomäki)

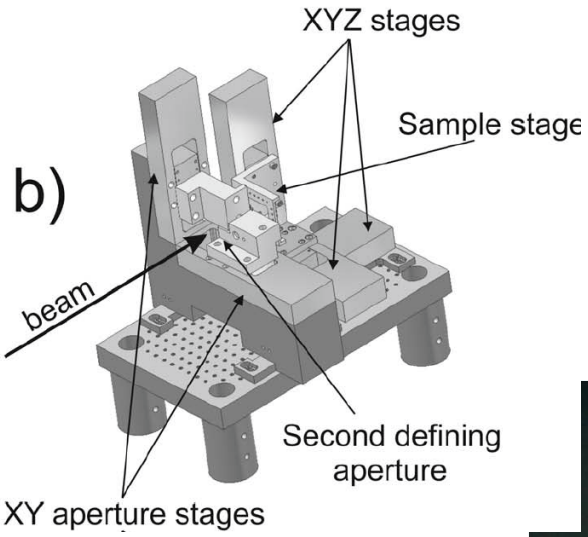
A RADICALLY DIFFERENT IDEA

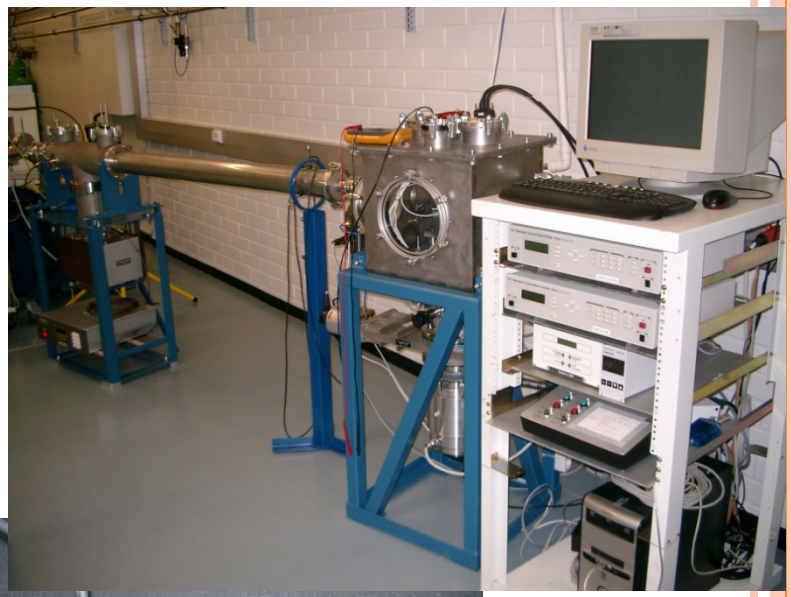
- In flourescence confocal microscopy the the target fluorphores are excited by short wavelength (~400 nm) light.
- In MIMMA MeV ions excite fluorophores within a 2-5 nm region.
- Resolution is no longer limited by the Abbe criteria

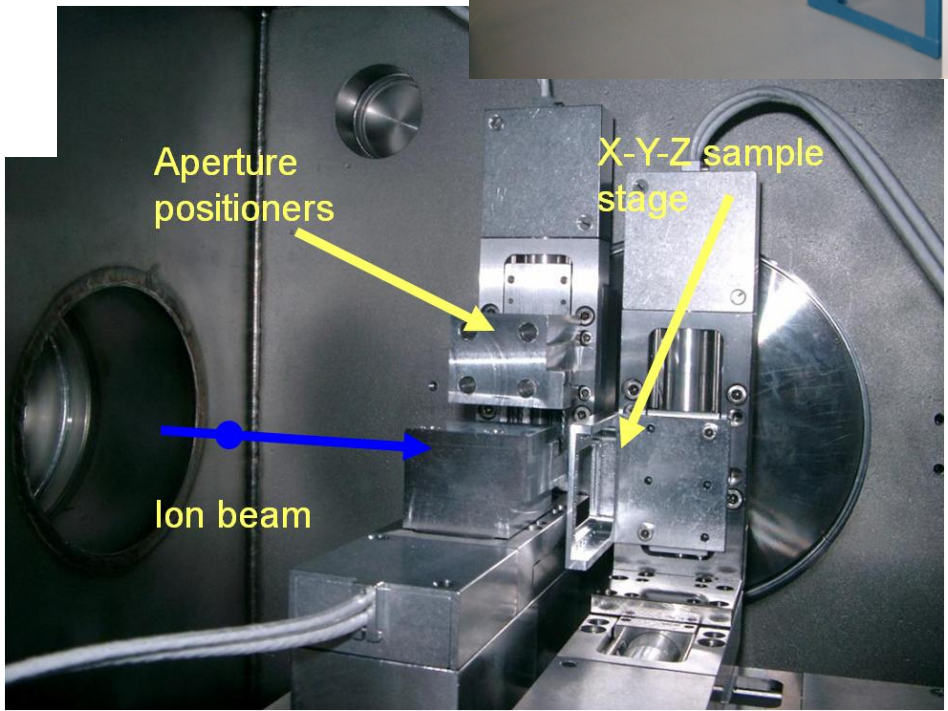
LITHOGRAPHY WITH SHAPED BEAMS



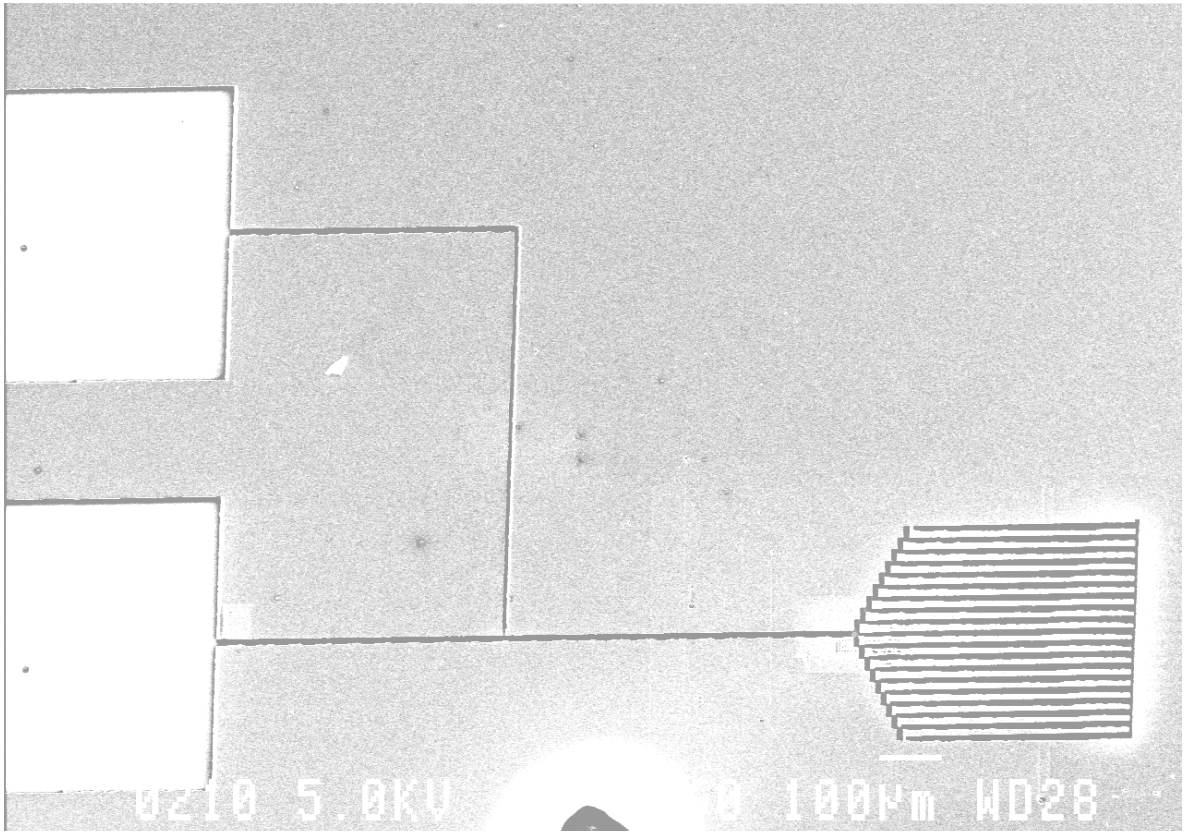
JYVÄSKYLÄ MEV ION BEAM LITHOGRAPHY SYSTEM





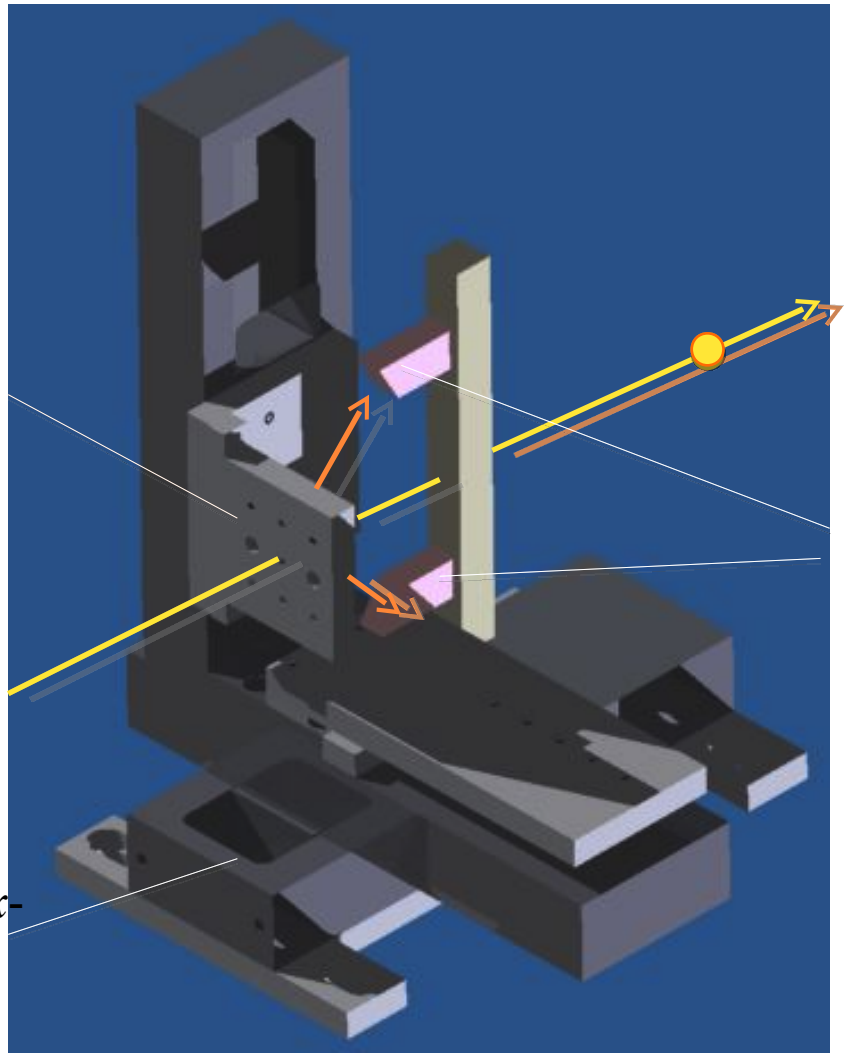


PROTOTYPE μ-FLUIDICS LOC DEVICE



L.P. Wang, L. Gilbert, R. Norarat and H. J. Whitlow
(unpublished results)

MIMMA TARGET AND DETECTOR SYSTEM



MeV ion path

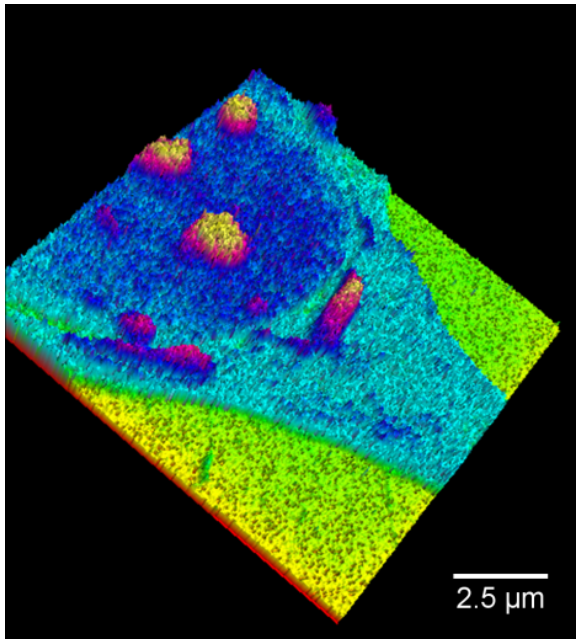
Sample holder
For TEM grid
specimens

Compact solid stage
Photomultiplier
fluorescence light
detectors

Existing *x*-
y-*z*
stage

INNOVATIONS

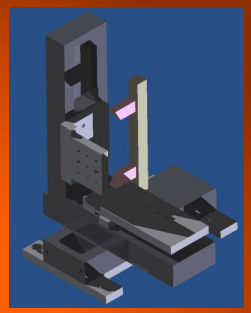
- Uses radically different physics to bust through the diffraction-limit
- Able to work with whole cells
- Uses conventional optical fluorescence confocal microscopy flurophores and dyes
- Extension to 3D nanotormography is straightforward
- Low-cost: Expensive ion or light lenses are not required.
- Advanced optical image processing gives high speed and resolution data collection.



Structural image of human cell taken using 1 MeV He^{+}

MIMMA AND DREAM

MIMMA



Ion Lens

Nov. 2009

Lithography

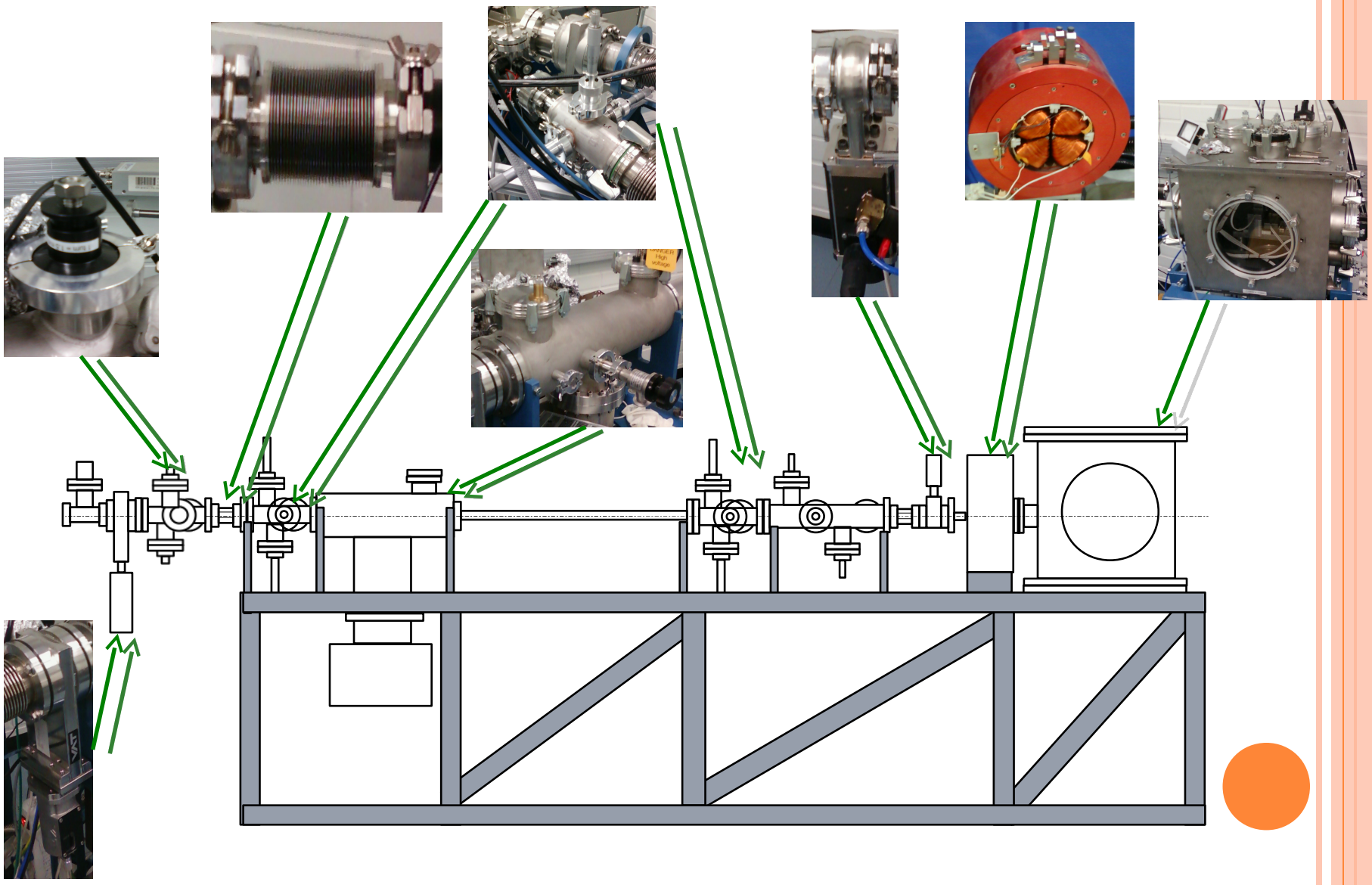
Jan. 2008

DREAM

Biomedical PIXE project 1, 2, 3,….

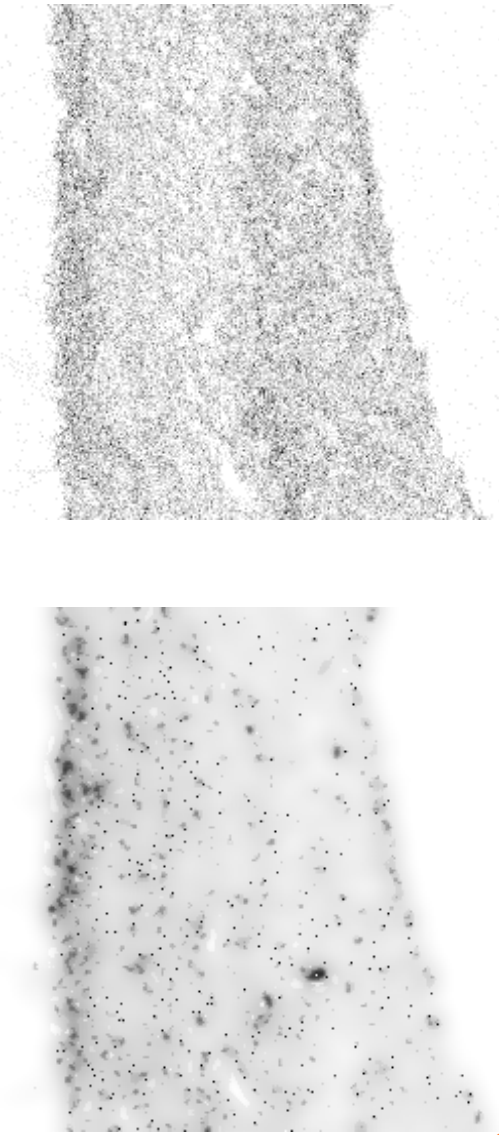
Lithography project 1, 2, 3,….

DREAM Construction



DREAM INOVATIONS

- First MeV ion microbeam to use time-stamped data collection time resolved studies
- First use of thermal-expansion compensated support system
- First with solid state photomultipliers
- First MeV ion microbeam with scan system for multi-resolution supported imaging.



Ca maps in rabbit aorta.
Top: raw data, Bottom wavelet filtered
Data from M.Q. Ren

COMMERCALISATION

- Develop MIMMA concept to prototype
- Develop MeV ion beam lithography (5 groups interested)
  - Make TEKES application

- Marketable developments
  - MeV ion beam lithography system
  - Bipolar high voltage amplifier with ± 1750 V differential outputs (Wide application)
  - Compact electrostatic deflector
  - Time-stamping data acquisition system for time dispersive ion microbeam measurements
  - Autofocus procedure for microbeam quadrupoles

THE END

People involved:

H.J. Whitlow, V. Marjomäki, Leona Gilbert

L.P. Wang, R. Norarat