Direct Detection of Electrons in a 525 by 525 pixel CMOS Sensor

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Cryo-Electron Microscopy

1. Aim: To image molecules in native aqueous environment, i.e in a hydrated form, in vitreous ice.
2. In older, lower resolution method, viz. negative staining, specimen coated with a heavy atom, e.g. uranyl
3. Trap important conformations by rapid freezing : equivalent to time-resolved measurements
4. Low contrast : need lots of averaging

Scientific Background

Three Main types of Analysis and resolution:

1. **Single Particle Analysis 7-10 Å**

2. **Electron Crystallography of ordered specimen, i.e. 2-D crystals ~3Å (in plane of crystal)**

3. **Electron Tomography ~100 Å**

Single Particle Analysis

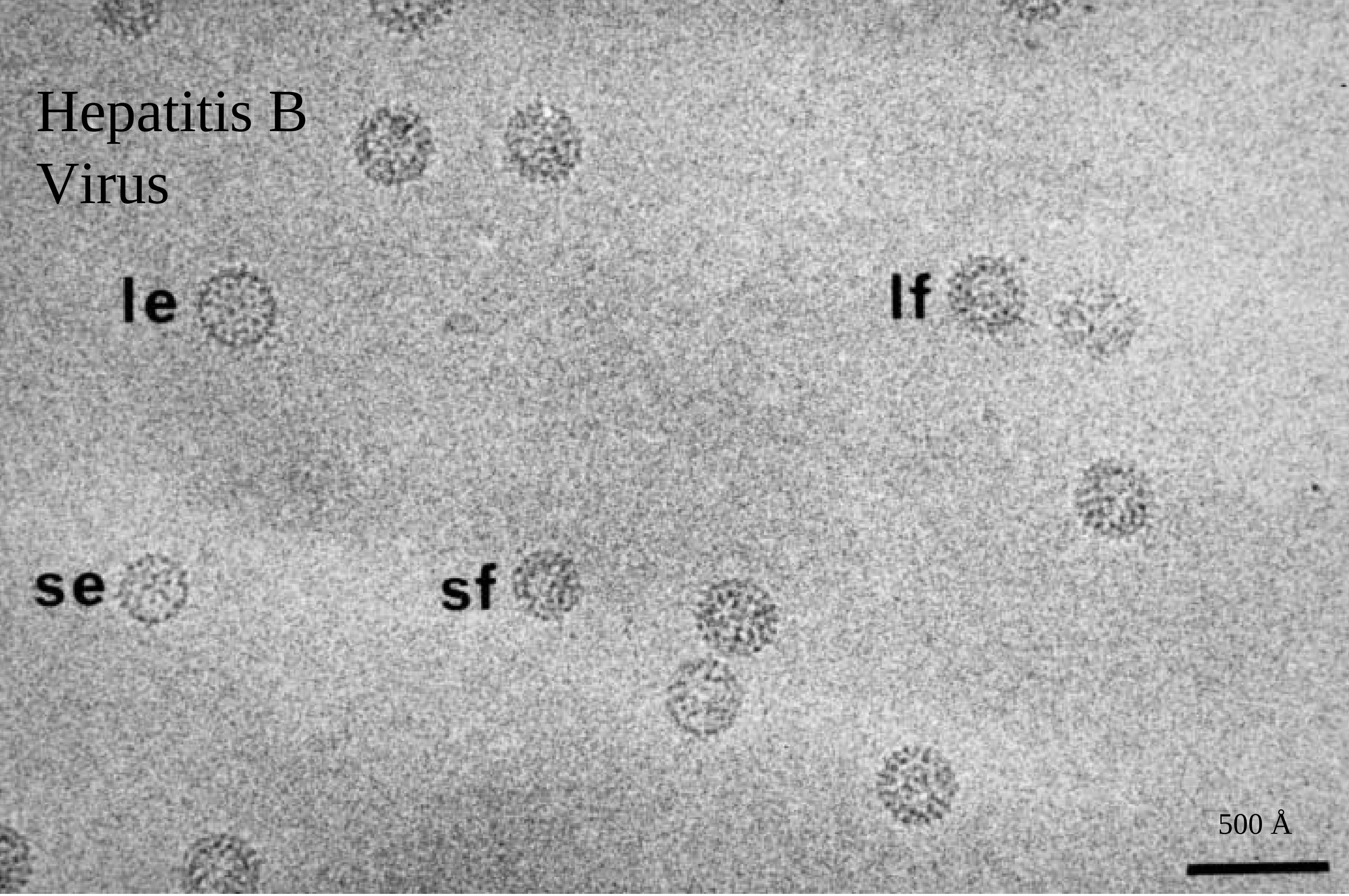
- Applied to large complexes, viz.
  Virus particles, ribosomes, etc

- Resolution 7.4 Å

- Need many views for averaging

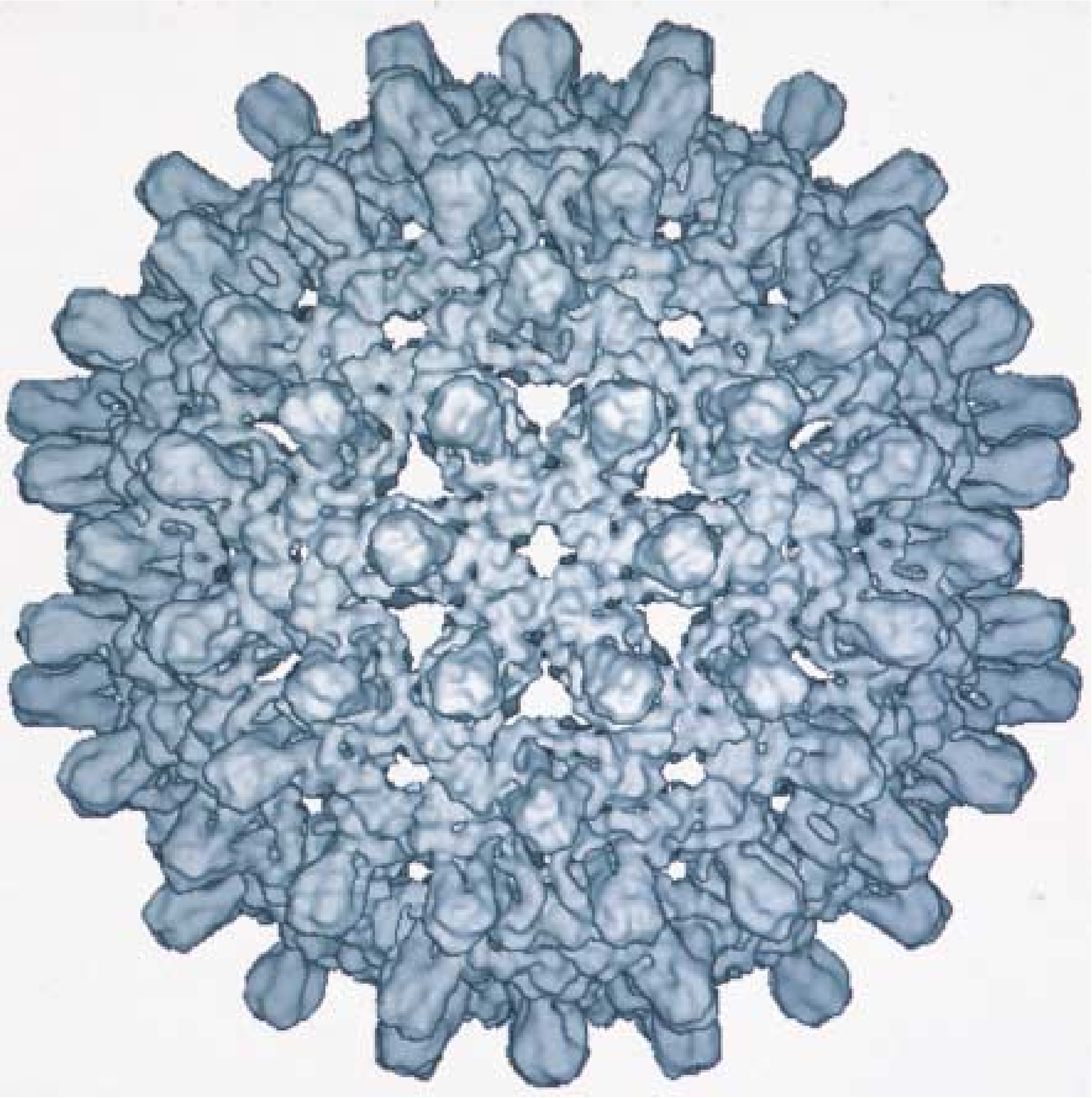
- No crystals required

Hepatitis B Virus



Bottcher,Wynne&Crowther Nature **386**,88-91 (1997)

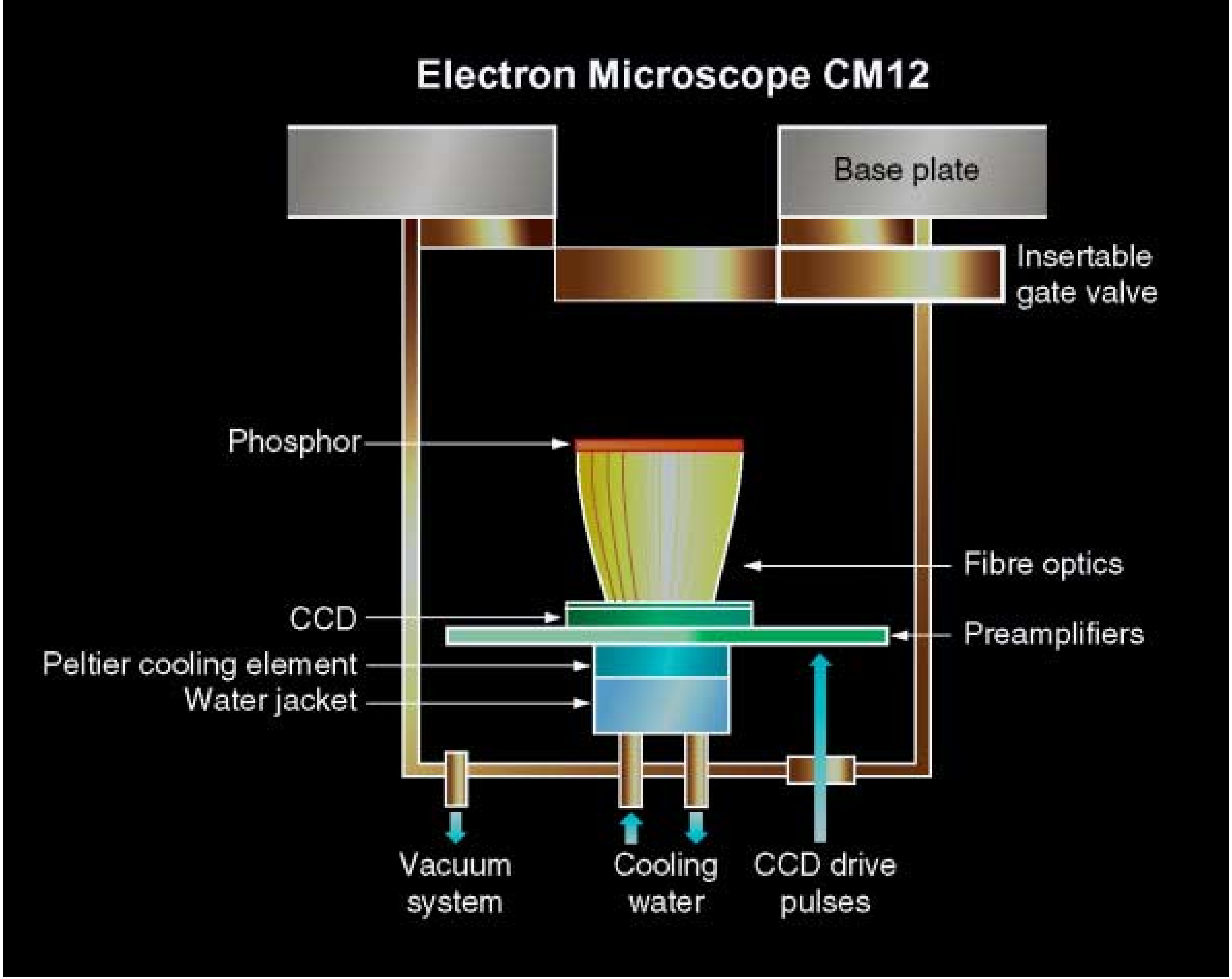
Hepatitis B Virus



Bottcher, Wynne & Crowther
Nature 386, 88-91, 1997

Electron Crystallography

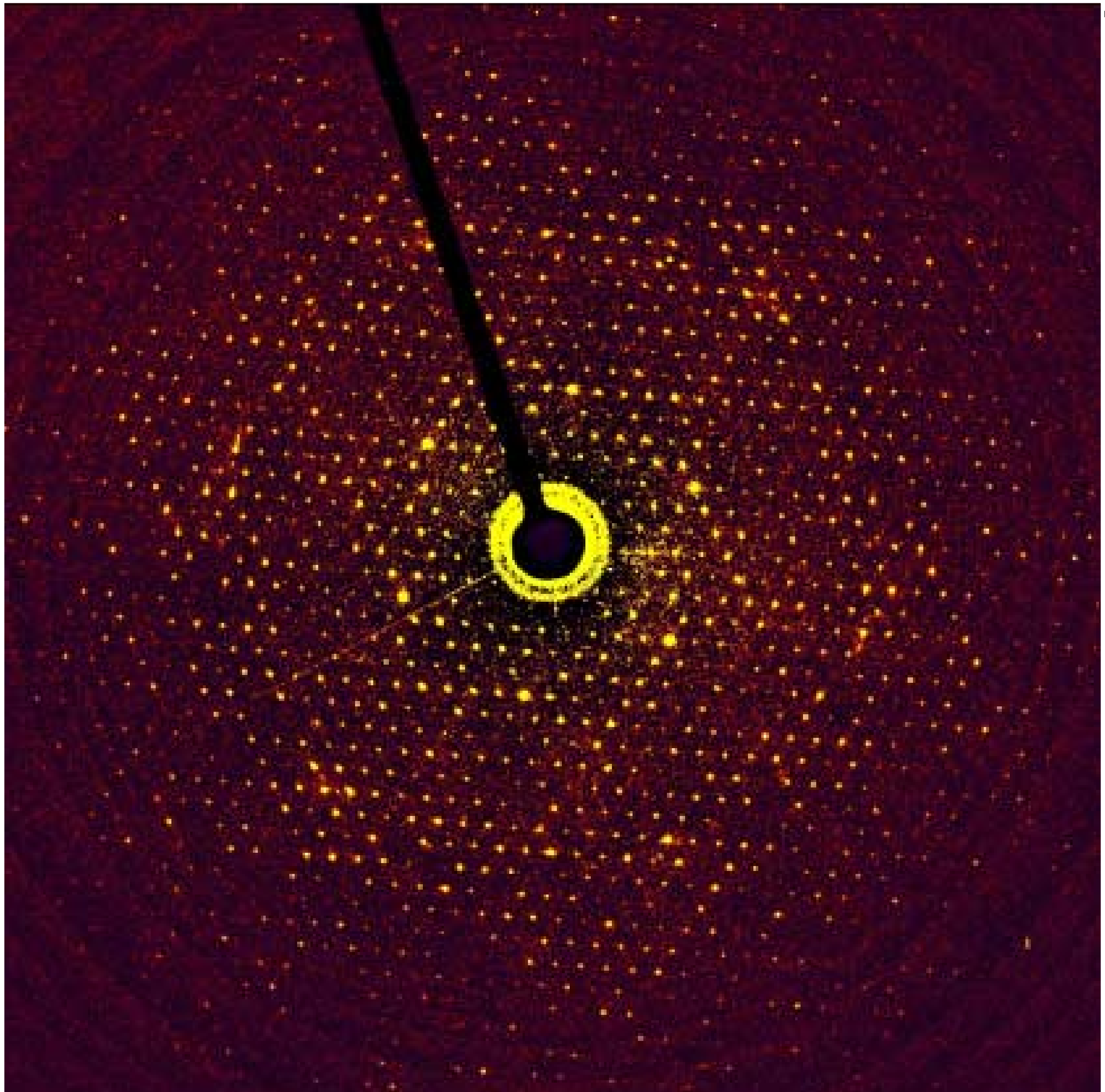
- 2-D crystals required
- Averaging done in crystal
- Main application: membrane proteins (but not exclusively)
- Near-atomic resolution (~2.5 Å).



Faruqi & Andrews NIM A392,233-236 (1997)

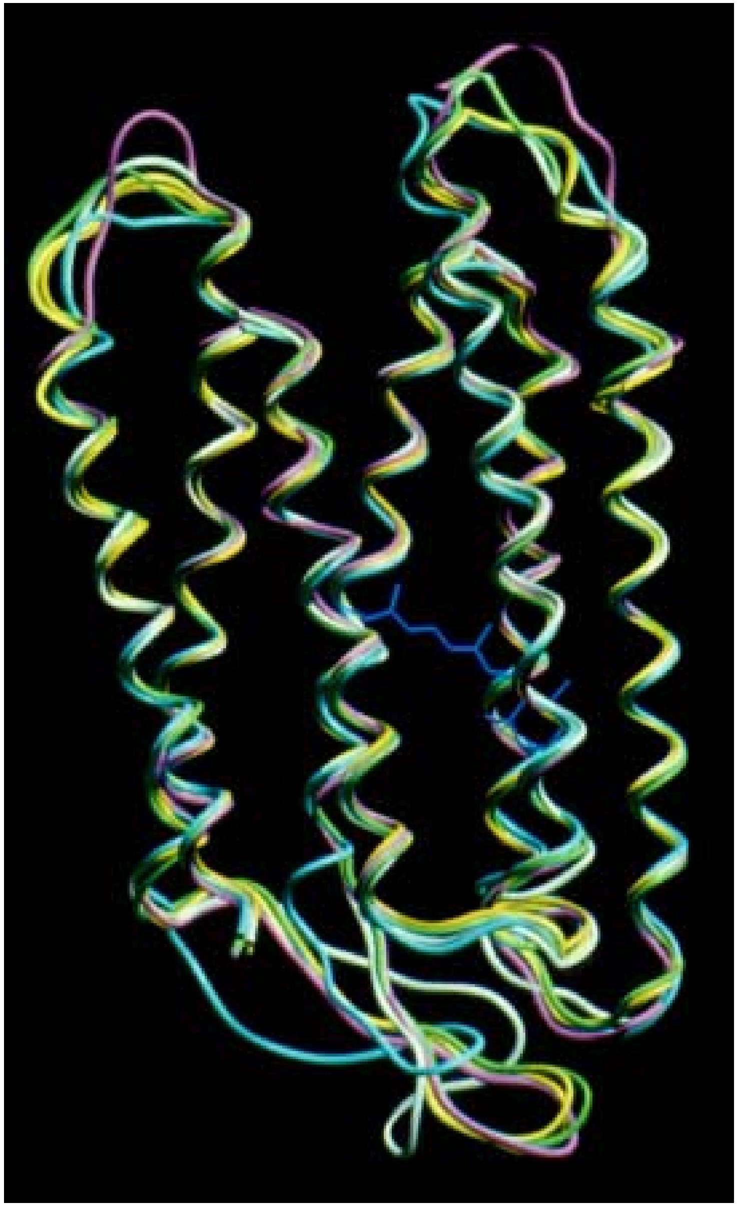
Electron Diffraction Studies on Bacteriorhodopsin

(with R.Henderson and S. Subramaniam)

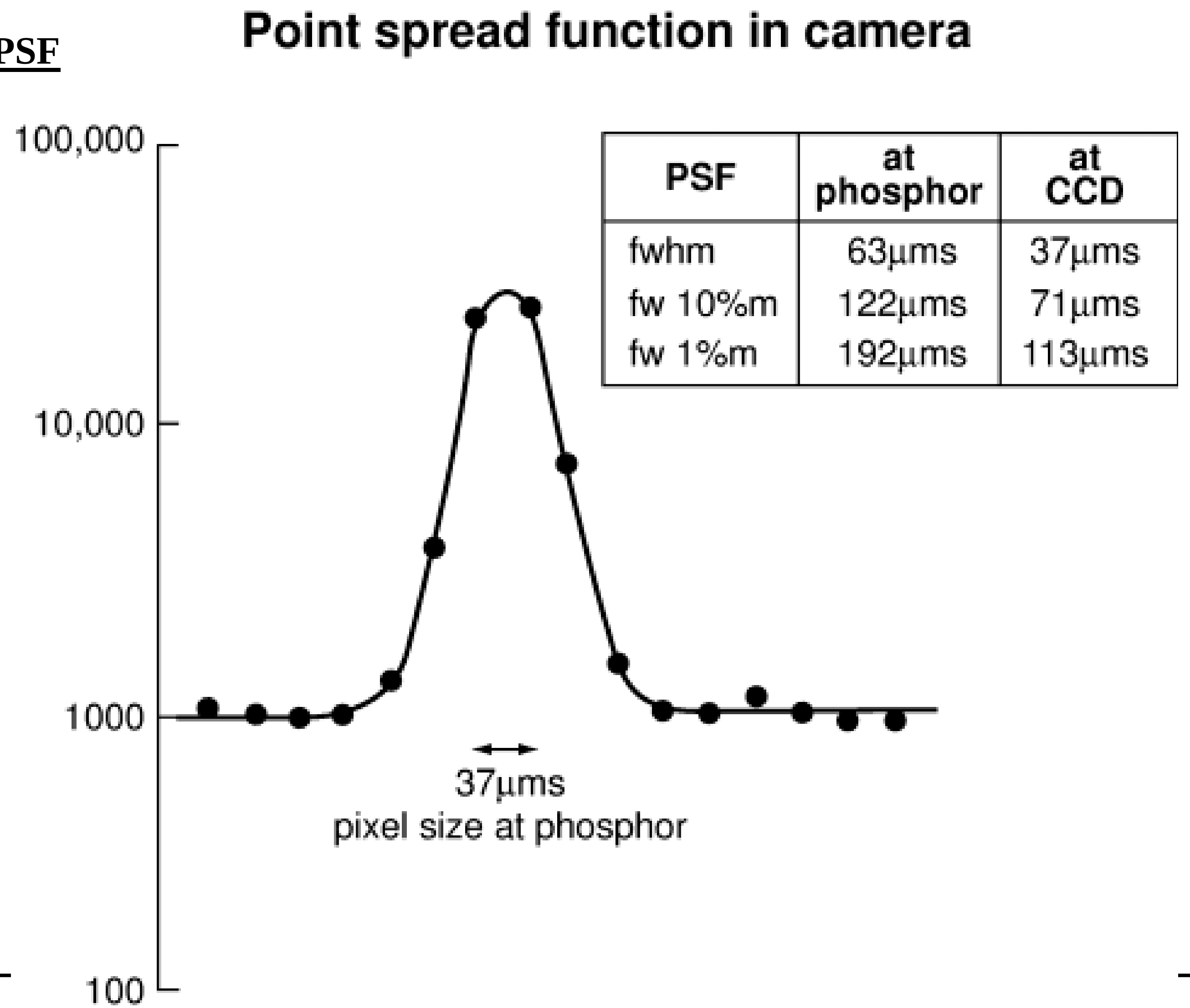


Faruqi,et al Ultramicroscopy, 75,235-250 (1999)

BR



PSF



PSF	at phosphor	at CCD
fwhm	63µms	37µms
fw 10%m	122µms	71µms
fw 1%m	192µms	113µms

Faruqi,et al NIM **A367**, 408-412 (1995)

FILM

Main Advantages

Very good resolution

Ease of archiving

New LMB Scanner (R.H.): *High speed, small programmable pixel size > 1 μm, very high accuracy in both position and optical density.*

Disadvantages

Not on-line, delays due to processing and scanning

Poor S/N for weak exposures – fog, dust.

High Resolution Imaging Detector Requirements

1. **Electronic detector with computer control**
2. **Number of *independent* pixels:4000 by 4000**
3. **Size 20 – 50 µm**
4. **High sensitivity, no noise**
5. **Radiation hardness important ~ 1 MRad**
6. **Readout time not critical (mostly)**

Semiconductor Detectors (pixel detectors)

Good spatial resolution(?); no intermediate light conversion step in the phosphor or fibre optics

Photon (electron) Counting – no noise(?)

Fast Readout – multiple frames per image

Compact size (limited space in microscopes)

Tiling essential for adequate area coverage

Cooling not required(?)

Direct Detection in Silicon Pixel Detectors

- **Hybrid Pixel Detectors (Poster…)**

  Pixellated silicon detector, bump-bonded to readout chip with same size pixels

CMOS Detectors (This talk)

Pixellated silicon, readout built into each pixel

MAPS Background

Monte Carlo simulations of 120 keV electrons in silicon, 4 µm thick

lateral spreading of charge, ~1 µm,.

energy deposited: ~2.4 keV - >> Readout noise (~ 100 e)

Monolithic Active Pixel Sensor (MAPS) –designed at RAL

Size: 525 by 525, 25 µm pixels

Non-Radhard, standard 0.5 µm CMOS technology

Each pixel in MAPS contains four diodes in the sensitive epi-layer

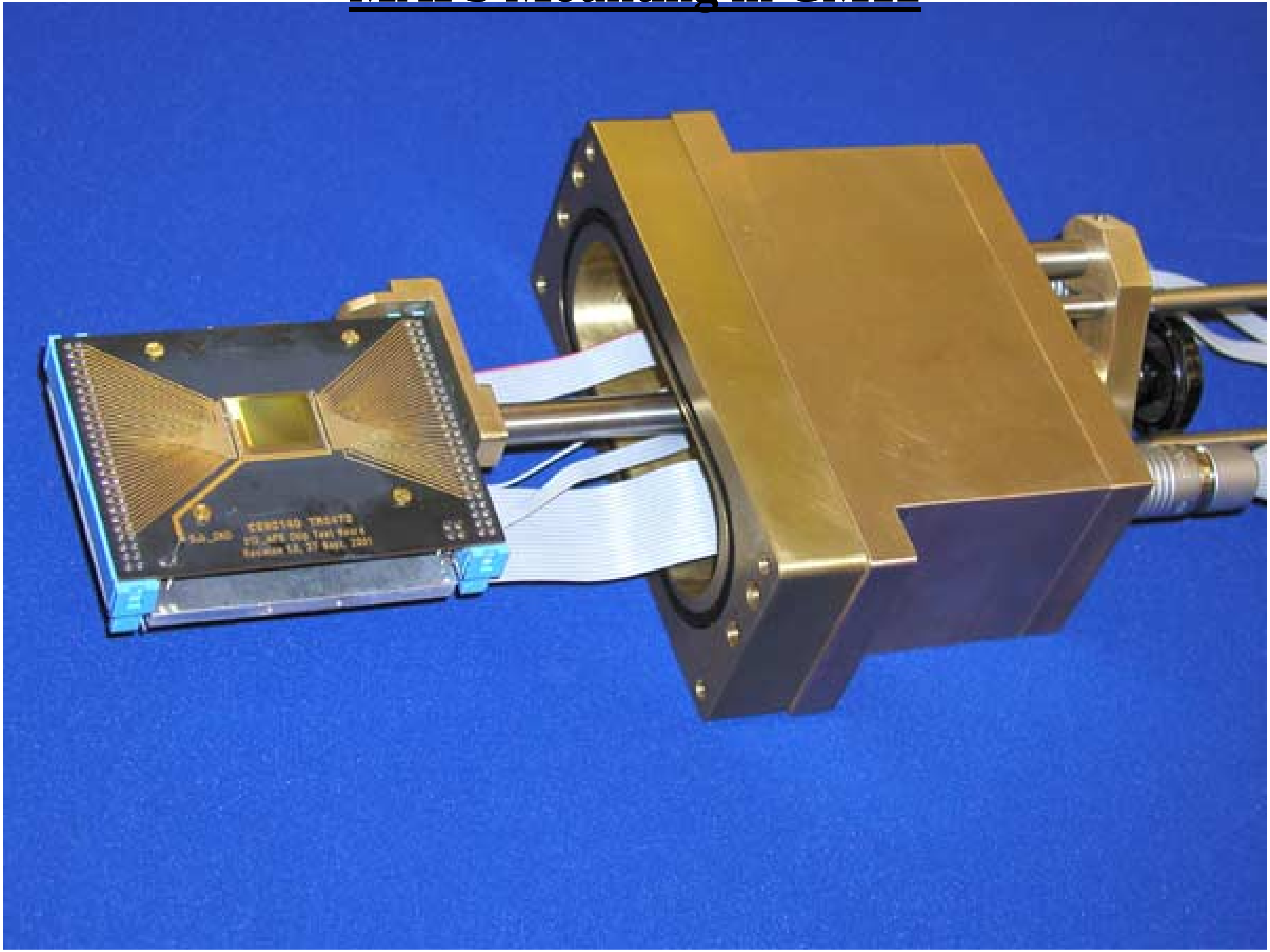
Electrons drift to one of the four diodes in pixel

Charge summed from all diodes and converted to a voltage

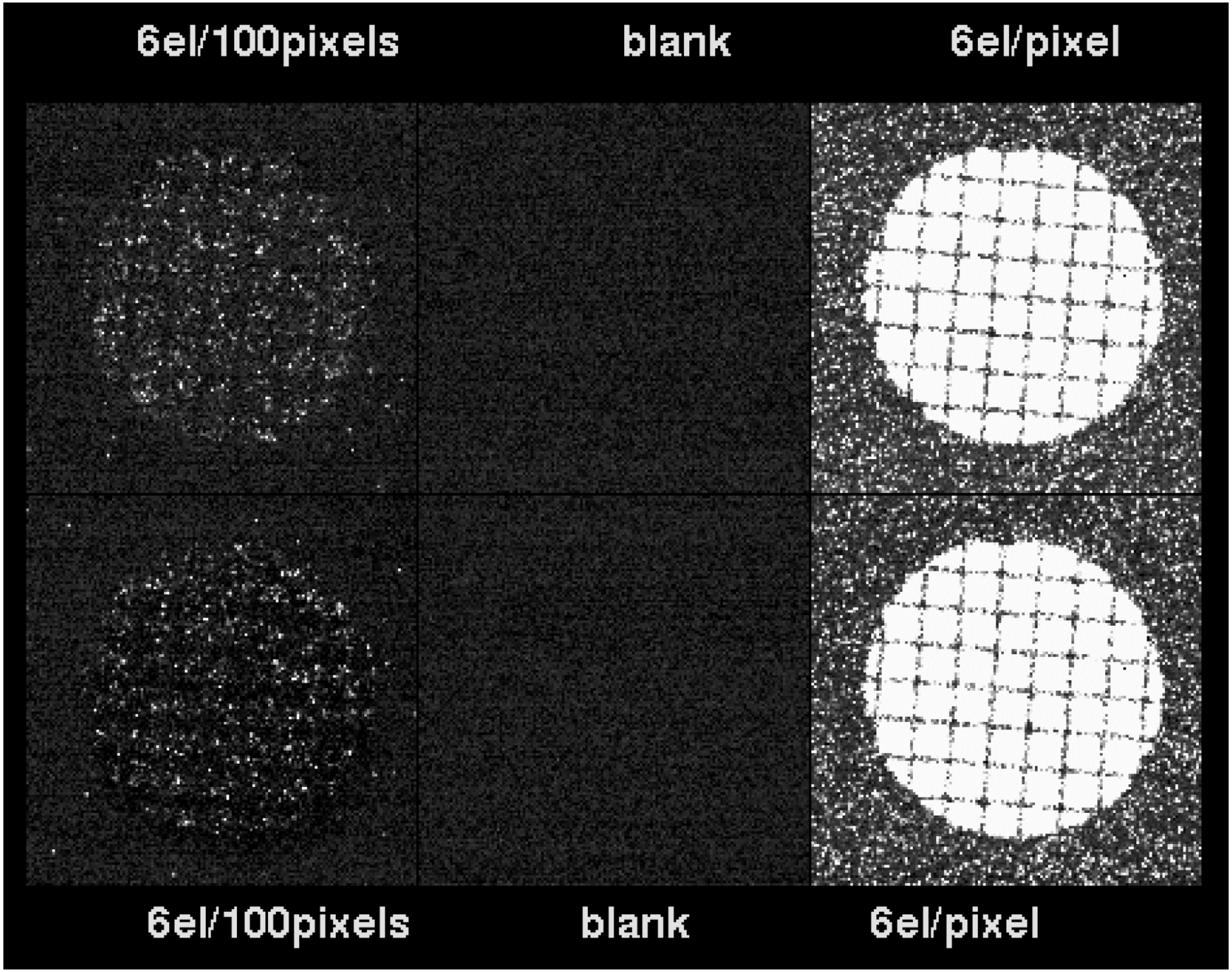
One ADC per column; all pixels in a row read out in parallel

Detector parameters tested so far: spatial resolution, sensitivity (or efficiency) and radiation hardness.

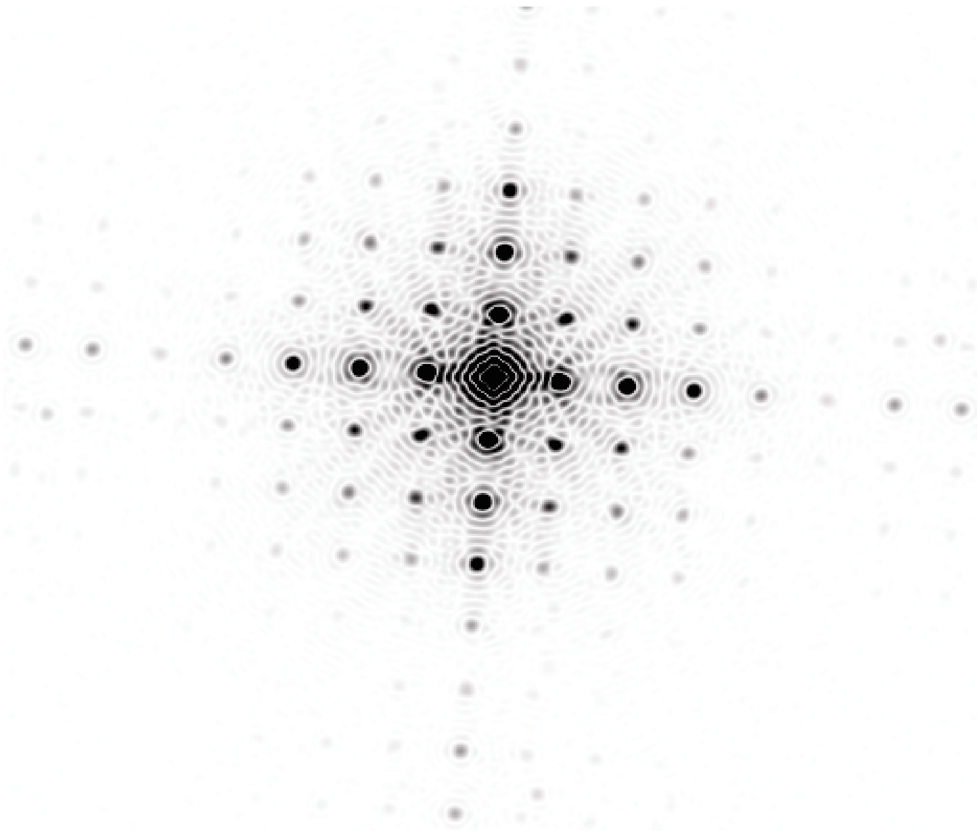
MAPS Mounting in CM12



Imaging of 100 mesh grid in MAPS

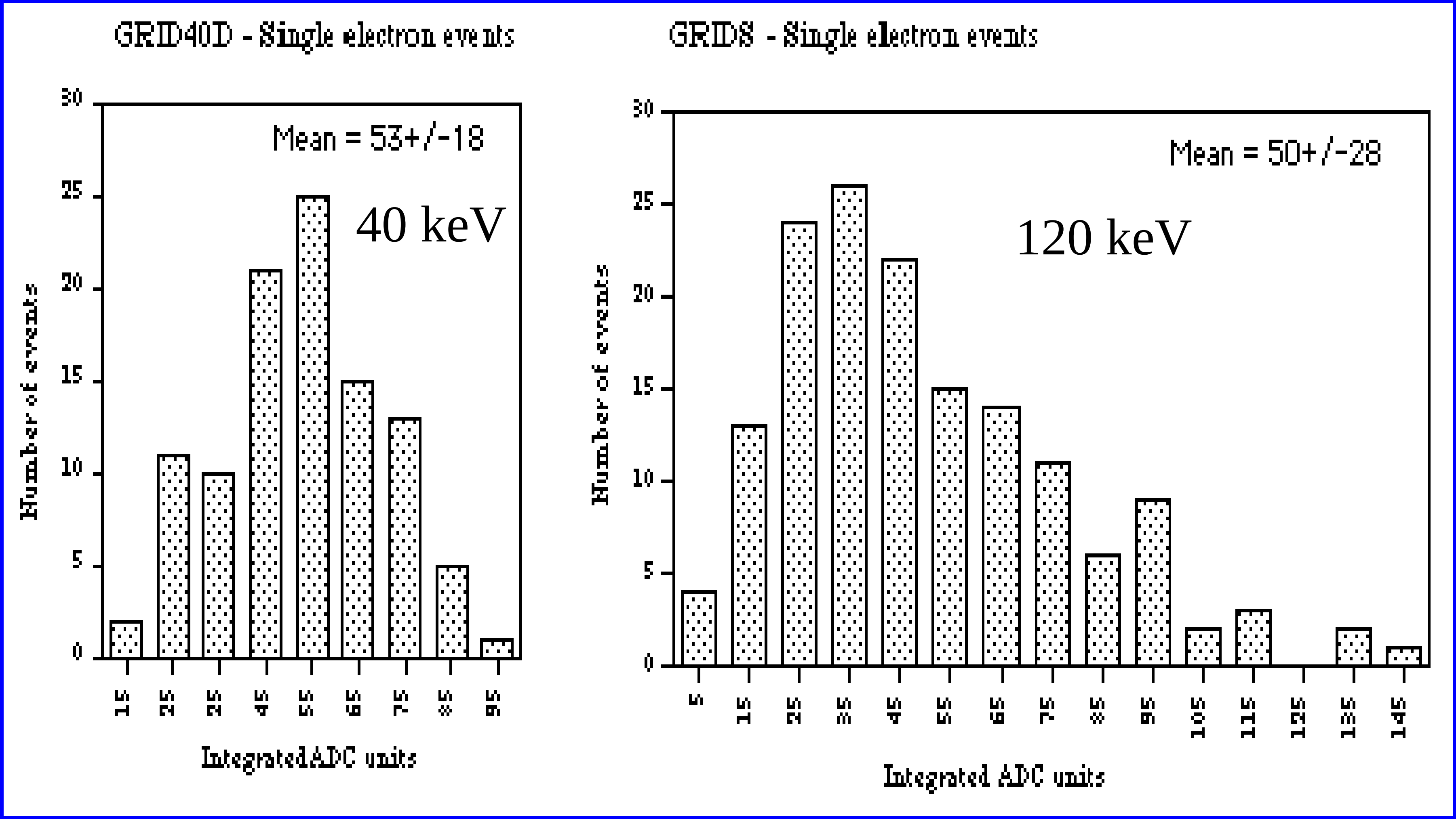


Fourier Transform of grid image on MAPS



MTF at Nyquist frequency : 52% compared to film

ADC Response for Single Electrons at 40 keV and 120 keV



Distribution of signal in ADC units from single electron hits at 120 keV

		0.2		
	0.8	5.2	1.4	
0.0	3.8	29.9	3.6	-0.2
	1.6	3.1	1.0	
		0.1		

Total = 50 ADC Units/electron from 152 events.
25% of signal in adjacent pixels (13% at 40 keV)

Radiation Damage

A series of exposures of the grid recorded on two detectors recorded as the accumulated dose was gradually increased. Both behaved in a similar way.
Even with ~10,000 electrons per pixel,
the change in the background level (pedestal?) could be seen in the form of an outline image of the previous grid pattern on blank exposures.
After 250,000 electrons/pixel, the detector was still usable, but after 600,000 to 900,000 electrons/pixel, the detector was unusable.

Total Dose: 10,000-15,000 Rads.

MAPS: Summary at 120 keV

Sensitivity:	**~50 ADC Units/electron**
Noise:	**~2 ADC Units**
Signal/Noise:	**~25**
Resolution:	**52% of film at Nyquist Frequency**
	(Similar to film at 40 keV)
Radiation Hardness:	**10-15 Krad . Needs improvement!**

Acknowledgements

- Richard Henderson, LMB
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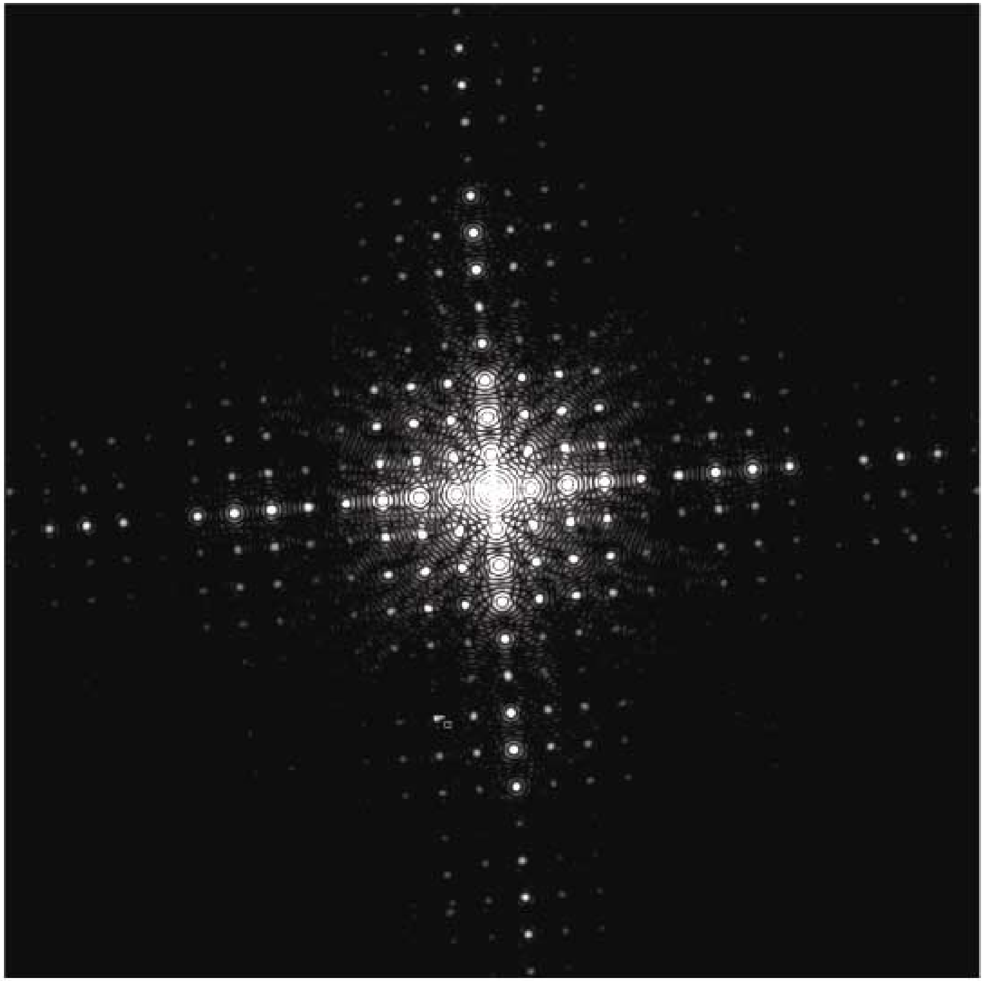
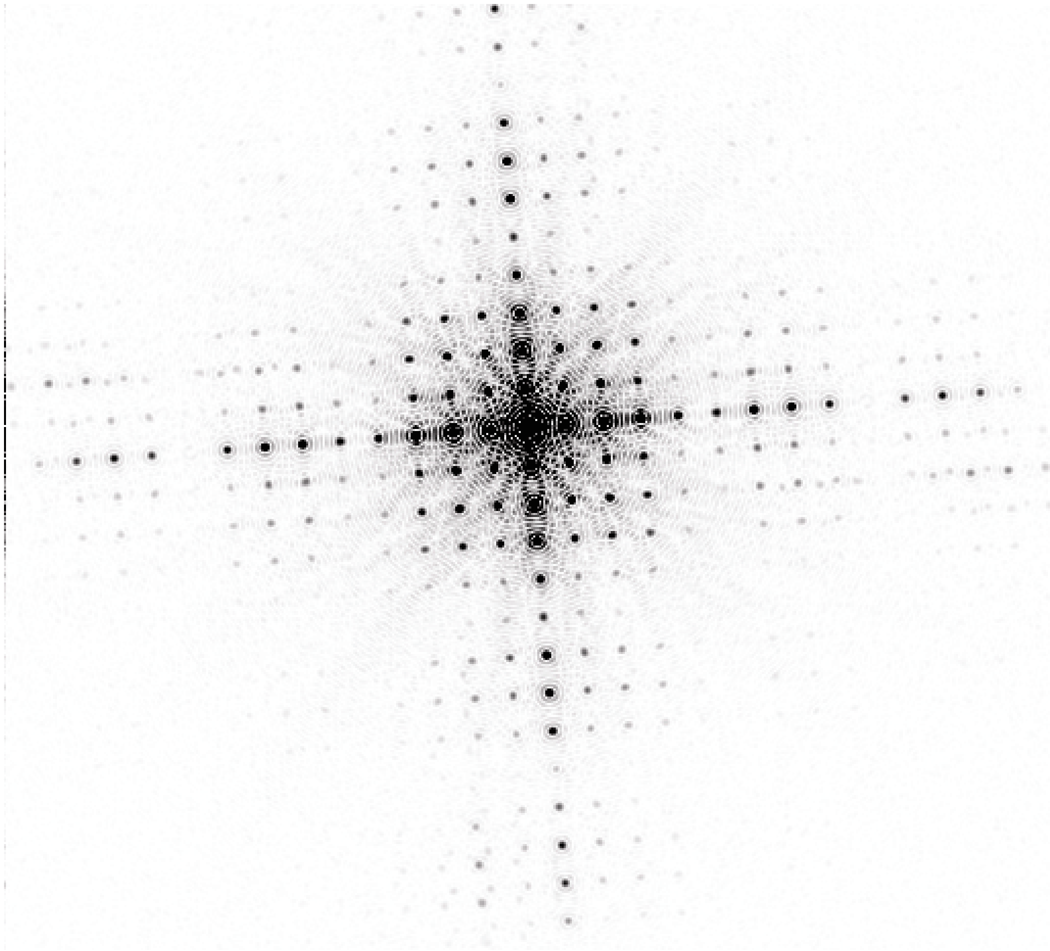
- Chris Raeburn, LMB
- RAL: R.Turchetta & Space Sciences Group, Arwel Evans Liverpool Univ.

FFT of 100 mesh grid at 120 keV: Medipix2



Nyquist Frequency, 76% compared to film

FFT of 100 mesh grid: Film



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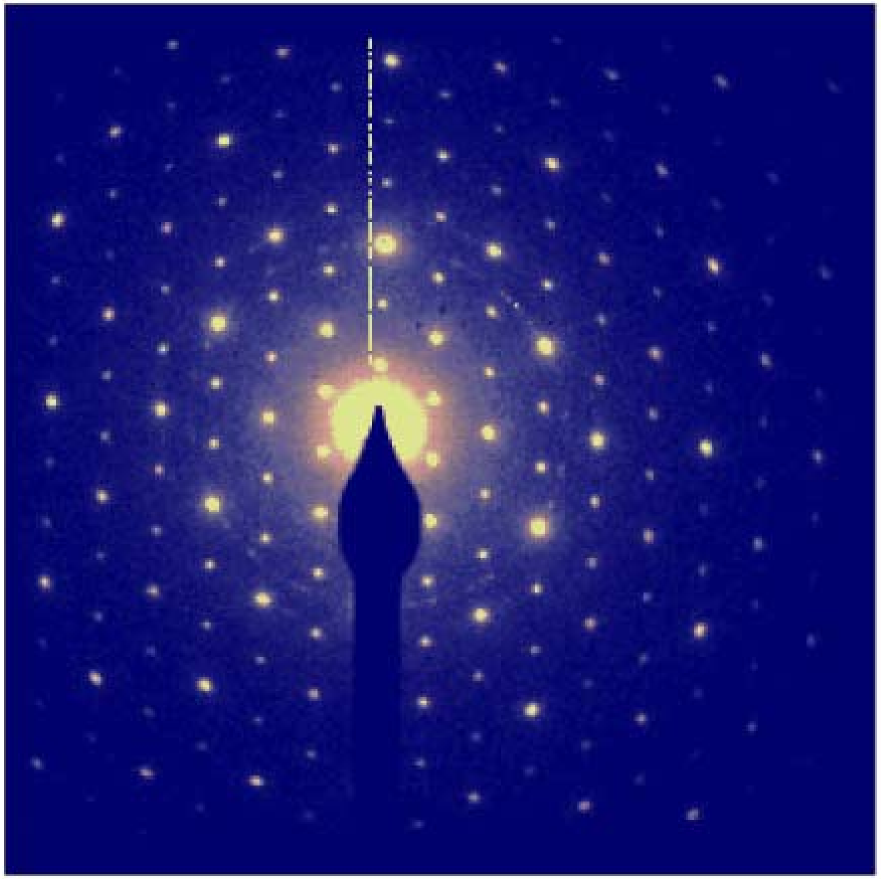
Vermiculite



Diffraction Pattern from Vermiculite

Medipix Summary

Efficiency: *very high, all energy absorbed in Si detector*

Resolution: *76% at Nyquist Frequency (if film 100%)*

Vth = (60 keV) eliminate charge sharing

Radiation Tolerance: *No signs of damage with 6 MRads of 120 keV electrons; readout electronics protected by 300 µm of Silicon*

Faruqi, Henderson and Tlustos, IWORID2004 (Glasgow) submitted