MAPS and Medipix2: Two direct detectors for Electron Cryo-Microscopy

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Motivation for Semiconductor Detectors

Main Aim of Project: Develop electronic version of film for all types of electron microscopy

Why consider direct detection detectors?

- Better MTF as no intermediate light conversion step
- High S/N ratio due to large signal and low noise
- Fast readout – framing possible
- Room temperature operation

Future improvements

- Larger number of pixels needed (~4000 x 4000)
- Radiation hardened designs (>1 MRad, ~ life 1-10 yrs)

Direct Detection in Silicon Pixel Detectors

- **Hybrid Pixel Detectors**

  MEDIcal imaging with PIXel detectors (Medipix)

  Pixellated silicon detector, bump-bonded to readout chip with same size pixels. Derived from (Centre for Research in Nuclear Physics) CERN designs.

- **CMOS (Complementary Metal Oxide Semiconductor) Detectors**

  (1) Monolithic Active Pixel Sensors (MAPS) designed at Rutherford Lab.

  Pixellated silicon, readout built into each pixel.

  Derived as successor to (Charge Coupled Devices) CCDs for optical imaging

- **(2) STAR250 Radiation hard detector designed at FillFactory, Belgium**

High Resolution Imaging Detector Requirements for Cryo-EM

1. Electronic detector with computer control.. eliminate film!
2. Number of *independent* pixels : 4000 by 4000
3. Pixel Size 10 – 50 μm (has to fit in commercial microscopes)
4. High sensitivity with no noise – ability to add multiple frames
5. Radiation damage; should be able to withstand at least 1 MRad
6. Readout time preferably short
7. Cost

Detectors: Quality Factors

Sensitivity: Detective Quantum Efficiency (DQE),
$(S/N)^2_{output} / (S/N)^2_{input}$ (=1 for perfect detector)

DQE(0) zero spatial frequency

DQE(Nyquist frequency)

Resolution: Modulation Transfer Function (MTF)

Framing Speeds… inverse of readout time

Radiation Hardness … lifetime before destruction

Dynamic Range … ability to record very weak and very strong parts of an image simultaneously (diffraction only)

Defects …… Faults in fabrication, etc

Detector basics for X-ray and Electron detection

(i) **Detection** (conversion of incident particle into signal, electron-hole pairs e^-h^+

(ii) **Readout** (transfer of signal to ADC, etc)

X-ray photon …… converts to photoelectron prior to detection in silcon

Electron ………… direct detection in silicon

Conversion of energy to signal: 3.6 eV/electron-hole pair in silicon

[1 eV/molecule …. 23kCal/mole]

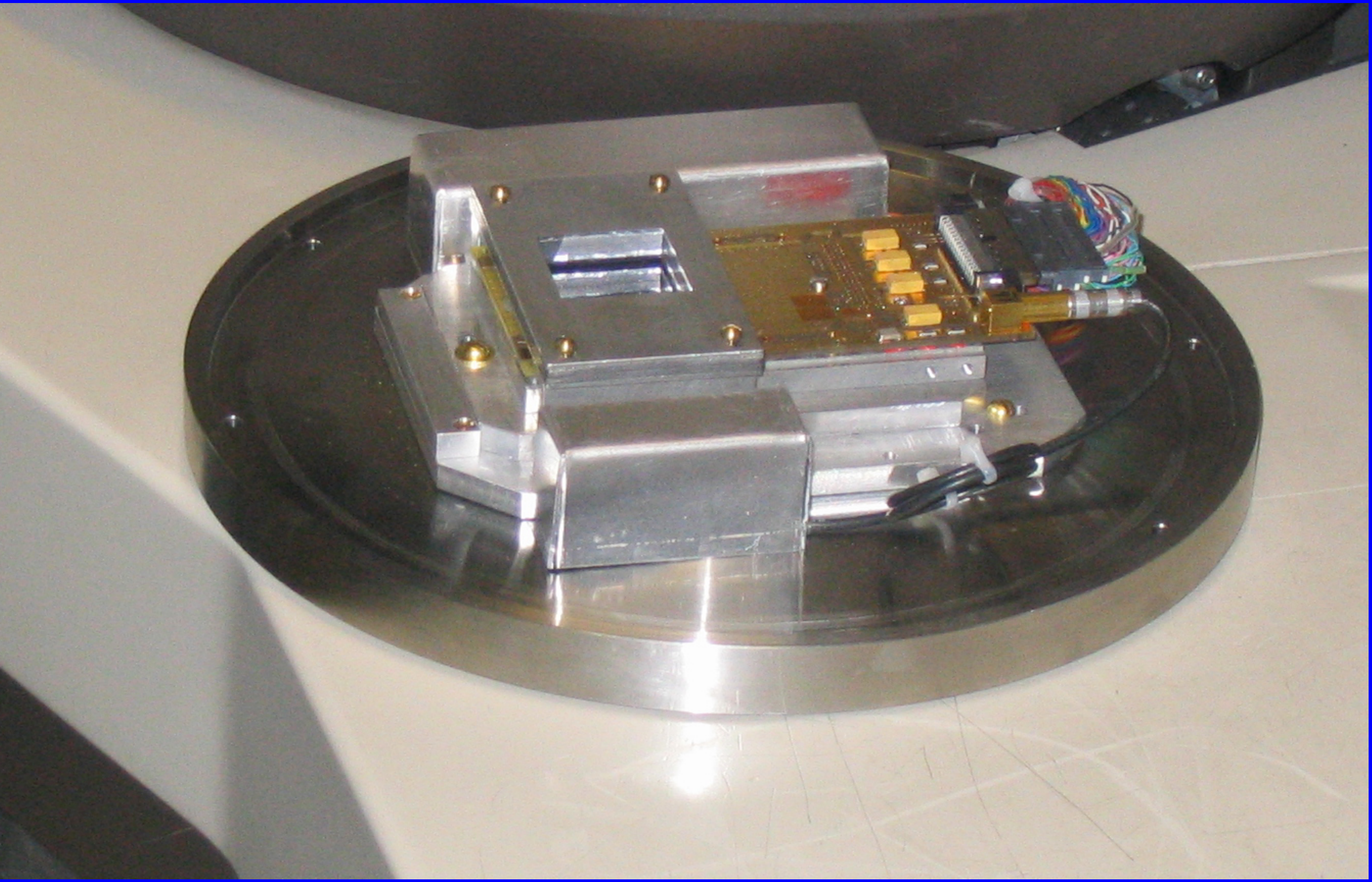
[Thermal noise (kT) = .025 eV]

120 keV electron ~33,000 electron-hole pairs

12 kev X-ray photon ~3300 electron-hole pairs

Noise is typically 100 e^- S/N pretty good (330 and 33).

Medipix2(Quad) in FEI F30 Mounting

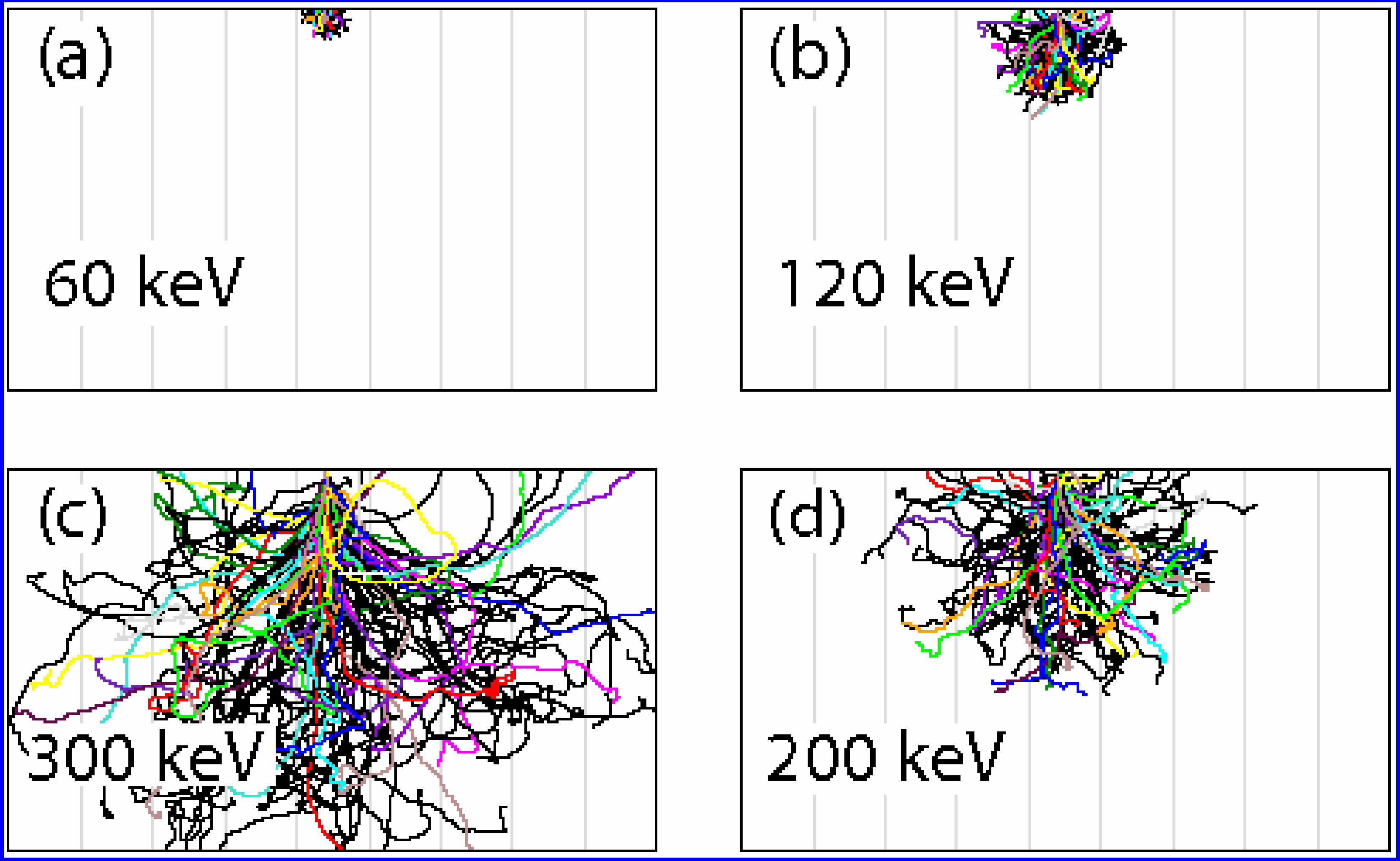


300 kV FEI EM with detector installed

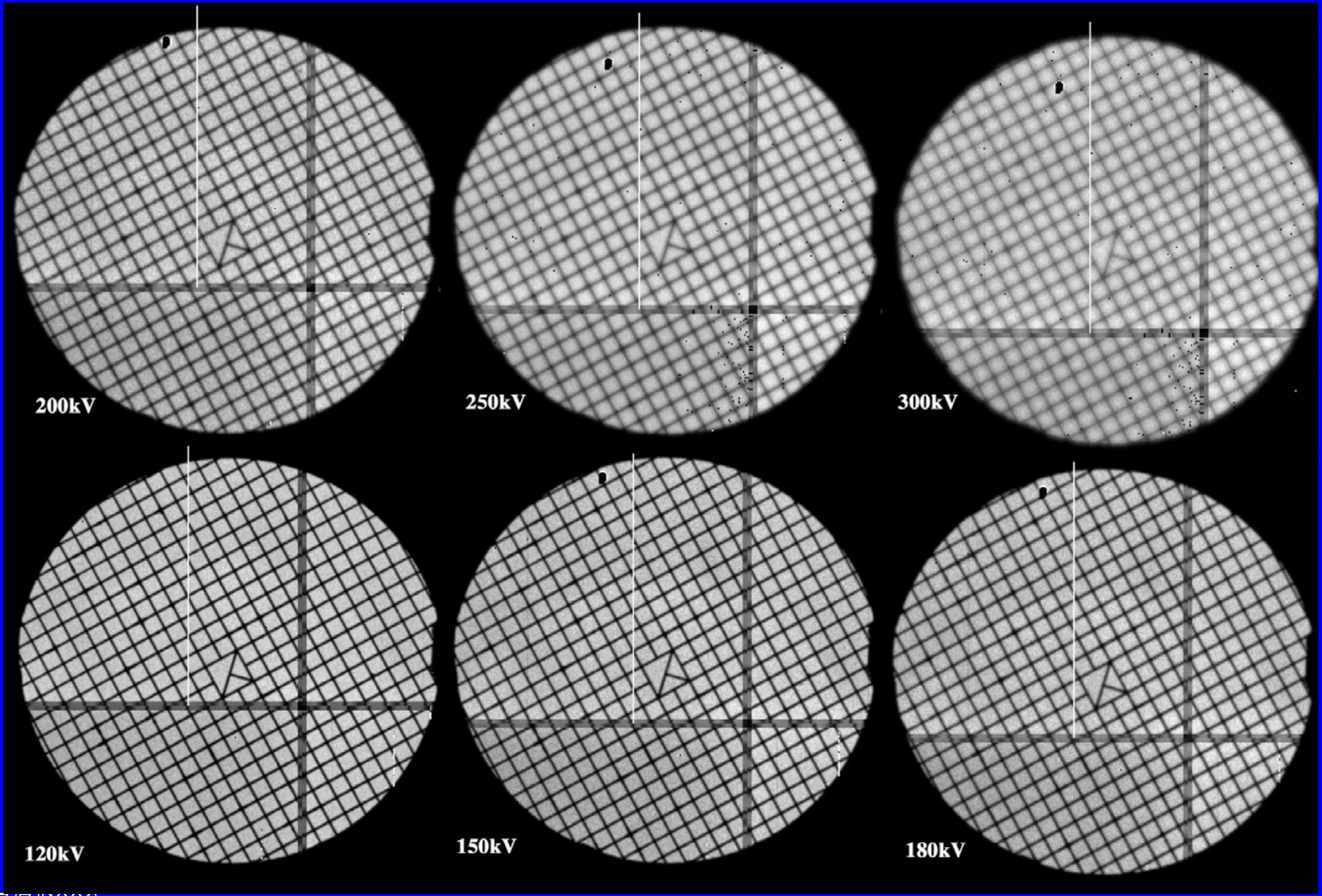
Medipix Quad

Monte Carlo simulation of electron trajectories in silicon. Detector thickness = 300 microns, pixel=55 microns

Extension of simulations to include energy deposition..(GM); More details in Poster 22. Also MTF, theory and experimental results



Resolution of Quad_Medipix2 from 120 – 300 keV

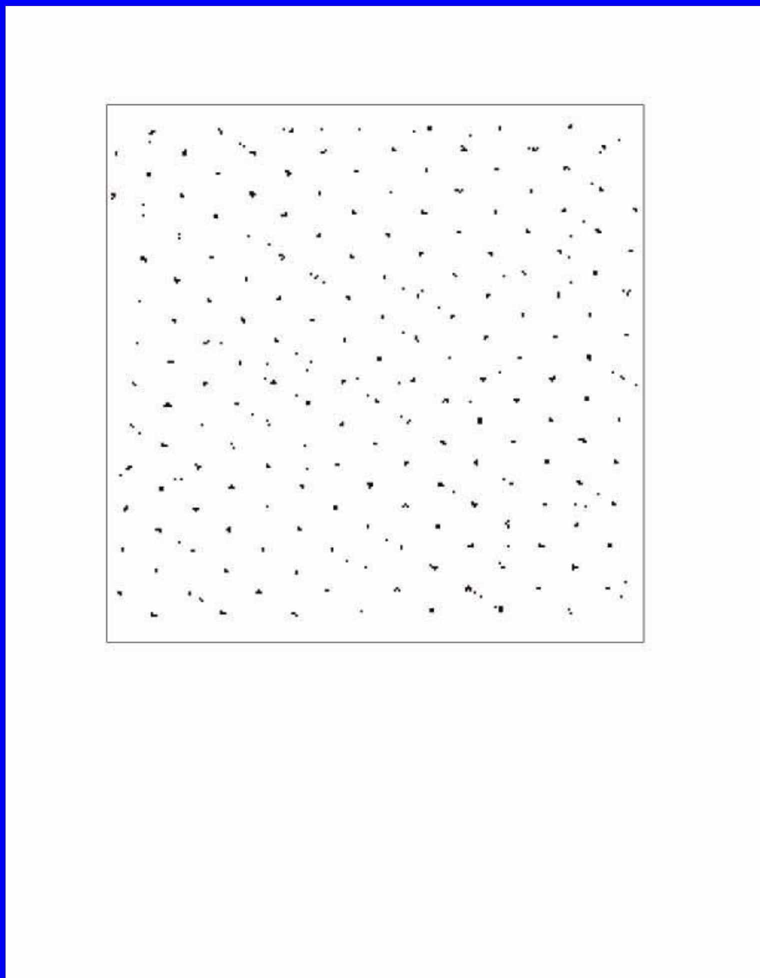


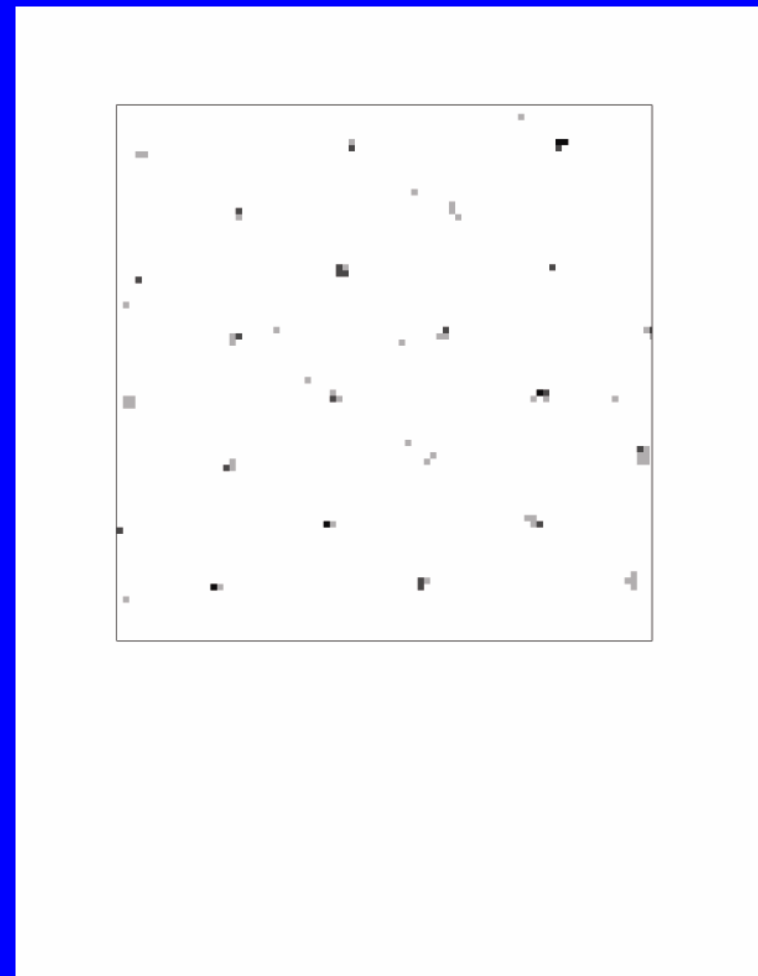
300 mesh grid, spacing ~650 microns in image

Raster of electrons at 120 keV

Spotscan **Magnified**

spots in a line – some electrons 'leak' in adjacent areas





Mean:4.7, standard deviation : 1.8

Comparison of Medipix2 with film

Spotscan1

	mean	std deviation
Medipix2	111	11
Film	116	24

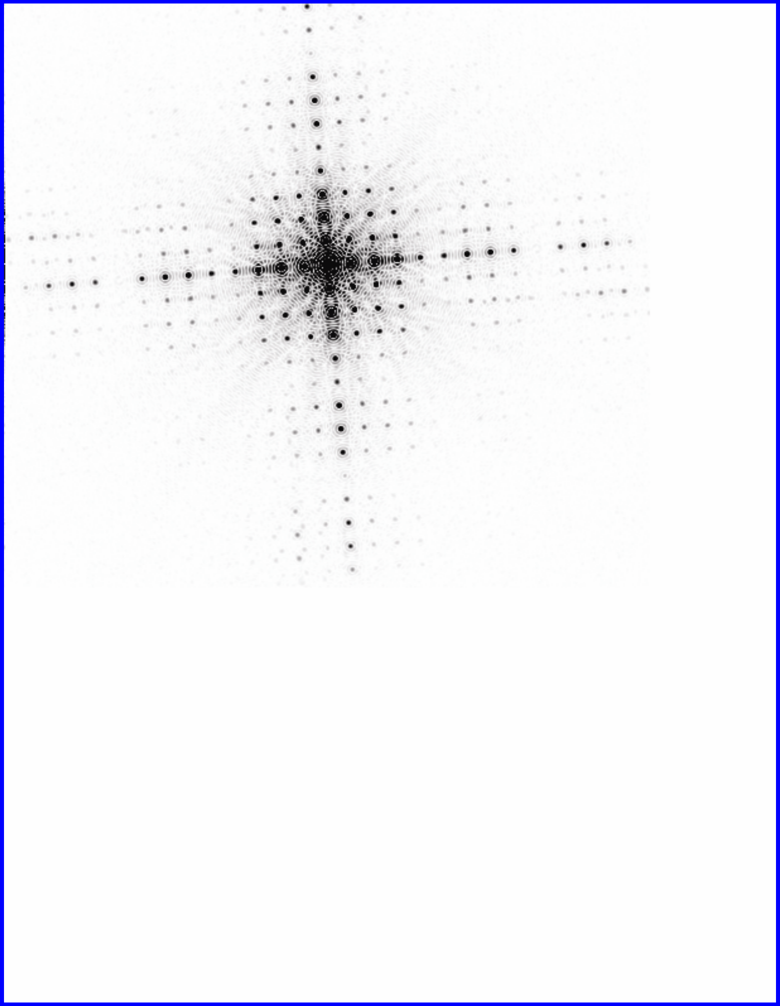
Spotscan7

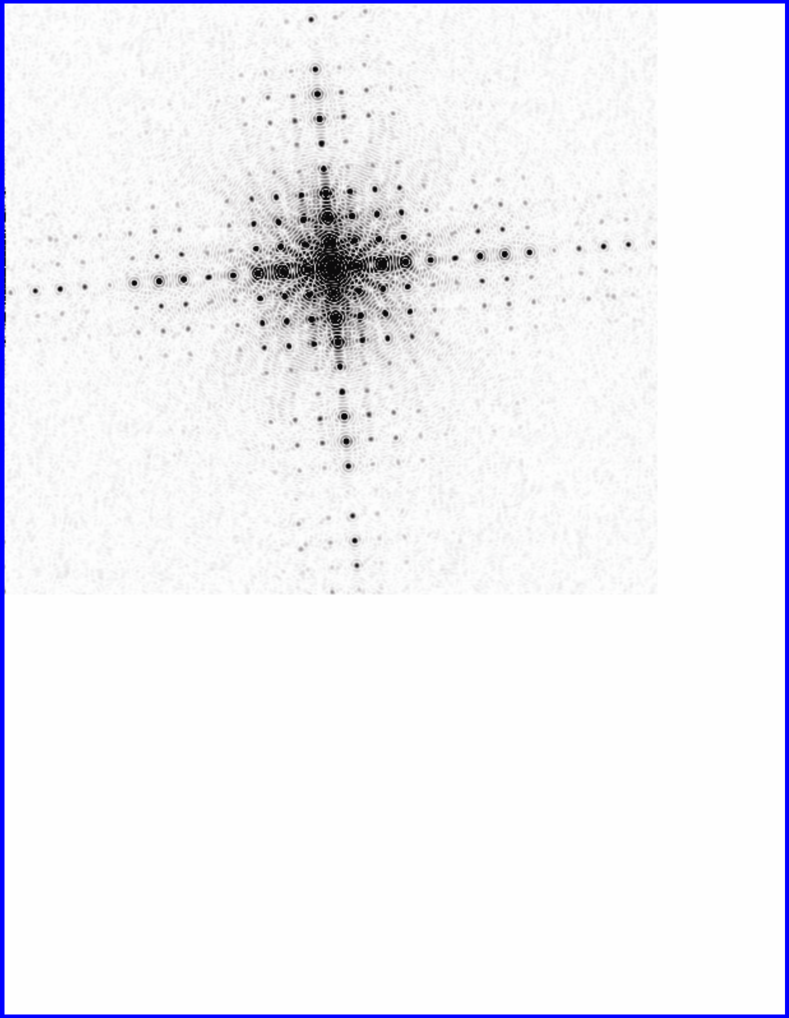
Medipix2	4.7	1.8
Film	spots invisible – merged with noise	

Medipix2 behaves like an electron counter with no noise.

FFT of Grid image recorded on:

Film **Medipix2**





17/7/2006

LMB, Cambridge

MTF and DQE for Medipix2

MTF: 50% of that expected of a perfect detector

DQE(0): ~85% independent of exposure

DQE(Nyquist): ~40% of that expected of a perfect detector

Hybrid Pixel Detectors (Medipix2)

Potential Advantages

Direct electron detection in Silicon with large signal

Excellent S/N due to absence of noise; specimen movement (RH,et al paper in preparation)

High dynamic range

Good spatial resolution since there is no light scattering

Detector and electronics separate – can choose detector material (Si, GaAs CdTe, …) for optimum efficiency

Fast readout – fast framing possible

No radiation damage at 120 keV

Downside

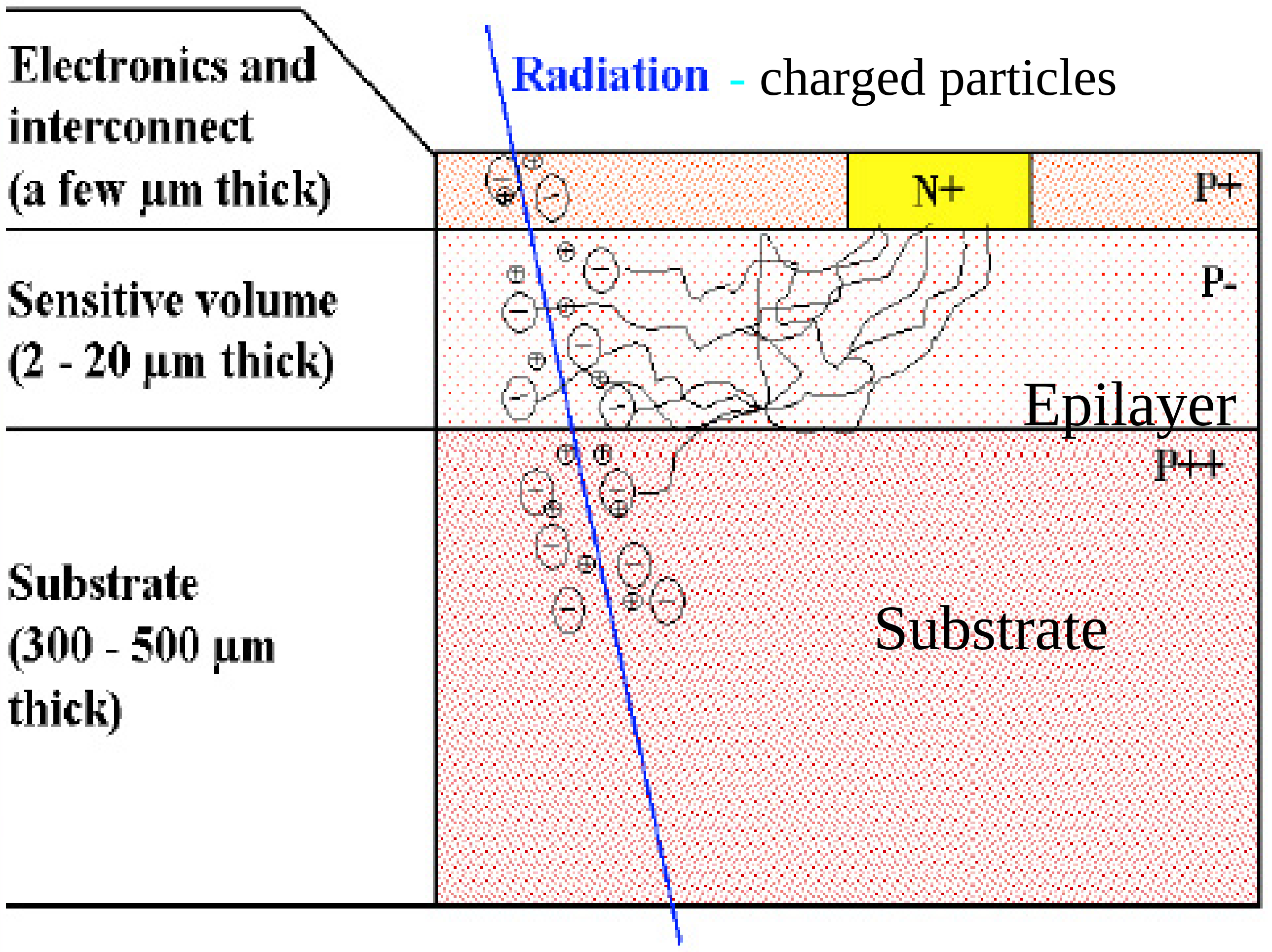
Large area detectors not yet built – but are being designed

Technology not yet mature – problems of ‘yield’

Radiation damage at 300 keV

(Monolithic active pixel sensor)MAPS CMOS Detector

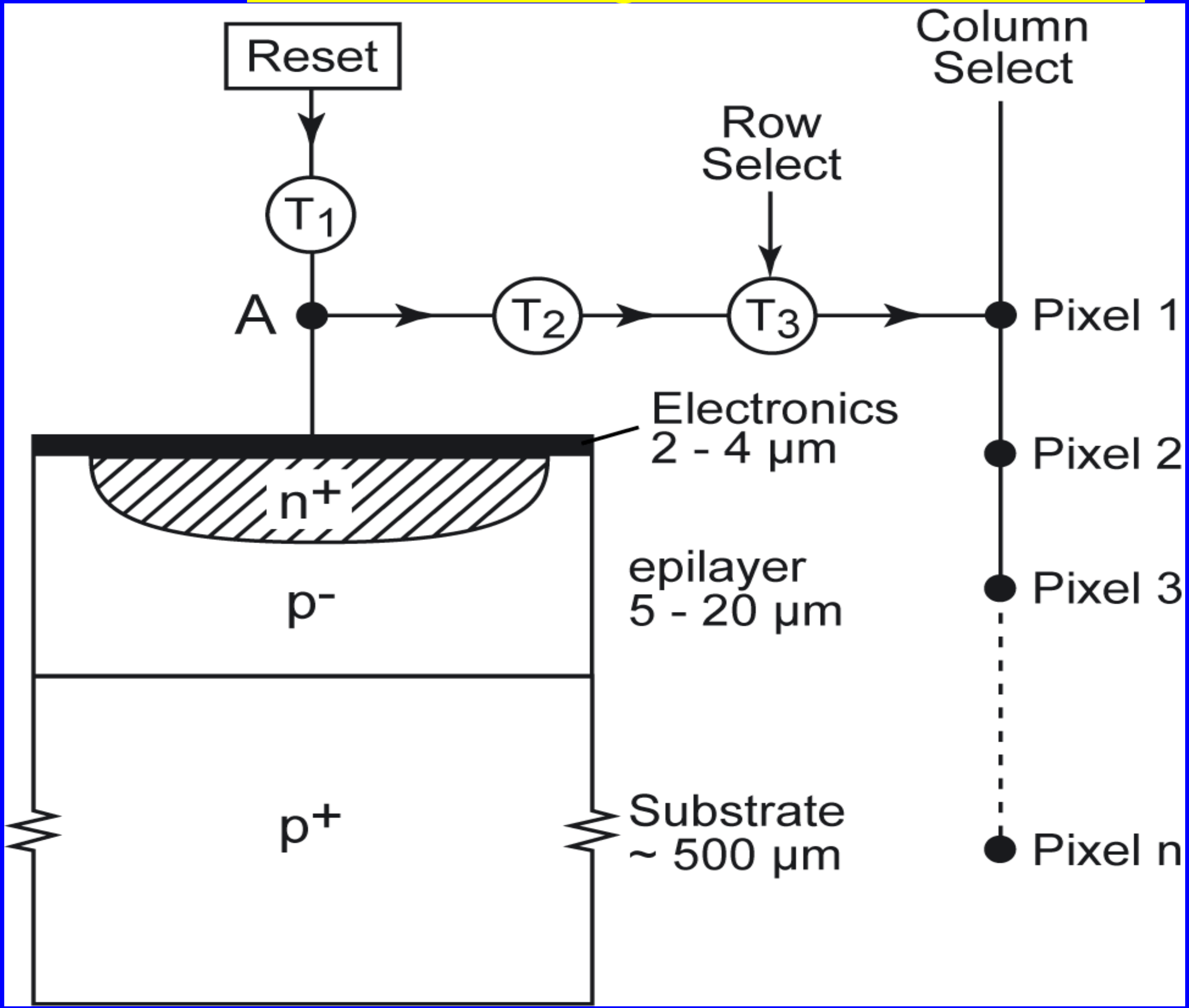
(detector and readout incorporated in the same layer)



- no bias voltages
- charge diffusion
- 100% fill factor

Turchetta et al
NIM A458 (2001) 677-689

CMOS: Single Pixel Readout

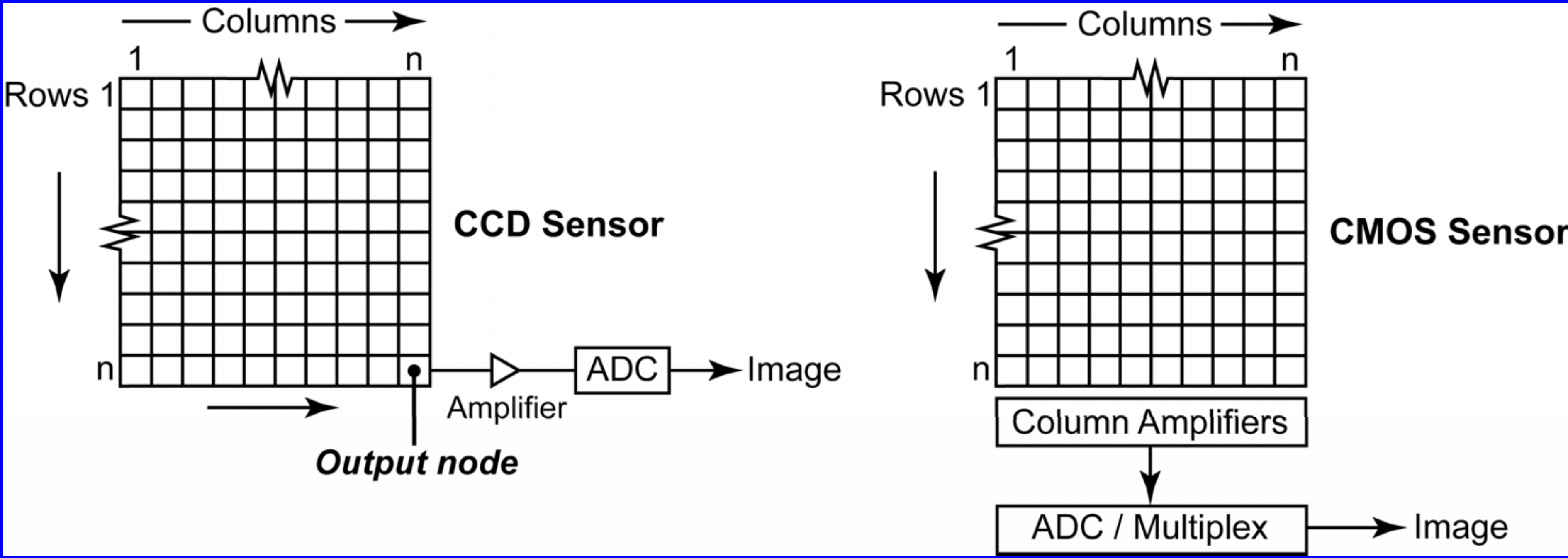


T1,T2, T3 are all transistors

Comparison of CCD and CMOS Readout

CCD

CMOS



Single (or few) node readout, slower

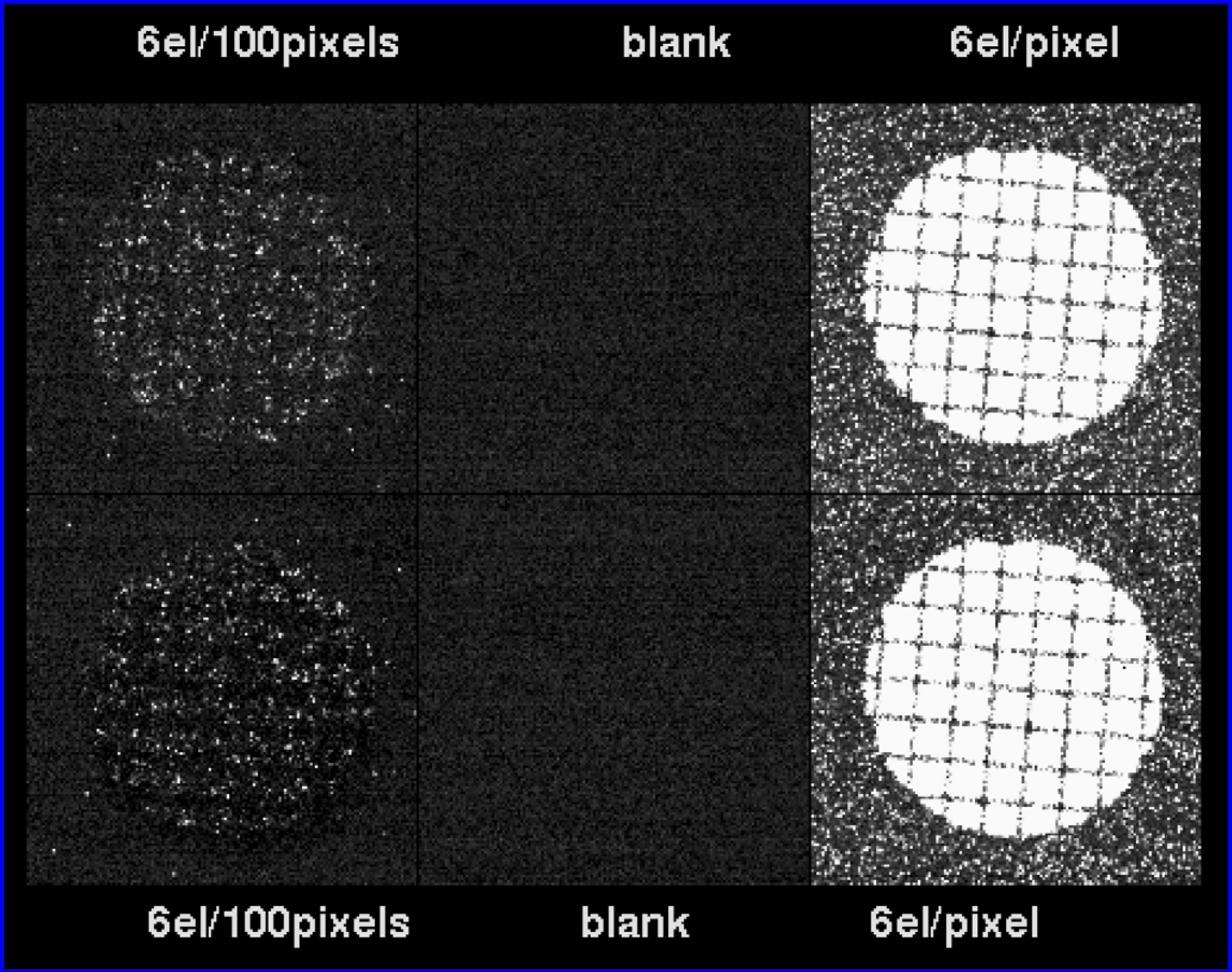
Charge shifted along columns/row

Parallel readout, faster

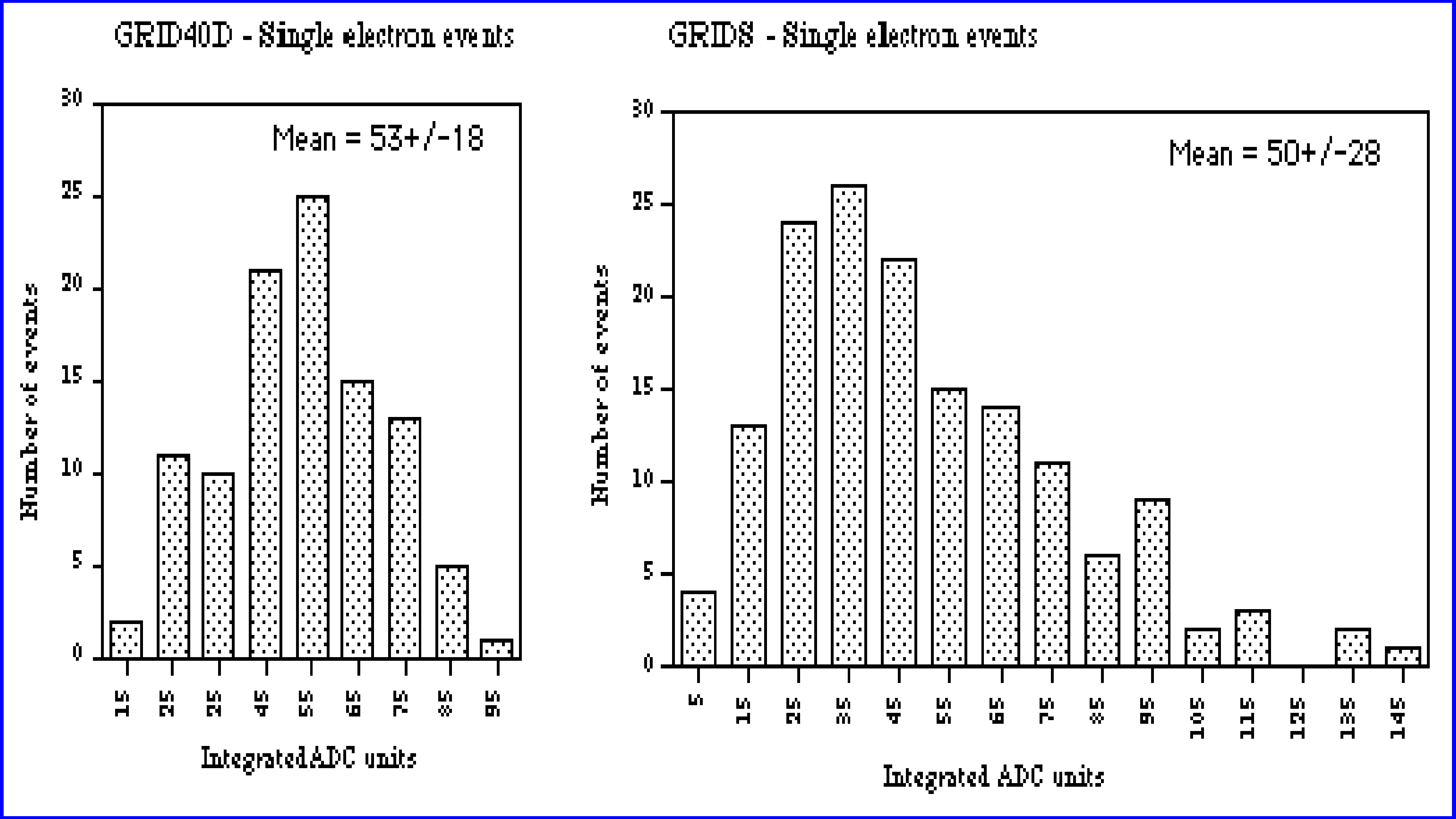
Charge converted to voltage

In pixel

Imaging of 100 mesh grid in MAPS at 120 keV



ADC Response for Single Electrons at 40 keV and 120 keV



MAPS Summary at 120 keV

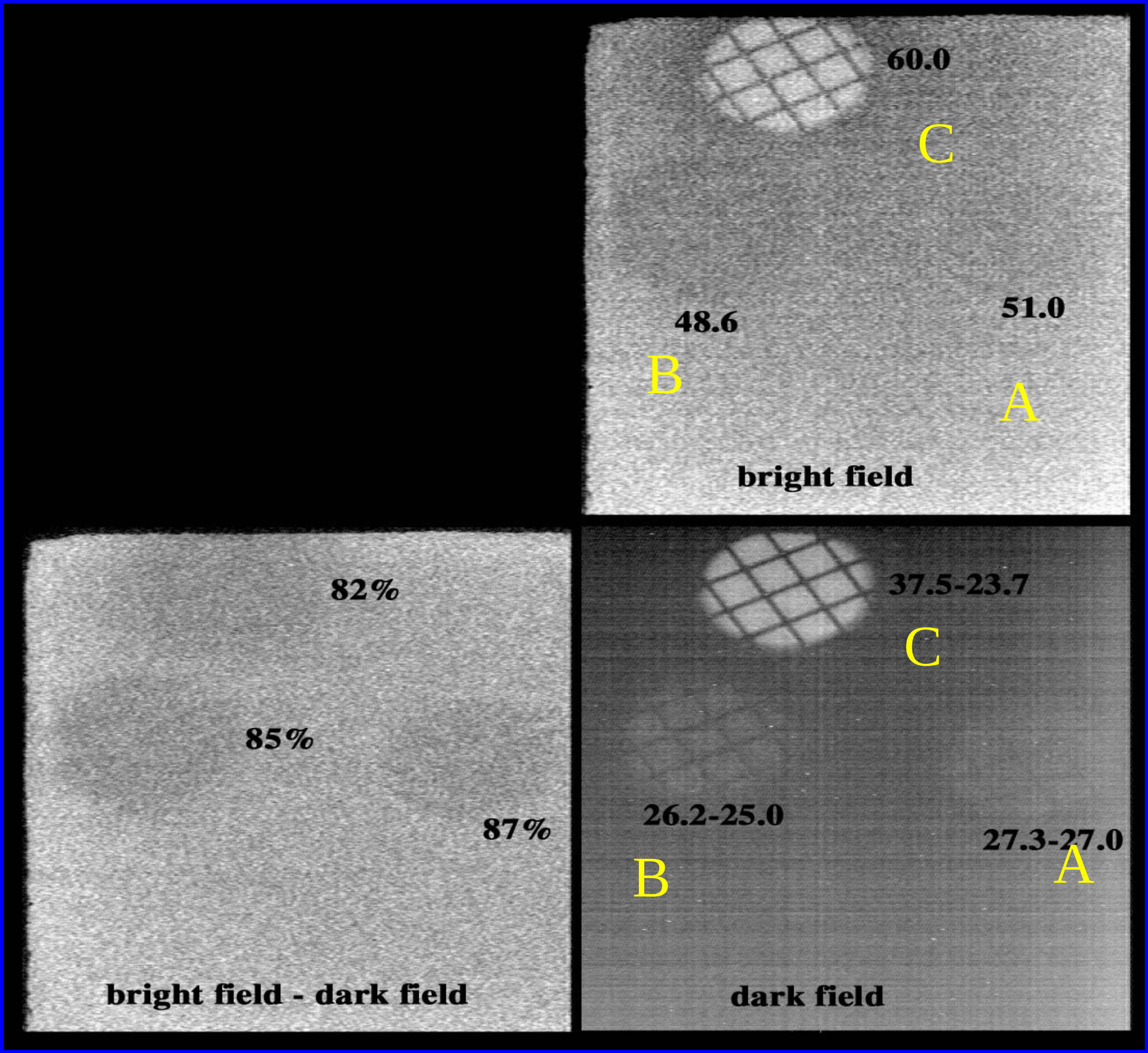
Sensitivity:	~50 ADC Units/electron
Noise:	~2 ADC Units
Signal/Noise:	20-25
Resolution:	52% of film at Nyquist Frequency
Radiation Hardness: Needs	10-15 kRad (only ~1% of what is required) improvement!
Active area	525 x 525 pixels need larger areas

Faruqi, Henderson, Turchetta et al Nucl. Instr.& Meth 546, 170-175, (2005)

Radiation Damage to STAR250 (FillFactory/Cypress Corp.) at 300 keV

Radhard Technology

512 x 512, 25 µm
Radiation Dose:
A: 200kRad
(annealed for 4 weeks)
B: 200 kRad
C: 1000 kRad
(80,000 e/µm^{2})
Contrast values labelled in bottom left image



Conclusions

- Medipix2 is a superb detector for electron energies up to 120 keV – noiseless readout makes it unique for dose-fractionated imaging
- But, it may prove expensive to design 4K square arrays without dead spaces
- Higher energies (300 keV) may be feasible but with higher Z and density detector material, e.g. Cd(Zn)Te, GaAs,……
- CMOS detectors offer a better chance of producing a radiation hard, 4K square detector – but need a lot more design effort. This may take a year or so to completion?

Acknowledgements

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CERN (Medipix2)

- Lukas Tlustos,
- Xavi Llopart,
- M.Campbell

http://medipix.web.cern.ch/MEDIPIX/

- **RAL-CCLRC (MAPS)**
- R.Turchetta, M. Prydderch, et al