

# Even better cameras?

*Are they needed, possible and  
will I be able to afford one?*

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MRC

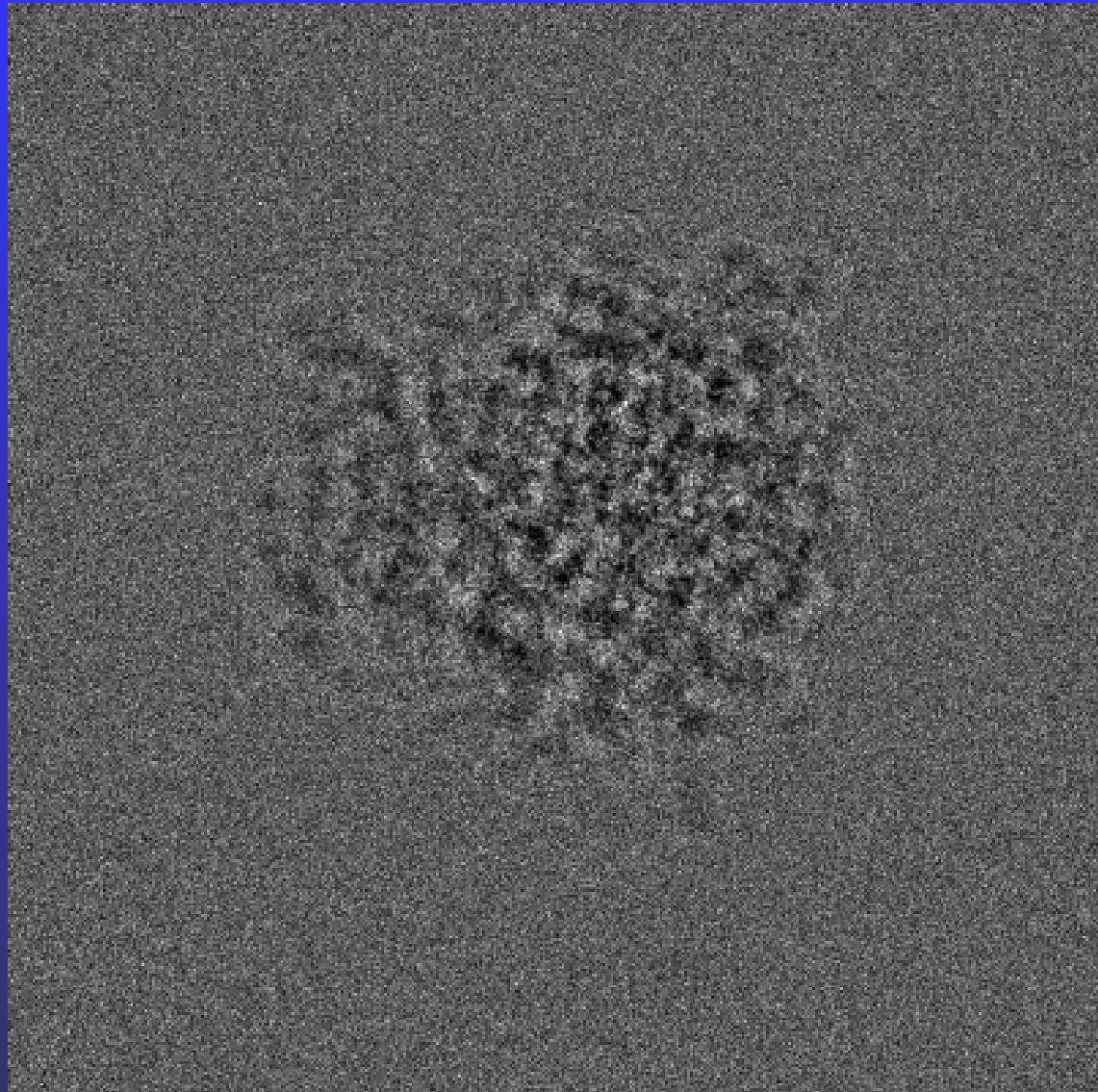
Laboratory of  
Molecular Biology

**Perfect image**

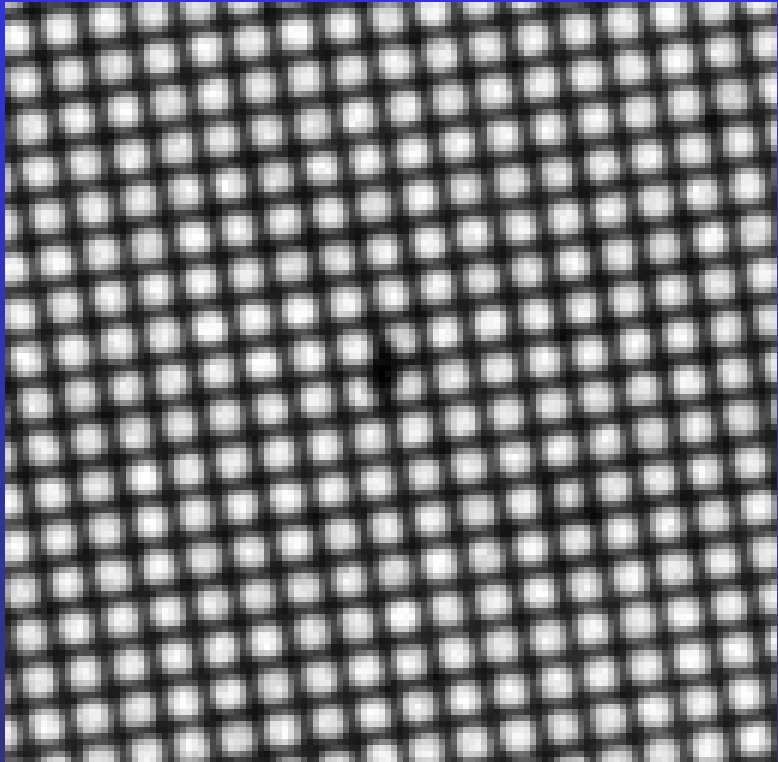
**Perfect detector**

**Perfect sample**

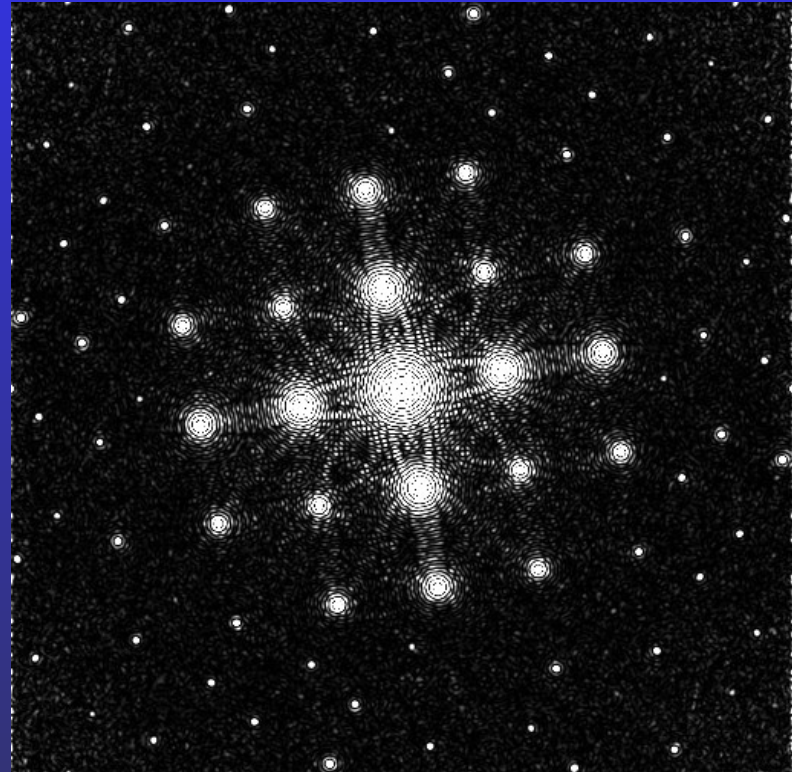
***20 el/pixel***



# Radiation Damage => DQE

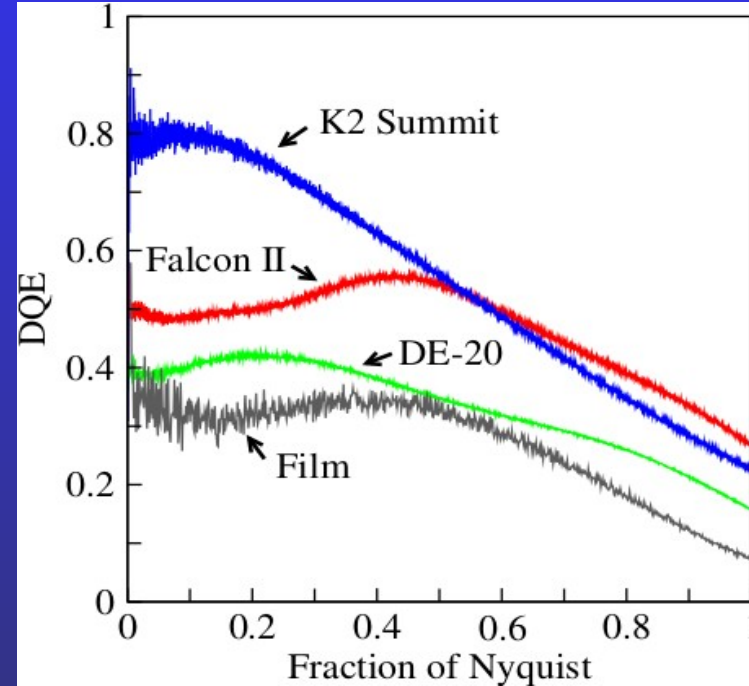


Falcon II image



# What do we have now?

- CryoEM maps now show  $\beta$ -sheets, side chains ...
- Higher resolution
- Smaller molecules
- Fewer particles



*McMullan et al, Ultramicroscopy*  
147, (2014) 156-163

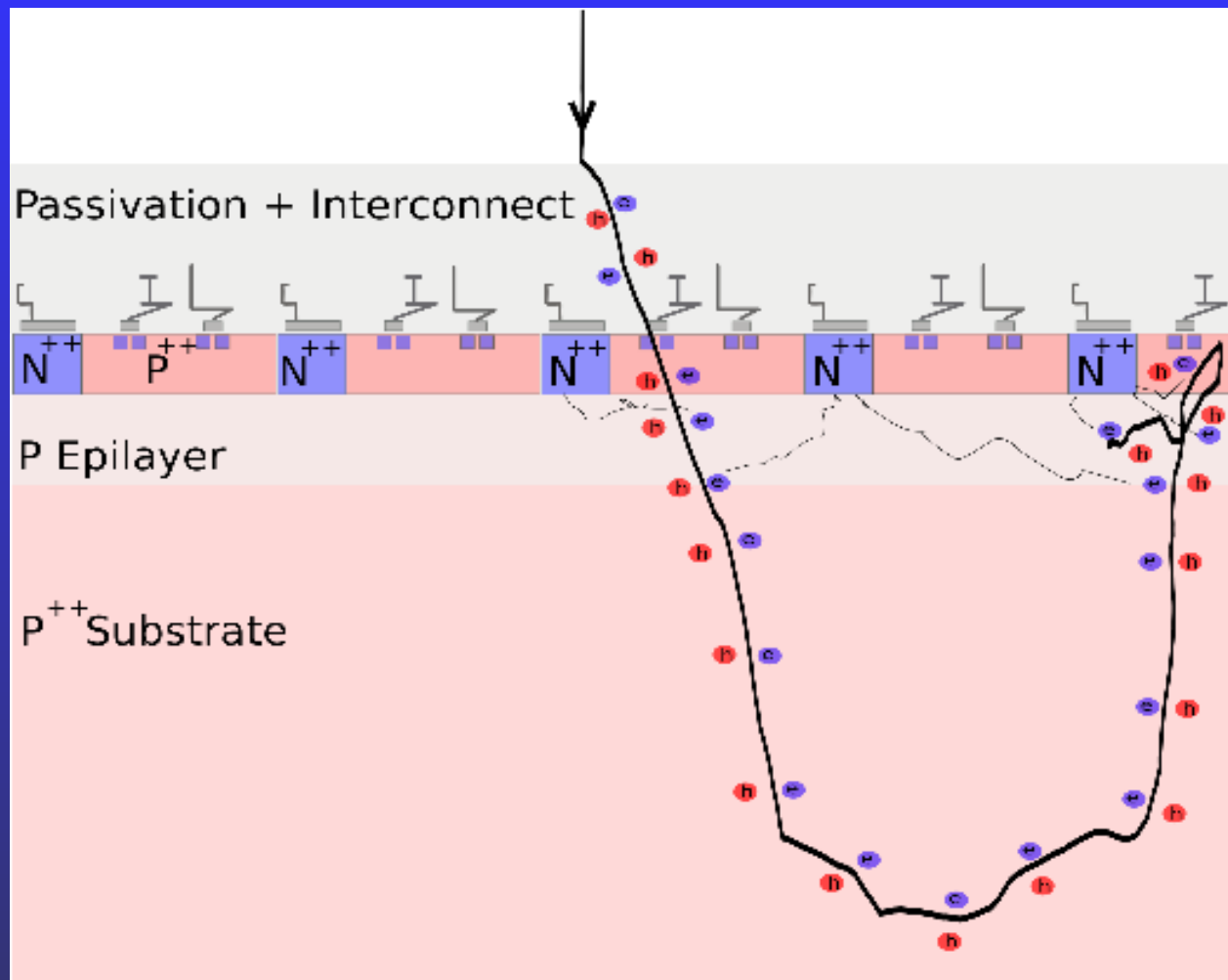
# What was wrong with film?

- DQE of film was not much lower
- Huge field of view
- Great archival media
- Fog level restricts imaging conditions ( $OD=1$ )

# MAPS Detector

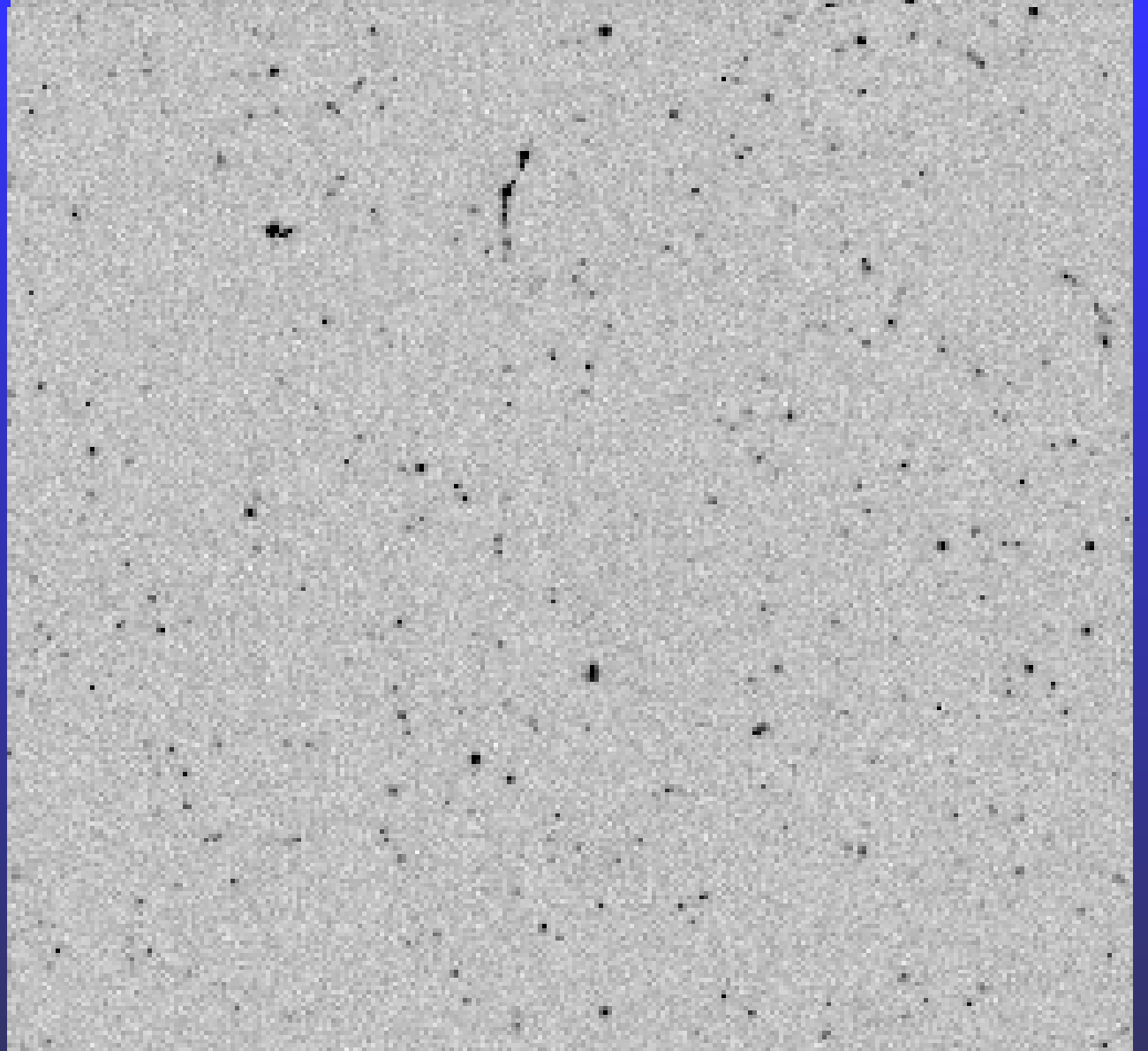
Detector must  
be  
backthinned!

Detector must  
be mounted  
carefully



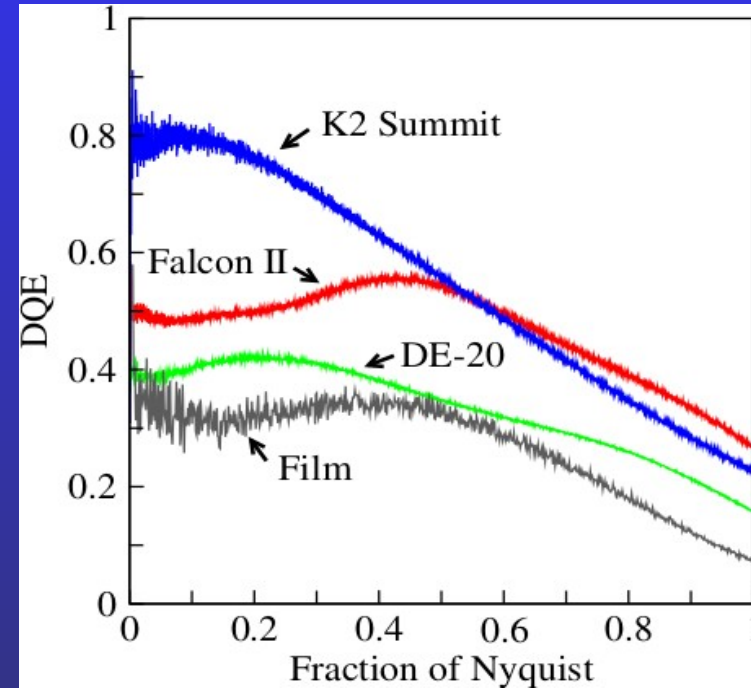
**Single  
electron  
events**

**All three  
can be used  
in counting  
mode!**



# Which is the better detector?

- All better than film
- All can collect movies
- All can be used in counting mode

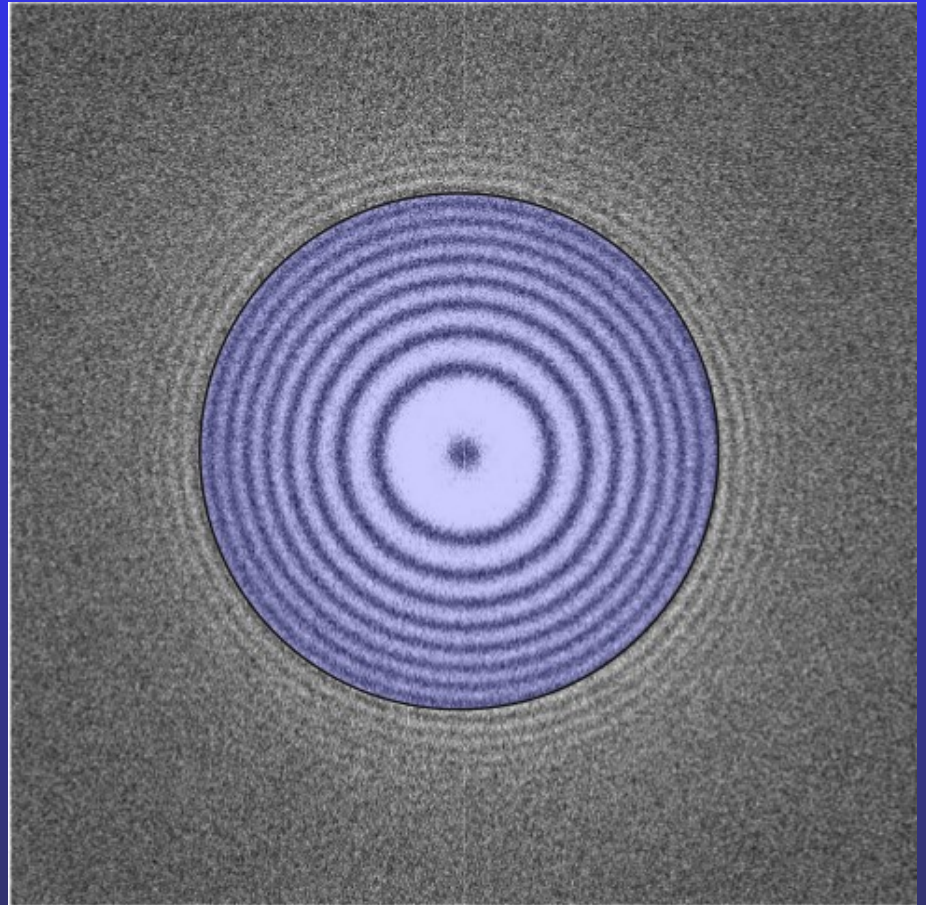


*McMullan et al, Ultramicroscopy  
147, (2014) 156-163*

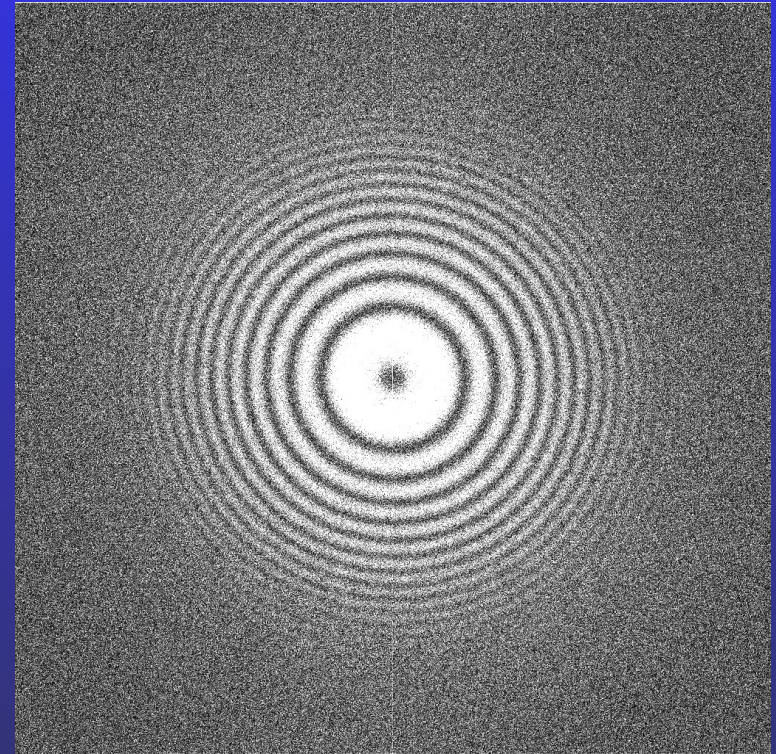
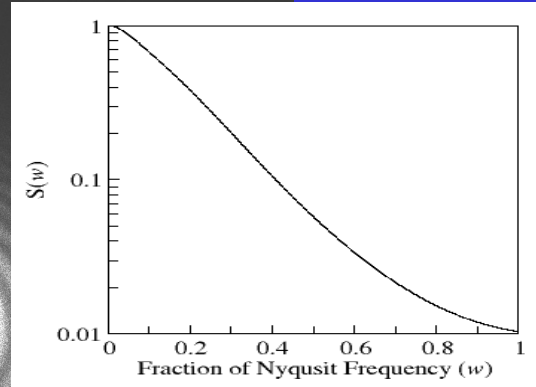
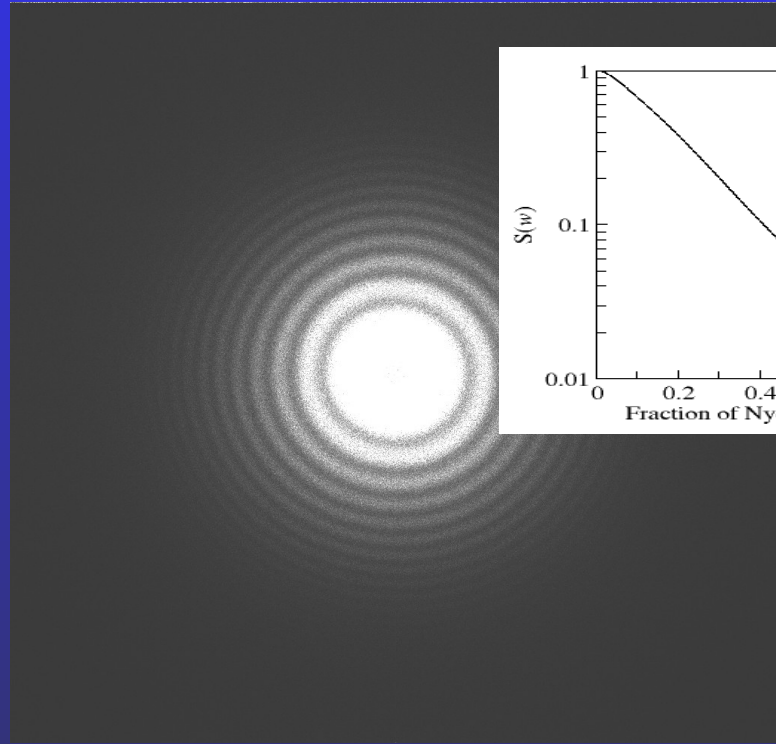


# Comparison of K2 vs Falcon II?

- K2 better at low resolution
- Falcon II better at high resolution
- Low resolution can be more radiation hard
- Tomography



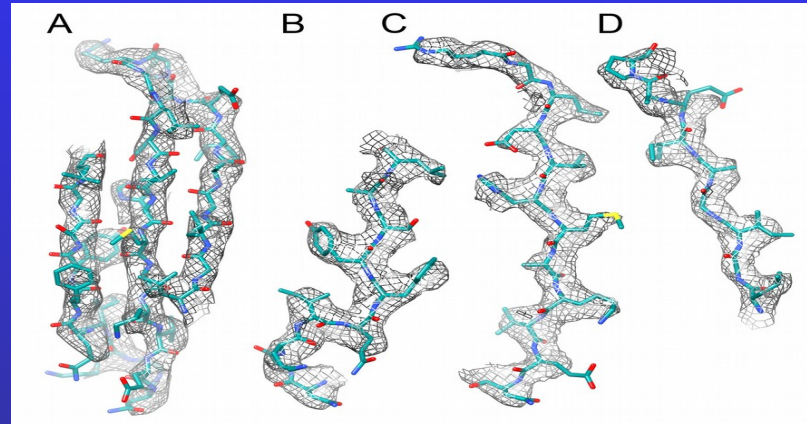
# Noise whiten Falcon II



**Pre-irradiated carbon 1.04 Å sampling**

# Are Better detectors needed?

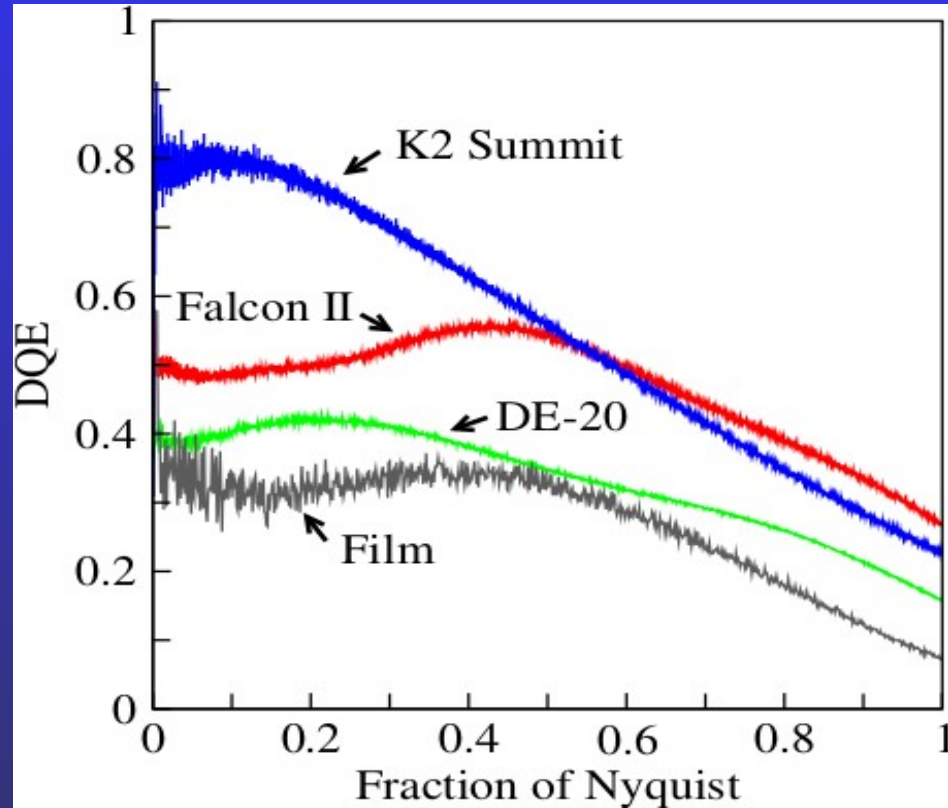
- CryoEM maps now show  $\beta$ -sheets, side chains ...
- Even higher resolution
- Smaller molecules
- Fewer particles



*Allegretti et al, eLife 3, e01963, 2014*

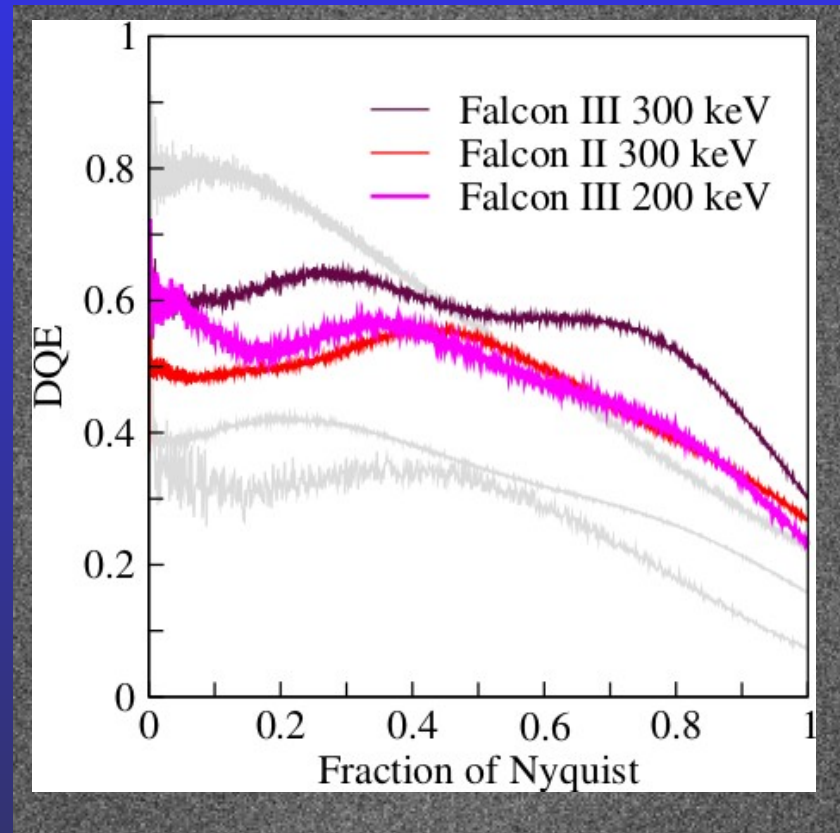
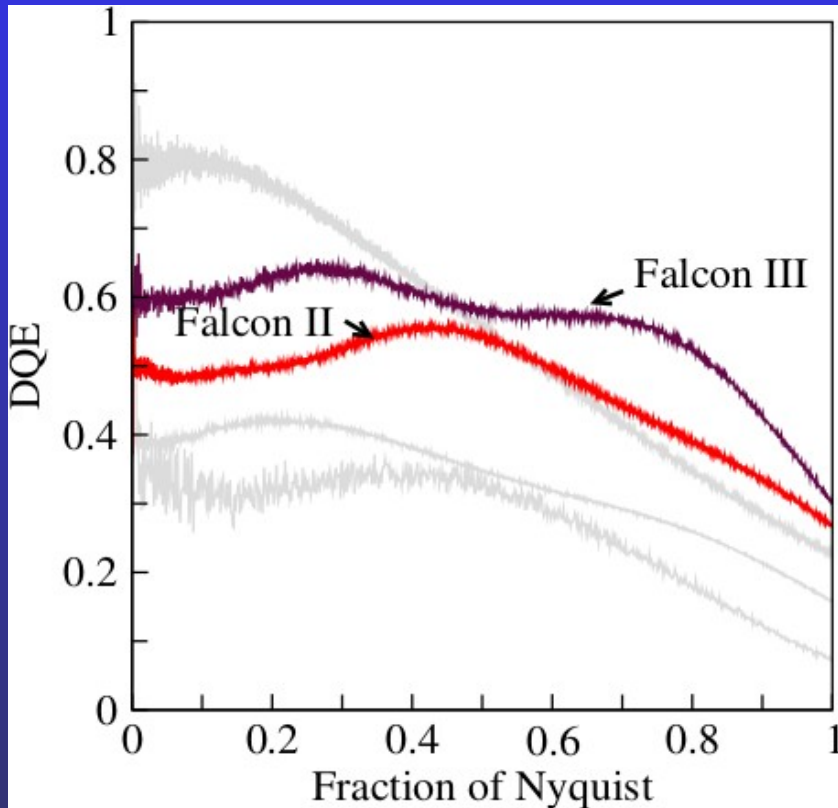
# Why the jump in resolution?

- Better detectors
- Better software
- Better computers
- Better samples
- Better ways of processing images
- More data
- Higher expectations



**Are better detectors possible?**

# Multiple companies → competition

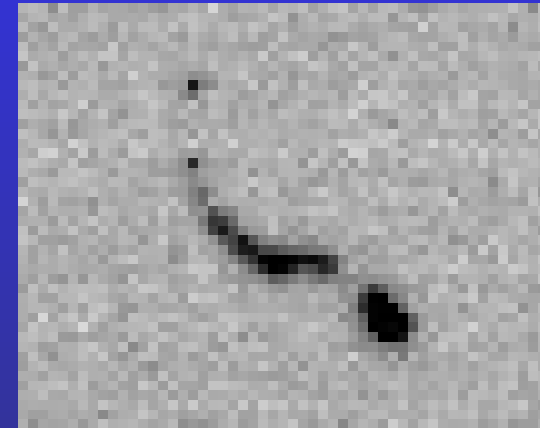
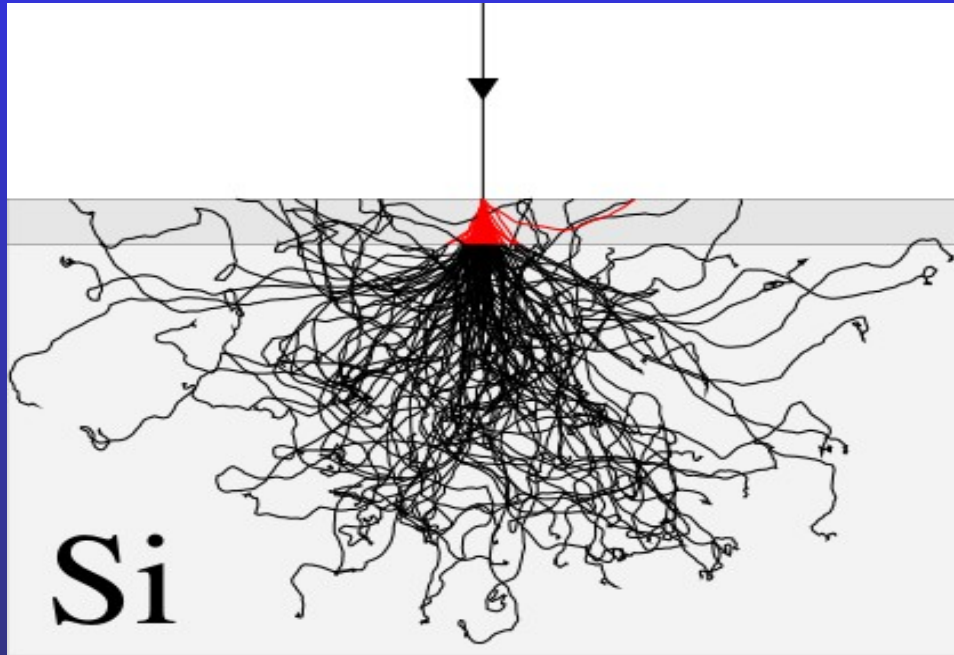


**Falcon III is probably as good as it gets for integrating detectors**

**The future is counting detectors**

**Want counting detector to be better than integrating detector over whole range (not just at low spatial frequency)**

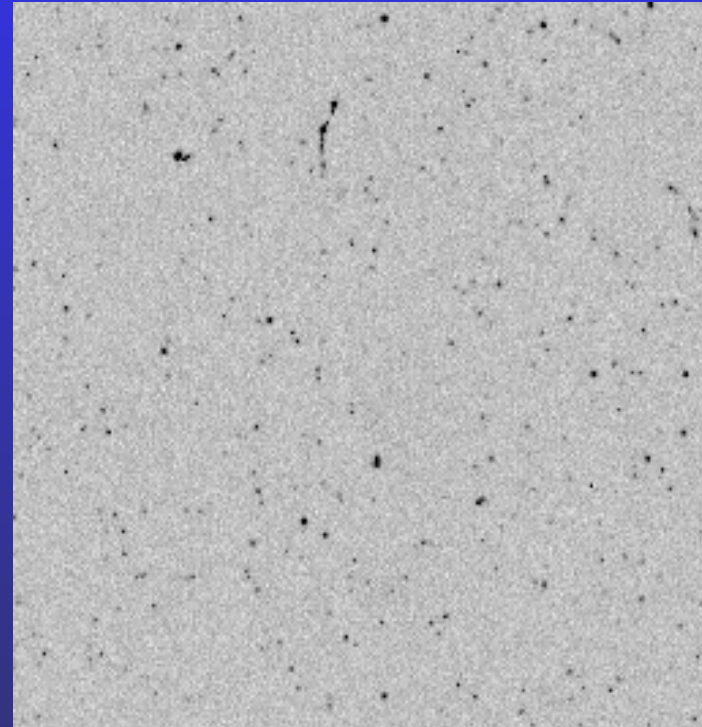
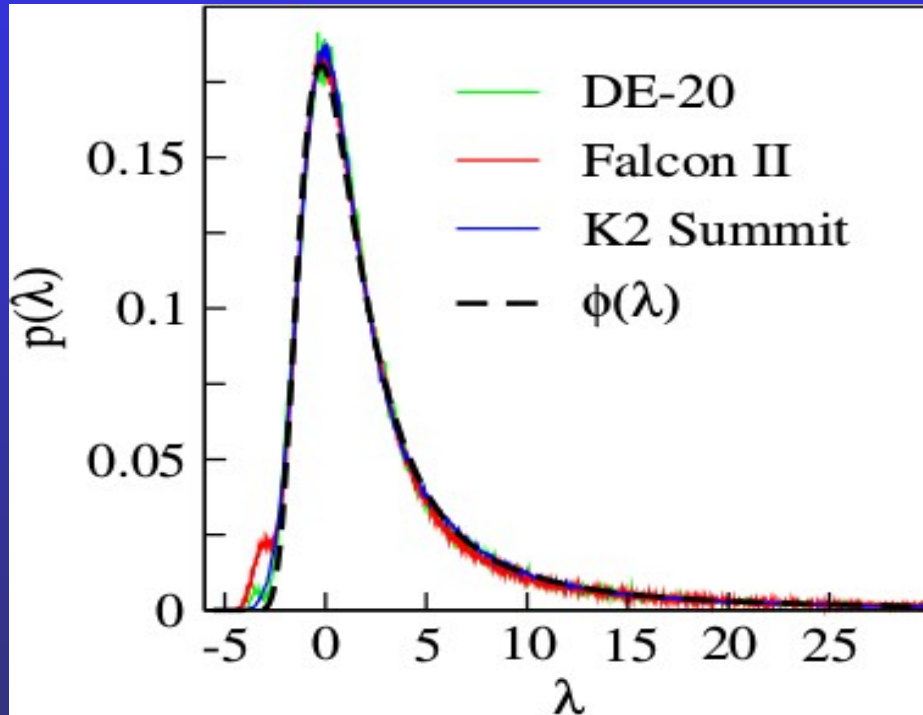
# 300 keV electrons are difficult



Taken with ~ one electron per frame!

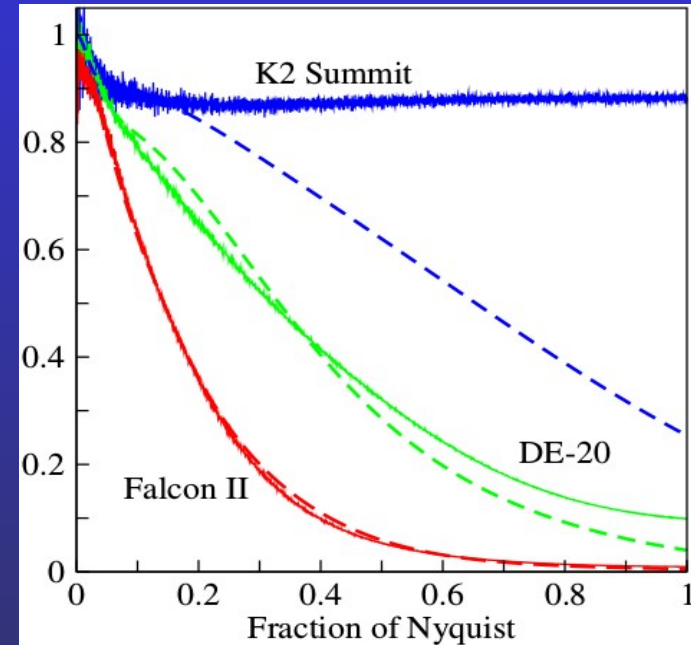
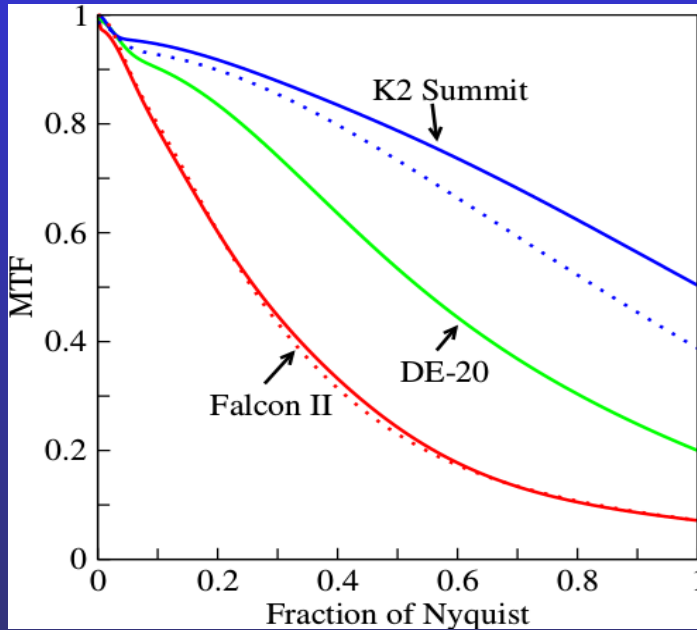


# Fundamental limit on the DQE for integrating detector



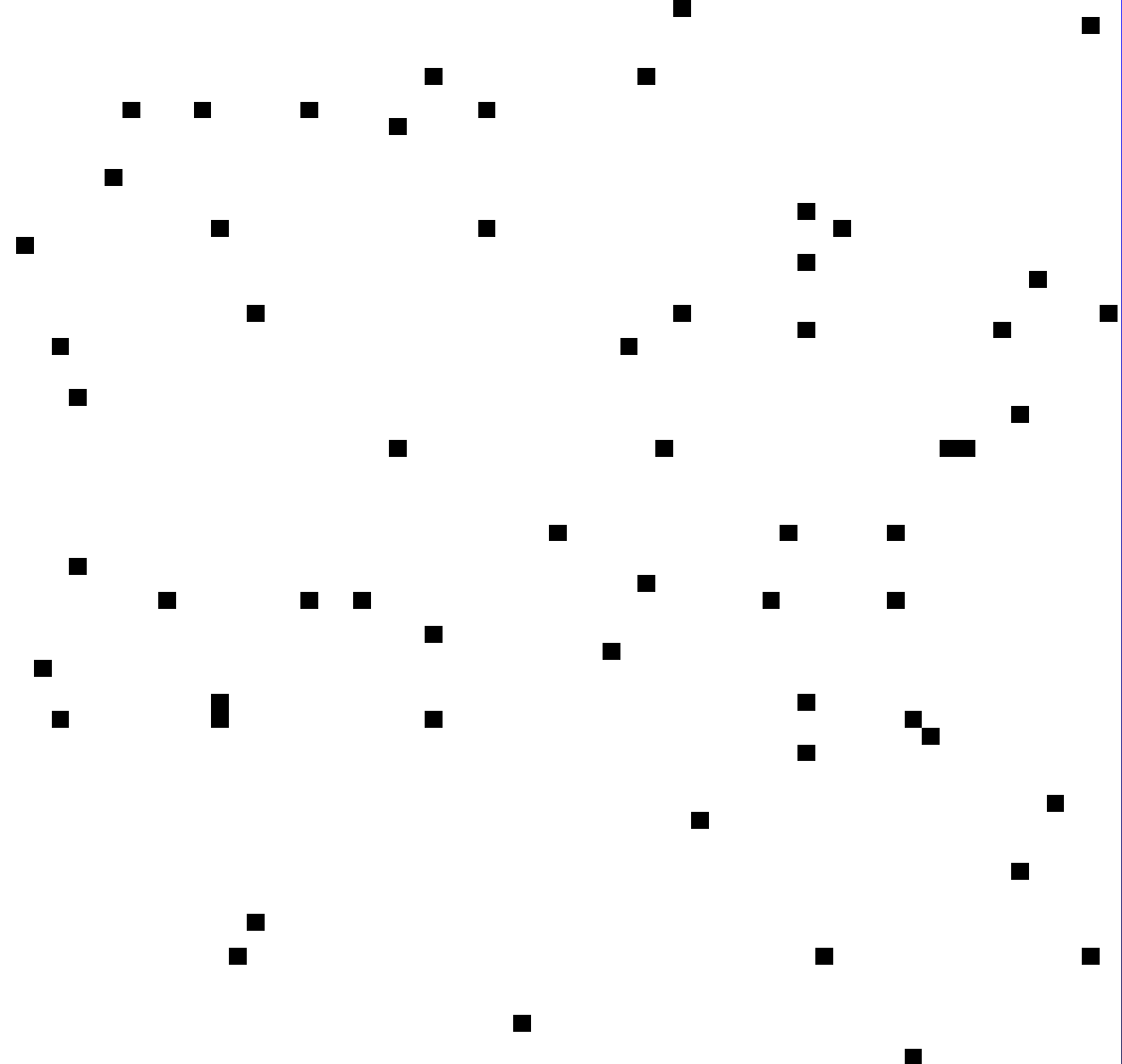
Reference: Hans Bichsel, *Straggling in thin silicon detectors* Rev. Mod. Phys 60, 701 (1988)

# Difference between integrating and counting



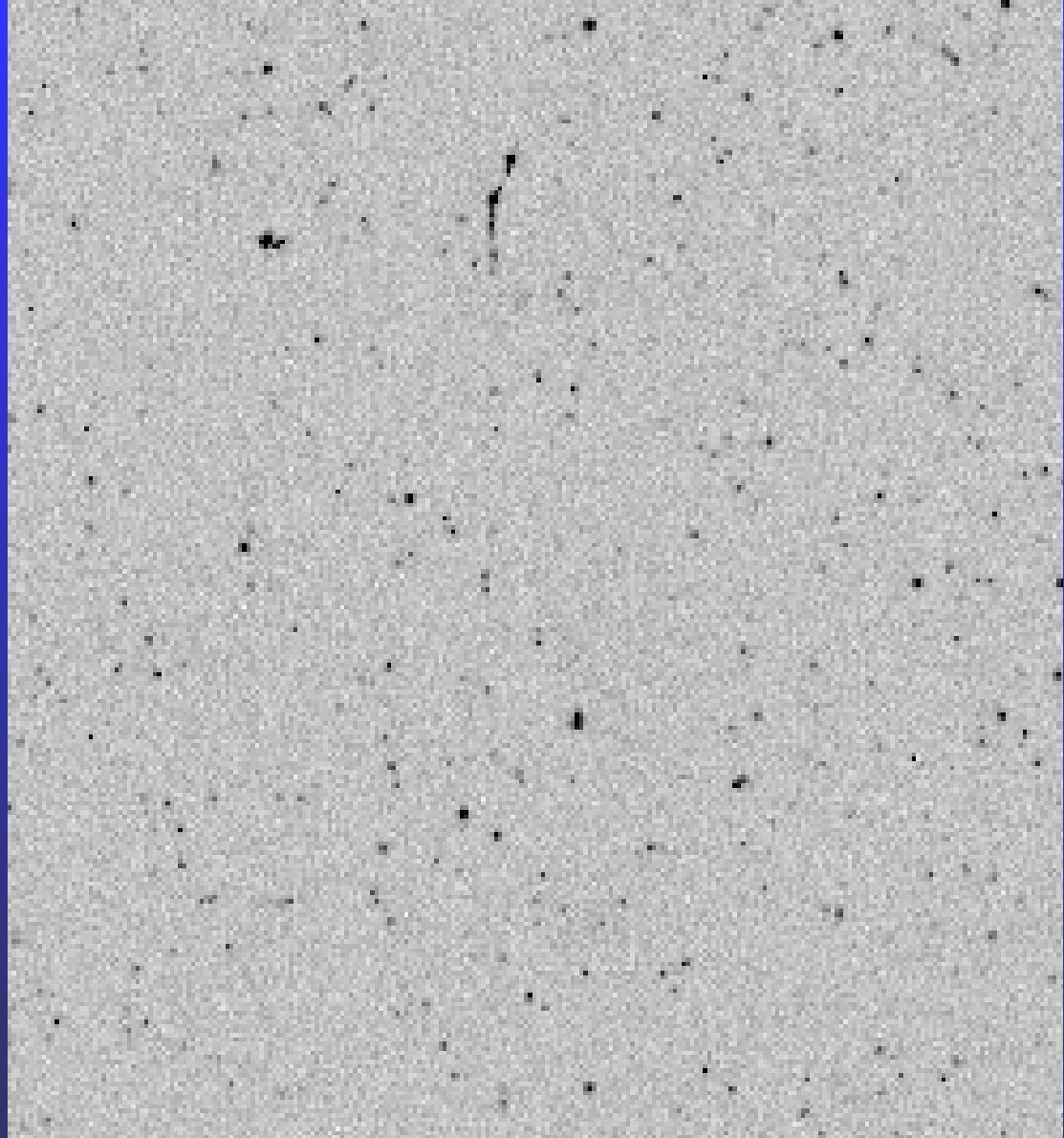
# Counting is hard

- Shows up every defect in your chip
- Can not distinguish between big and multiple events
- 1 in 80 (5 el/pixel/s)



# Counting is hard!

- Gatan have done a very good job.
- How do you do better!
- (1) A thin as possible
- (2) Better algorithms
- (3) Better hardware

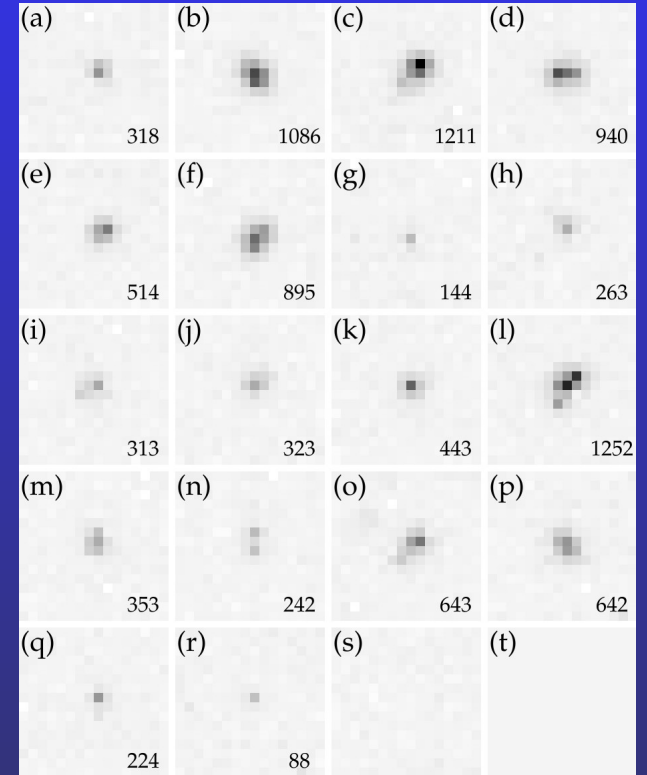
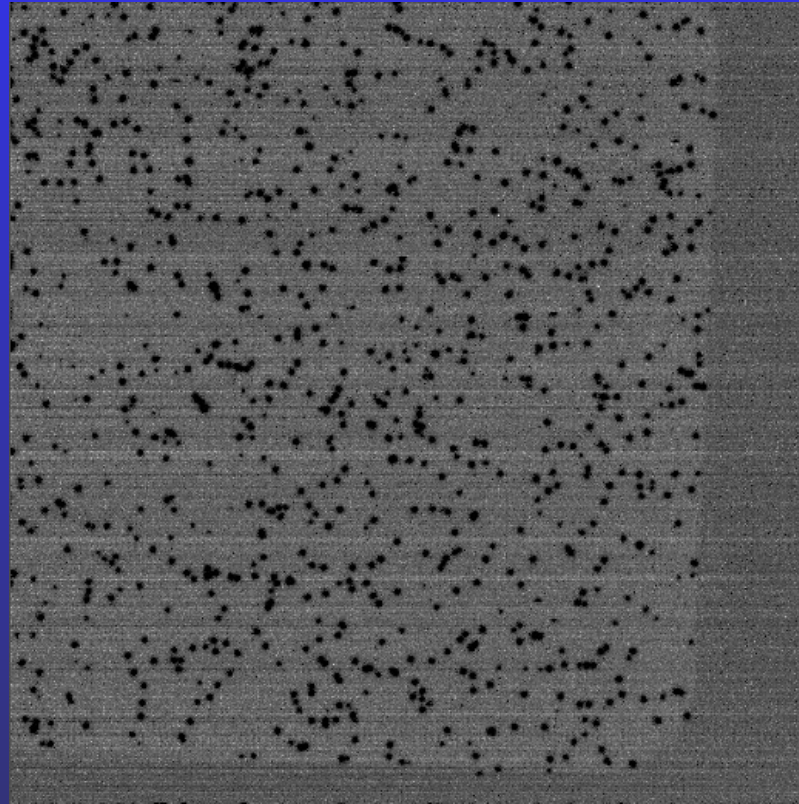


# Vanilla detector

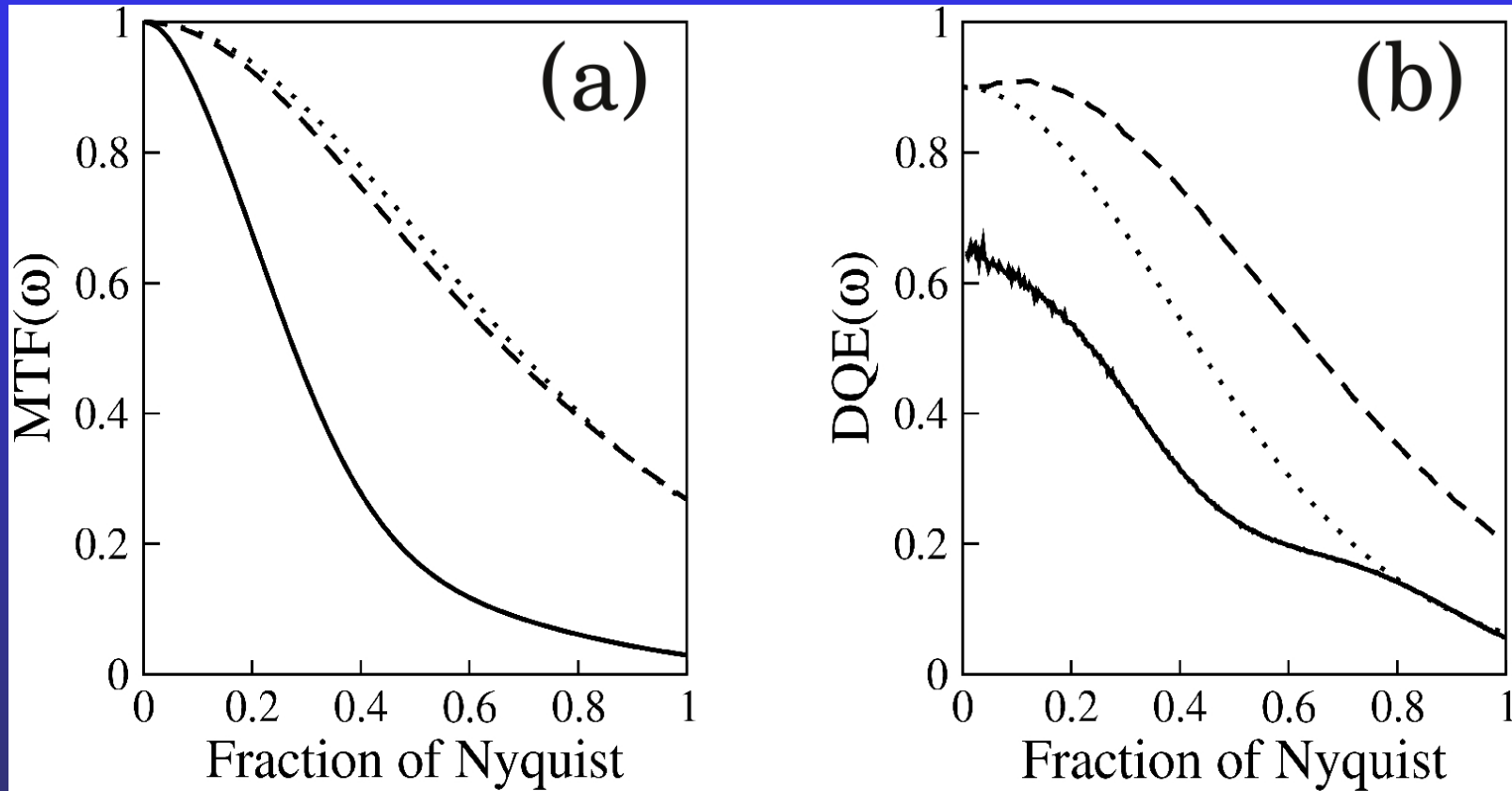
**Vanilla  
detector**

**120 keV**

**7416  
frames**



# Vanilla detector

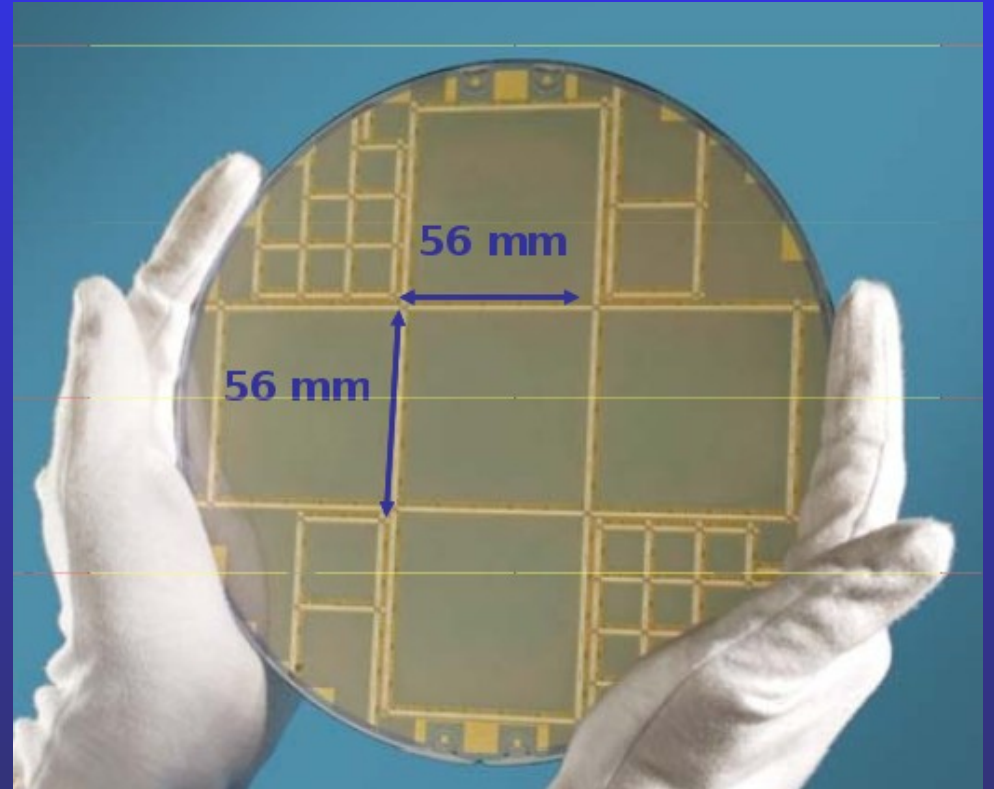


# Counting algorithms

- Don't commit to FPGA too early
- Don't put events in a single particle
- Every defect hurts
- Filter images

# MAPS detector design parameters

- Number of pixels
- Size of pixels
- Pixel design
- Technology to use
- Thickness of sensor layer
- Type of sensor layer
- Speed
- Low noise (use CDS)





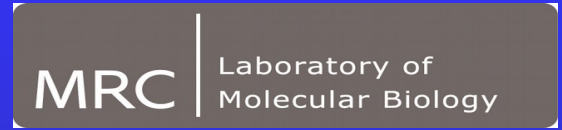
# Future

- Show counting can be done better
- DE and FEI will introduce counting modes (hopefully)
- Gatan will improve the K2
- Prices will come down!

# Summary

- Counting is the future (but not yet)
- Must be better than integrating
- Perfect images will still be horrible
- Prices will come down!

# Thanks



- Richard Henderson
- Wasi Faruqi
- Shaoxia Chen
- Vinoth Kumar
- Sjors Scheres
- ....
- Renato Turchetta
- Nicola Guerrini
- Matthijn Vos