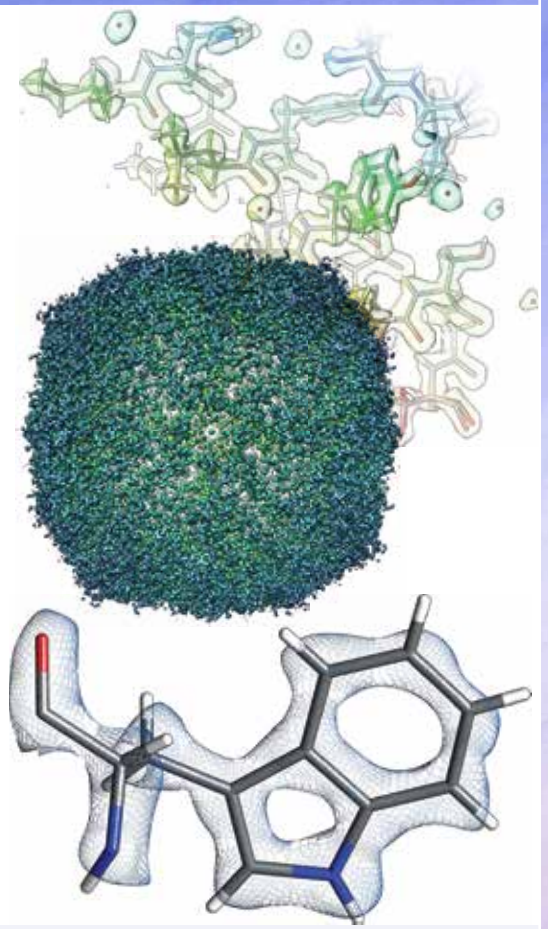
APOLLO CAMERA

Ultra-Fast Electron Counting For Cryo-EM

Delivering Bigger | Better | Faster | Cameras For Electron Microscopy

NEXT-GENERATION DIRECT DETECTOR FOR ELECTRON COUNTING

- Our novel direct detection device (DDD®) delivers ultra-low noise and extraordinary resolution for nearly any beam current for cryo-EM.
- Electron counting *in hardware* is elegant, fast, easy-to-use, and more cost effective.
- Change the paradigm for cryo-EM by removing camera limitations.
- On-chip CDS and digital output of detected events minimizes noise.
- 4k × 4k (16.8 million) physical pixels with larger 8 µm pixel size to maximize resolution.
- Super-resolution 8k × 8k (67.1 MP) counted movies saved to the computer for motion correction, dose filtering, etc.
- Integrated with SerialEM, Leginon, etc., for automated acquisition.
- Generate better results than you've ever achieved before.



1.46 Å resolution cryo-EM structure of apoferritin (EMD-33707) from Apollo on a JEOL CRYO ARM 300 II, acquired at 12 e-/physical pixel/s (eps).

DETECTOR APPLICATION:

Biology

Direct Electron®
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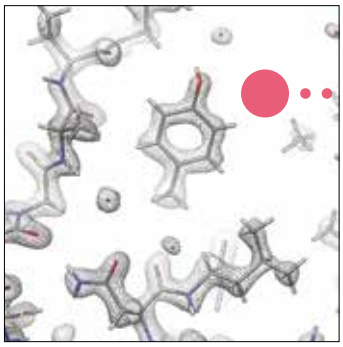
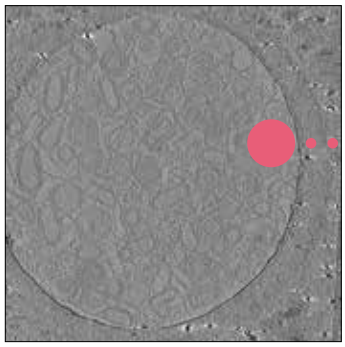
OPTIMIZED FOR DEMANDING TEM APPLICATIONS

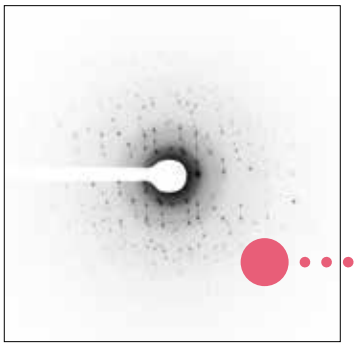


High-Resolution Single-Particle
Ultra-large search mode images without montaging

High-Throughput Automation
Ultra-fast electron counting enables short exposure times



Cryo-Tomography
Large field-of-view and high contrast

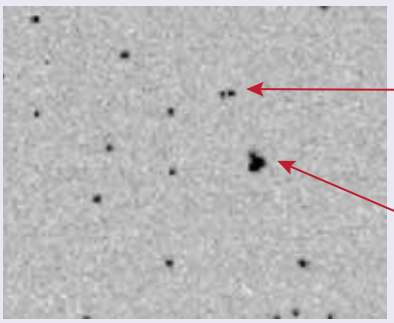


Continuous Rotation & *in situ*
Real-time counting enables dynamic applications

MicroED (Diffraction)
High dynamic range & large area for crystallography

MEASURING COUNTING SPEED: EPS, NOT FPS

PREVIOUS-GENERATION CAMERAS



It is impossible to determine if more than one electron has hit a the sensor at the same place and time. This results in coincidence loss. When the electron beam is too bright, it is likely that multiple electrons will be coincident (same time and place on the sensor) and thus be missed. **Coincidence loss is a failure to detect** electrons when the beam is too bright compared to the speed of the sensor.

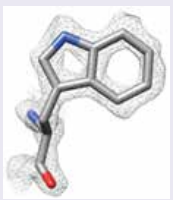
Older direct detection cameras use an internal frame rate to spread the beam over multiple frames. **On older cameras, higher fps means lower coincidence loss.**

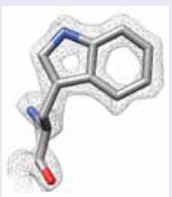
APOLLO

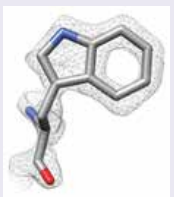
Next-generation event-based detection does not rely on internal integrating-mode frames to ensure the sparsity necessary for counting, so internal fps does not make sense.

To compare counting speed between older and newer technology, the critical measure is how much coincidence loss occurs as the beam gets brighter. In other words, **how well does electron counting work versus the input electrons per pixel per second (eps)?**

Apollo's ultra-fast counting is unmatched.

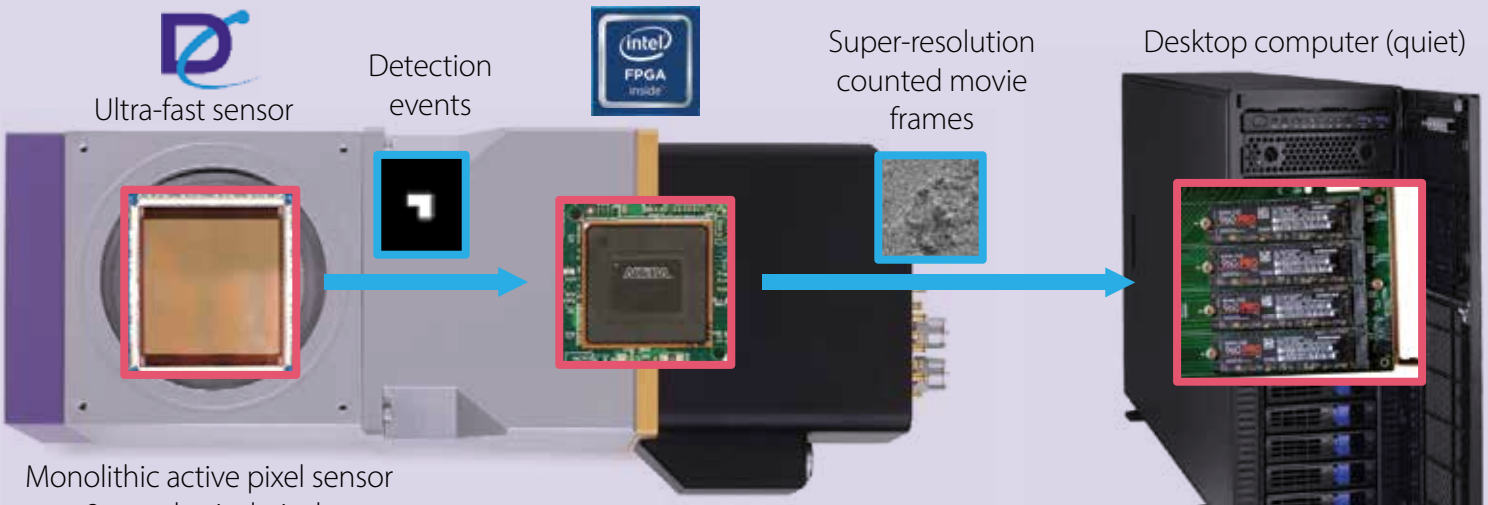

16 eps → 1.68 Å


34 eps → 1.68 Å


78 eps → 1.68 Å

Reconstructions courtesy of Scott Stagg, Florida State University (Tallahassee, FL).

A NEW STRATEGY FOR ELECTRON COUNTING: EVENT DETECTION IN HARDWARE

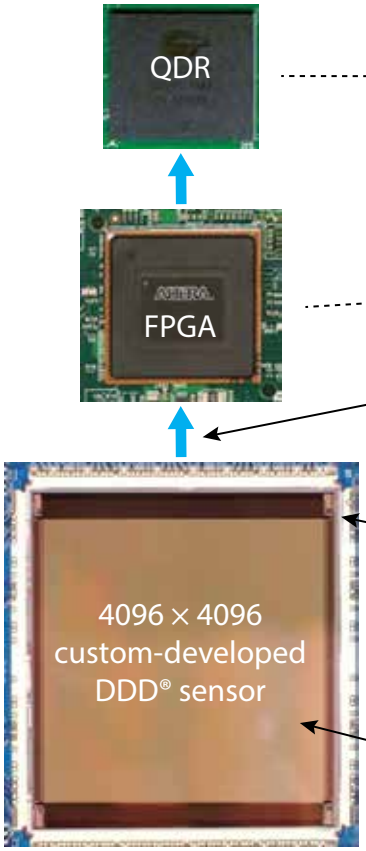


Monolithic active pixel sensor
8 µm physical pixels
4096 × 4096 physical pixels
On-chip CDS
On-chip thresholding
On-chip event detection
Event encoding

Field-programmable gate arrays
Sensor control
Real-time event processing
Super-resolution centroiding
Generation of output frames

User interface
TEM automation
Data storage/transfer
Post-processing

NEXT-GENERATION REAL-TIME ELECTRON COUNTING



US patent #10,616,521

Digital output of event blocks

Integrated circuitry on the top and bottom edges of the sensor (shielded from the electron beam)

Monolithic active pixel sensor (MAPS) for direct detection of TEM electrons

QDR memory stores each movie frame until it is output

FPGA isolates and centroids each detection event

FPGA isolates and centroids each detection event

Sense amplifier checks pixel values against a threshold

Pixel array uses on-chip CDS to minimize noise

On-board functionality

On-chip functionality

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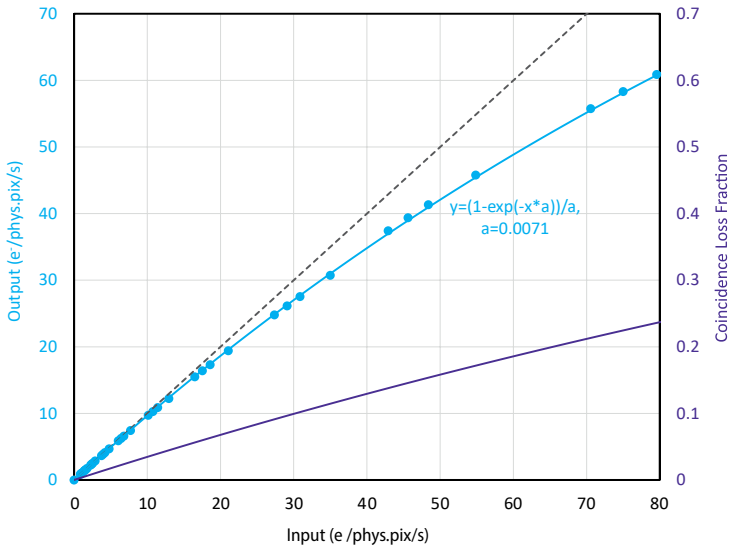
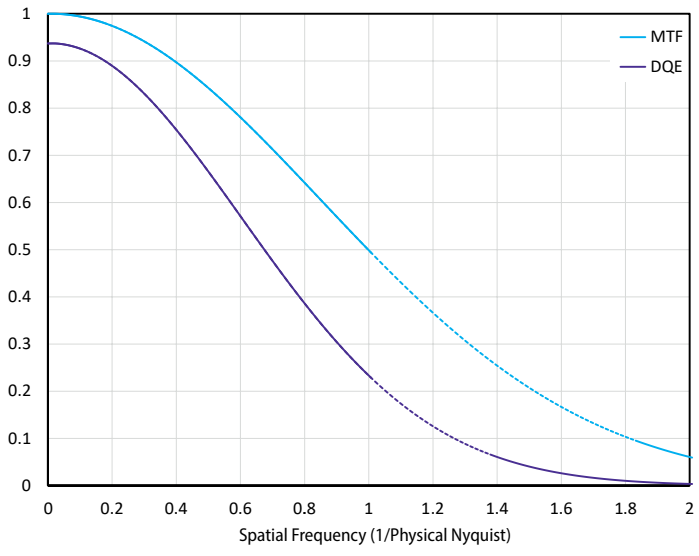
Tem Electron Energy	Sensitive to 80 keV – 1.25 MeV | optimized for 200 - 300 keV
Pixel Array Size	4096 × 4096 (16.8 million pixels) | 8 µm pixel pitch
Sensor Design	Novel event-based ultra-fast DDD® sensor on-chip correlated double sampling (CDS) | on-chip thresholding | digital readout backthinned | radiation hardened
Acquisition Modes	Event-based electron counting, *always*
Detection Efficiency	>90% For 200 - 300 kV
Exposure Rate	~0.01 - 75 e-/pixel/second (ranging ~4 orders of magnitude)
Linearity	>95% linear up to ~15 e-/pixel/second
Dose Fractionation	8192 × 8192 (67.1 Million pixels) super-resolution counted movies flexible dose fractionation time | 16.7 ms minimum
TEM Compatibility	All major TEM manufacturers & models
Mounting Position	Fully retractable | compatible with a wide-range of configurations typically in TEM bottom port, pre- or post-energy filter, or in JEOL film drawer
Sensor Protection	TEM blanking/shuttering | failsafe software
Computer System	High-performance computer | Windows 10 | Nvidia GPU(s) | up to 55 TB storage
Image Format	Non-proprietary | MRC, TIFF, or TIFF LZW
Automation Software	SerialEM | Leginon | JADAS (JEOL) | open API (supporting Python, C, C++, C#, etc.)
Integrations	CEFID post-column energy filter (CEOS)





DQE curves are shown for 300 kV electrons with Nyquist meaning the physical (non-super-resolution) Nyquist | Specifications and performance are subject to change.