

Selectris and Selectris X Imaging Filters

Experience the thrill of atomic-resolution cryo-EM

Designed for stability and speed, the Thermo Scientific™ Selectris™ and Selectris X Imaging Filters are post-column imaging filters that improve the contrast of TEM images, resulting in high-resolution structures up to atomic resolution.

The zero-loss filtering of the Selectris Filters removes noise caused by inelastically scattered electrons, producing an increased signal-to-noise ratio (SNR). This is a benefit not only for relatively thicker cryo-electron tomography samples, but also for thin samples used in single particle analysis (SPA), where a strong contrast enhancement is observed. Designed for high stability, ease of use, and paired with the latest generation Thermo Scientific Falcon 4i Direct Electron Detector, Selectris Filters enable you to obtain high-resolution structures quickly for novel biological insights.

Cryo-electron microscopy (cryo-EM), the imaging of biological molecules suspended in a thin layer of vitrified water, is often challenging as radiation damage inevitably restricts the electron dose that can be applied. This, in turn, results in long acquisition times, unless contrast can be enhanced otherwise.

Zero-loss energy filtering provides a means to improve image SNR, resulting in enhanced contrast, higher resolution reconstructions and increased throughput. This can lead to new biological insights and allows further increases in cryo-EM workflow productivity.

With the Selectris Filters, zero-loss energy filtering is straightforward due to the thorough integration of software and hardware along with extensive automation and exceptional stability. Every mechanical and electron-optical element has been designed for stability and reproducibility, enabling the unattended and reliable acquisition of large datasets with narrow energy slit widths (<10 eV). Particularly for the thin samples often used in SPA, the capability to use <10 eV slits provides an additional boost in contrast, enhancing signal strength, resolution and throughput.

Key Benefits

Designed for stability

- Contrast enhancement on thin and thick samples thanks to <10 eV zero-loss energy-filtered transmission electron microscopy
- Sophisticated aberration correction, low image distortions, and uniform energy resolution over entire field of view
- Minimized sensitivity to temperature variations

Straightforward operation

- Fully integrated in Thermo Fisher Scientific instrument operation software as well as Thermo Scientific EPU and Tomography Software for data collection
- Filter tuning is only needed occasionally and is completely automated
- No need to interrupt data collection for zero-loss centering

Falcon 4i Direct Electron Detector

- High throughput for more images per hour
- Unsurpassed imaging quality with high DQE
- Lossless data compression with patented Electron Event Representation (EER)

The Selectris Filters are paired with the latest generation Thermo Scientific Falcon™ 4i Direct Electron Detector and are fully integrated into the instrument's operation and application software. Selectris Filters are available on the award-winning Thermo Scientific Krios™ and Glacios™ Cryo-TEMs.

Selectris X Filter – taking the next step toward atomic resolution

Expanding on the stability, ease-of-use, and performance of the Selectris platform, the Selectris X Imaging Filter offers an even more sophisticated electron optical system for further aberration correction. This results in extremely low distortion characteristics in both the image and energy domains, opening the way to true atomic-resolution structures in single particle analysis cryo-EM.

Designed for stability

The Selectris Filters feature a symmetrical design that is robust against changes in ambient temperature, resulting in minimal impact on the relative positions of prism, multipoles, slit and beam. This stability allows the use of narrow energy-slit widths (<10 eV) during longer experimental periods, without the need to interrupt data collection for re-centering.

Furthermore, the bending prism was designed with a large radius (135 mm), thereby producing intrinsically small aberrations and thus a low need for tuning. In combination with the high mechanical accuracy of the multipoles, this leads to low image distortions and uniform energy resolution over the entire field of view.

Selectris Filters have also been carefully designed for low power dissipation, such that water cooling is not required, enhancing stability even further.

Fully integrated and automated tuning

To ensure smooth daily operation and efficient data acquisition, Selectris Filters are fully integrated into the instrument's operation software, Thermo Scientific EPU Software, and Thermo Scientific Tomography Software.

The high stability of these filters also means that tuning is rarely required, but when it is necessary, tuning can be completed automatically within minutes.

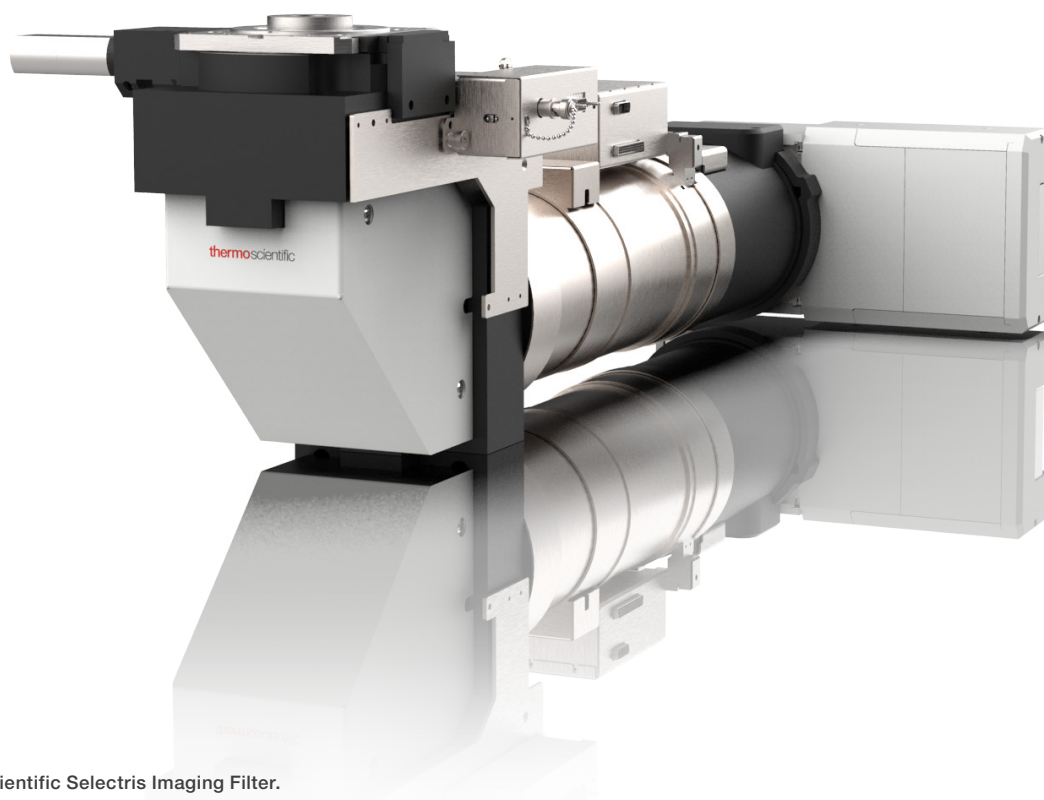
Falcon 4i Direct Electron Detector

Selectris Filters are paired with the latest generation Falcon 4i Direct Electron Detector, which features a high DQE over the entire spatial frequency range, making it particularly suited for small or difficult to detect proteins, as well as for low-dose cryo-electron tomography.

Without any compromise on SNR, the Falcon 4i Detector has an increased internal frame rate of 320 fps, so typical exposure times are decreased by a factor of 1.3 compared with those in the previous generation Falcon 4 Detector (at 250 fps). With ever shorter exposure times, the "overhead" time of an acquisition becomes a dominant factor in total experiment throughput. Data stream optimization and camera control improvements have enabled a five-fold reduction of camera overhead, to only 0.5 seconds per acquisition.

In addition to improved speed, the Falcon 4i Detector also benefits from an improved DQE at high spatial frequencies. It now fully exploits the sensor's accurate sub-pixel localization potential by using Electron Event Representation (EER) as its native file format. EER format uses lossless data compression and retains full spatial and temporal resolution, allowing super resolution, and avoids the need for fractioning data.

The increased internal frame rate in combination with improved overhead yields a significant increase in throughput, depending on the use case: 1,200 images per hour have been demonstrated.



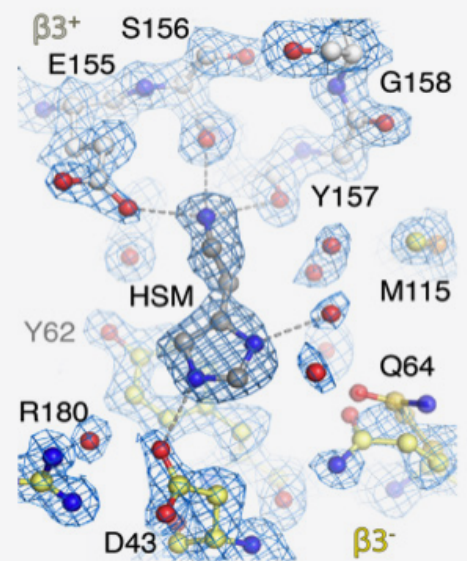
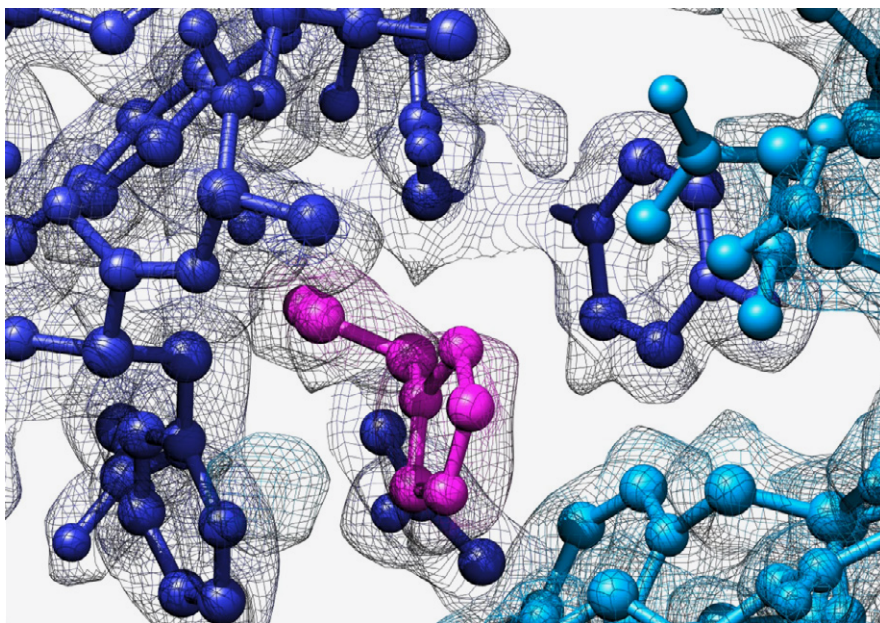
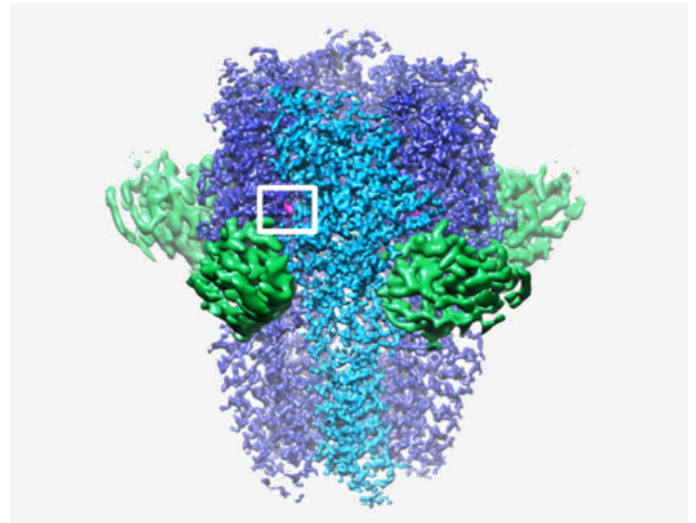
The Thermo Scientific Selectris Imaging Filter.

Human GABA_A receptor resolved at 1.7 Å

GABA_A is a 200 kDa human membrane protein, and carries the primary target sites for a wide range of clinically-relevant drugs, including general anaesthetics, benzodiazepines, barbiturates and neuroactive steroids. Here, a GABA_A receptor, bound to its small molecule agonist, histamine, was analyzed.

Experimental details:

- Filter slit width = 5 eV
- Falcon 4 Detector EER mode
- Reconstruction generated from approximately 370,000 particles
- 1.7 Å map with B-factor of 47 Å²



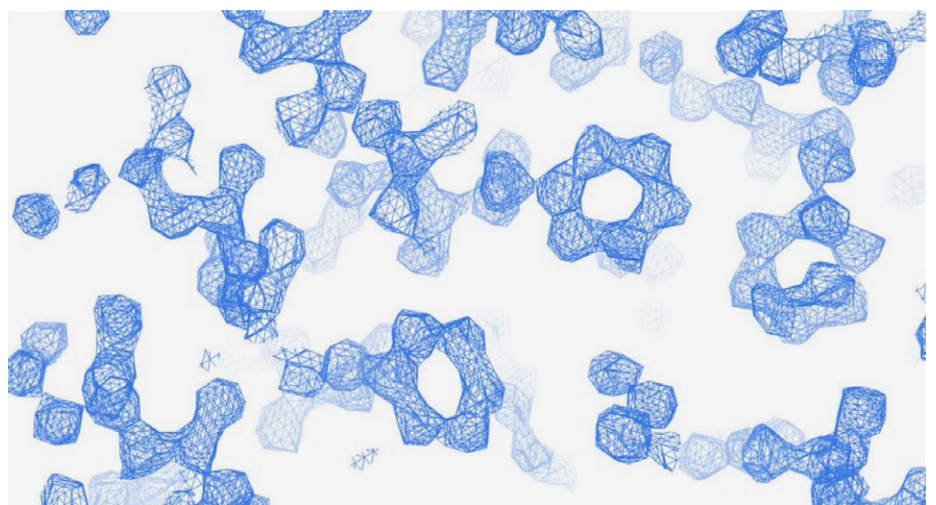
GABA_A receptor resolved at 1.7 Å shown from a side view (top right). Detail of the binding pocket is shown in the bottom left. Histamine coordination and a number of water molecules (red spheres) are shown on the bottom right. Adapted from Nakane, T. et al. Nature (2020), CC-BY 4.0. Image courtesy of Andrija Sente and Radu Aricescu, MRC-LMB Cambridge.

Mouse apoferritin resolved at 1.2 Å

Apoferritin is an iron-storing protein that is often used to characterize cryo-EM performance because of its high stability. Here, it was used to demonstrate the structure determination of a protein at true atomic resolution.

Experimental details:

- Filter slit width = 10 eV
- Falcon 4i Detector EER mode
- Reconstruction generated from approximately 297,000 particles
- 1.2 Å map with B-factor of 28 Å²



A 1.2 Å resolution reconstruction of apoferritin was created from 3,600 images of 297k particles acquired in 6 hours (EPU data was acquired on the Thermo Scientific Krios G4 Cryo-TEM). Recorded at a dose rate of 5.4 e/p/s.

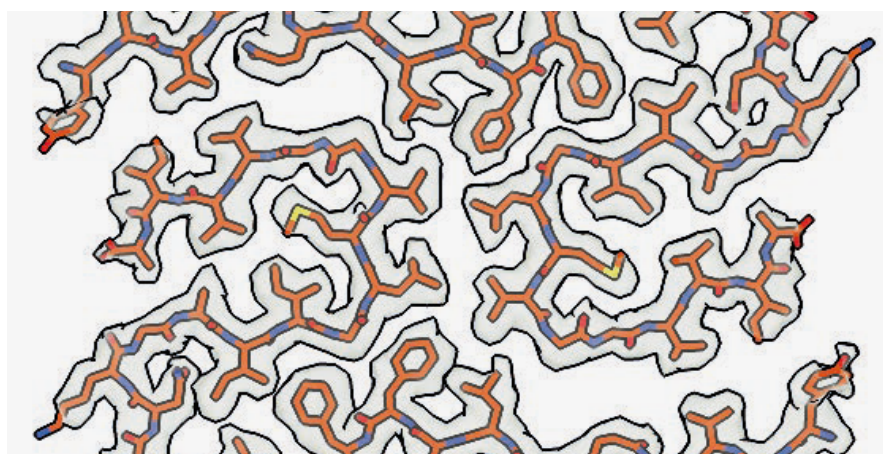
System requirements

Compatibility: Selectris and Selectris X Filters are available on new Krios and Glacios Cryo-TEMs. Retrofits to existing microscopes are possible on most Thermo Scientific cryo-TEMs operating under Windows 10.

Filter performance	200kV		300kV	
	Selectris Filter	Selectris X Filter	Selectris Filter	Selectris X Filter
Zero Loss Peak (ZLP) stability (eV / 24 hours)	<±1.5 ⁽¹⁾		<±1.5 ⁽¹⁾	
Slit width minimum (eV)	2	1	2	1
Geometrical Image distortions - max (%)	<0.5	<0.1	<0.5	<0.1
Chromatic distortion – max (%)	<0.4	<0.2	<0.4	<0.1
Non-isochromaticity - max (eV)	<1.0	<0.3	<1.0	<0.3
Falcon 4i Direct Electron Detector performance				
Camera architecture	Direct electron detection			
Sensor size	4,096 × 4,096 pixels ~ 5.7 x 5.7 cm ²			
Pixel size	14 x 14 μm ²			
TEM operating voltages	200 kV, 300 kV			
Internal frame rate	320 fps			
Frame rate to storage	320 fps (EER mode)			
Camera overhead time	0.5 s per acquisition			
File formats	EER (native), MRC, TIFF, LZW TIFF			
Lifetime (<10% DQE degradation)	5 years in normal use (1.5 Ge/px)			
Modes	Electron counting mode Survey mode (fast linear mode)			
Imaging performance in EER mode (4k x 4k) ⁽²⁾	300 kV		200 kV	
DQE (0)	0.92		0.91	
DQE (½ Nq)	0.72		0.62	
DQE (1 Nq)	0.50		0.33	

⁽¹⁾ Disturbances from doors opening/closing, air-con units and ventilation valves switching etc are excluded from the measurement. Krios room must be within specifications from Krios pre-installation manual (< 0.8 °C p-p/ 24 h).

⁽²⁾ For each sensor, DQE is guaranteed by factory validation of Critical to Quality (CTQ) parameters in a Certificate of Compliance; these measurements cannot be repeated on-site.



Cryo-EM structures of Amyloid-β 42 filaments isolated from human brain. Data was collected at a flux of 8 e/p/s; magnification of 0.74 Å/pix; 40 e/Å² total dose and a throughout of 570 movies/hr resulting into a 2.5 Å reconstruction. (Data collected in collaboration with MRC – Laboratory of Molecular Biology, Cambridge) doi: <https://doi.org/10.1101/2021.10.19.464936>

Learn more at thermofisher.com/Selectris

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