

Glacios 3 Cryo-TEM

Outstanding 200 kV performance meets undeniable practicality

Cryo-electron microscopy (cryo-EM) has transformed the landscape of biological research and drug discovery by enabling the visualization of biomolecules in their native states, revealing critical structural details of proteins, viruses, and cellular machinery.

The Thermo Scientific™ Glacios™ 3 Cryo-TEM expands on the established Glacios platform, creating a high-performance 200 kV solution for high-resolution single particle analysis (SPA), cryo-electron tomography (cryo-ET), and microcrystal electron diffraction (microED) that supports biological discovery, drug design, and more.

With the built-in Thermo Scientific™ READY™ System, the Glacios 3 Cryo-TEM is easier to install in more lab spaces, reducing renovation costs and installation timelines.

Easier installation brings cryo-EM to more lab spaces

Built-in environmental mitigation with the READY System

The installation of a cryo-TEM can be complex, often requiring expensive and time-consuming renovations with specialized HVAC systems, vibration-isolating flooring, faraday cages, etc.

To address these challenges, the Glacios 3 Cryo-TEM features the built-in READY System for the mitigation of environmental disruptions; this would have eliminated the need for facility renovations at 80–95% of sites previously surveyed by Thermo Fisher Scientific for electron microscopy installations over the last decade. As a result, Glacios 3 Cryo-TEM installations can be completed with substantially lower costs, reducing installation timelines from a year or so to a few months.

Key features

High-performance 200 kV imaging that supports multiple high-resolution cryo-EM techniques, including single particle analysis, cryo-electron tomography, and microcrystal electron diffraction

AI-powered software facilitates cryo-EM workflows with real-time feedback to guide decisions, screen samples, and automate complex tasks

A compact size, with built-in protection against environmental disturbances provided by the READY System, substantially lowers renovation costs and shortens installation timelines

Enhanced optical innovations lower acquisition time and data storage demands

Remove the guesswork from experimental set-up with an AI-trained optical model, making the process faster and easier, particularly for less experienced users



Figure 1. The Glacios 3 Cryo-TEM brings cryo-EM to more lab spaces with its compact design and built-in READY System, which mitigates external disturbances.

The READY System protects against the following environmental disturbances:

- **Acoustic:** The patent-pending enclosure includes five layers of acoustic insulation that significantly reduce sound-related interference by approximately -25 dB
- **Temperature:** The acoustic isolation layers also protect against temperature variations, allowing for shifts of up to 2°C peak to peak in 24 hours, which can be maintained by standard HVAC systems
- **Electromagnetic interference (EMI):** Optional sensors and an active suppression system can be integrated into the frame to detect and reduce EMI
- **Vibration:** Optional active vibration blocks are integrated into the system base to compensate for floor vibrations; these blocks also protect against unforeseen new sources of vibration, such as construction



Figure 2. The Glacios 3 Cryo-TEM enclosure features five layers of acoustic and temperature insulation

Compact design with a shorter height

All system configurations of the Glacios 3 Cryo-TEM fit in rooms with minimum dimensions of 4.2 x 3.8 x 2.7 m (WxLxH). This represents a 22% reduction in size compared to the largest configuration of the previous Glacios system, and helps ensure compatibility with standard United States ceiling heights.

High-performance 200 kV cryo-EM

The Glacios 3 Cryo-TEM can be fully integrated with our most advanced components and software, including the READY System, the Thermo Scientific™ Falcon™ 4i Direct Electron Detector, and a low-energy-spread cold field emission gun (E-CFEG). Together, these result in an information limit validated to 1.4 Å, as measured using Young's interference fringes.

Falcon 4i Detector for fast, high-quality imaging

The Falcon 4i Direct Electron Detector delivers a fast frame rate and reduced overhead to enable efficient data collection. Its high detective quantum efficiency (DQE) helps ensure outstanding image quality across all spatial frequencies. Additionally, the

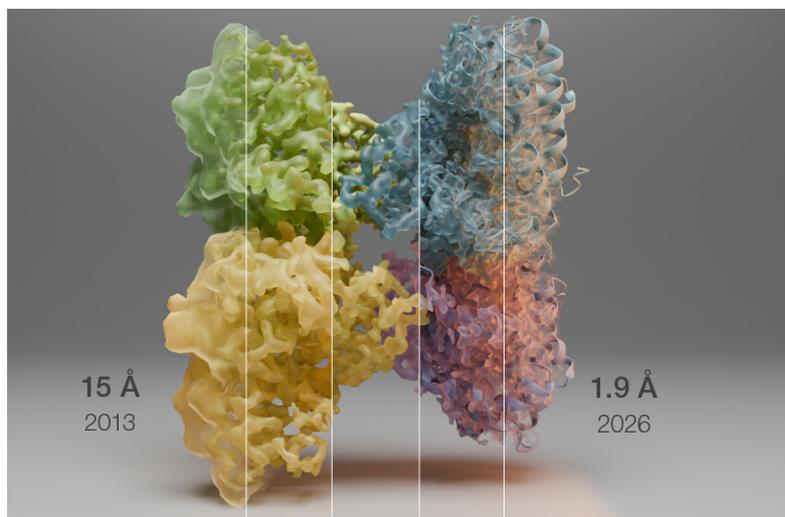


Figure 3. Structural determination with 200 kV cryo-TEM has dramatically improved over the years with advancements in both hardware and software. With the Glacios 3 Cryo-TEM, a structure at 1.9 Å of aldolase could be determined from 8,925 images, which were collected in 12 hours (EMD-74335). To achieve the previous 2.1 Å resolution from 2020 (EMD-21023), only 4 hours of data collection would have been needed.

innovative electron event representation (EER) mode boosts DQE at high resolutions, supporting super-resolution imaging and lossless data compression without upfront fractionation.

Selectris Imaging Filters for enhanced image contrast

Thermo Scientific™ Selectris™ Imaging Filters are post-column filters with a highly stable energy slit that provides narrow widths (<10 eV) for imaging. By allowing only the zero-loss peak to pass through, inelastically scattered electrons are removed. This improves signal-to-noise ratio and image contrast, enhancing image quality for both single particle analysis and cryo-ET. Additionally, fewer images are needed to achieve high-resolution reconstructions, reducing acquisition time and increasing throughput.

E-CFEG for high image contrast and resolution

The low-energy-spread E-CFEG is a high-brightness, high-coherence electron source that produces a highly stable electron beam. It offers significant benefits for cryo-TEM, including high image contrast and resolution, which makes it easy to visualize small or low-contrast biological structures. An additional benefit of E-CFEG is its inherently longer lifetime, which reduces service costs and minimizes system downtime.

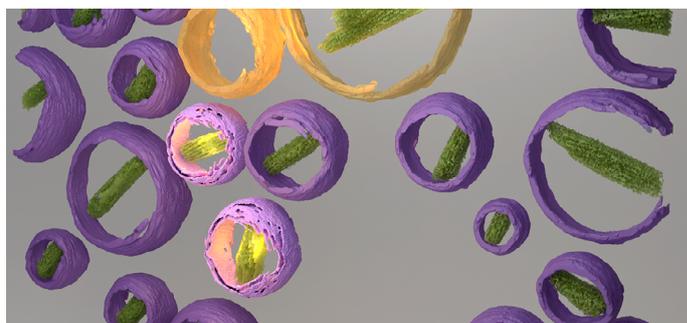


Figure 3: Liposome-encapsulated doxorubicin, a chemotherapy drug formulation, imaged with 200 kV cryo-ET. Purple shows correctly packaged liposomes for drug delivery while yellow indicates improperly packaged liposomes. Data segmentation with Thermo Scientific™ Amira™ Software. 3D rendering created in Blender.

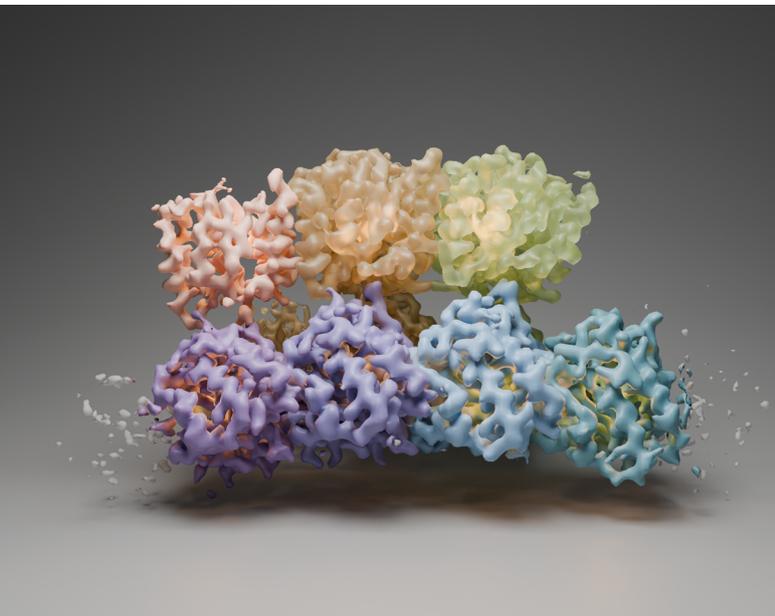


Figure 4. High-resolution visualization of gene editing complexes. Single particle analysis of the active SAVED-CHAT protease filament, which is associated with certain type III CRISPR systems, generated with 200 kV cryo-TEM. Recreated from EMD-41358. Original study by Steens *et al.* doi: [10.1126/science.adk0378](https://doi.org/10.1126/science.adk0378)

Improved optical features

Faster data acquisition with more accurate aberration-free image shift

AFIS (aberration-free image shift) is a standard optical mode in Thermo Scientific cryo-TEMs that speeds up data collection by moving the electron beam rather than the sample stage. Newly improved with the Glacios 3 Cryo-TEM, AFIS now provides enhanced targeting accuracy (i.e., greater than 100 nm within a 12 μm radius), ultimately accelerating data acquisition with higher quality imaging across the grid. The result is faster imaging with greater accuracy.

[Watch the video](#)

Increased data yield with enhanced fringe-free imaging

Fringe-free imaging (FFI) is an optical mode that reduces damage around the beam impact point on a sample, thereby increasing the usable sample area within the grid. New with the Glacios 3 Cryo-TEM, an automated beam centering routine for FFI helps ensure that the beam is always in the center of the field of view, enabling long-term data acquisition and higher data yield per sample. Overall, this means that less data collection is required per experiment for high-resolution protein reconstructions, with the additional benefit of lowering long-term data storage demands.

[Watch the video](#)

Easier instrument set-up with new optical model

A new optical model in the Glacios 3 Cryo-TEM takes the guesswork out of cryo-EM experimental set-up. In a single click, it calculates all the lens current required along the optical path and sets the electron beam in parallel with the desired flux. This makes set-up faster and easier, particularly for less experienced users. This also shortens the learning curve for new users.

AI-powered software for improved productivity and faster time to results

Smart EPU Software for automated single particle analysis

Thermo Scientific Smart EPU Software enables fast, unsupervised grid screening through AI plugins, delivering high-resolution imaging in about 20 minutes per grid, even when operated remotely. It allows you to run multiple grid sessions unattended, reducing microscope idle time while providing real-time feedback on image quality, imaging parameters, and optical status. Embedded CryoSPARC Live Software generates preliminary 3D models during acquisition, allowing you to assess sample quality more quickly, shortening the overall time to results.

CryoTomo Software Suite for efficient cryo-ET

The Thermo Scientific CryoTomo Software Suite enhances cryo-ET efficiency through Tomo Multishot, which acquires multiple tomography series in a single sweep, thereby increasing throughput. Tomo Multisite allows you to navigate and utilize the software during search map acquisition, accelerating session setup. Tomo Multigrad seamlessly schedules long data acquisitions across multiple grids without interrupting ongoing collection, maximizing microscope usage. You can also evaluate sample quality with on-the-fly reconstruction and easily analyze key parameters such as sample thickness.

CryoFlow Software for integrative data management

An integral part of both Smart EPU Software and the CryoTomo Software Suite, Thermo Scientific™ CryoFlow™ Software unifies image acquisition, processing, and analysis into a connected and collaborative environment. It enables remote visualization of real-time image processing results and allows you to filter and export raw or pre-processed data in multiple image formats for use with common cryo-EM post-processing programs. Collaborators can simultaneously view and work on the same project in real time, and users can create shareable reports that summarize key results and microscope settings.

Connected cryo-EM workflows

Vacuum Capsule compatibility enhances cryo-EM sample transfer

The Thermo Scientific Vacuum Capsule is designed to avoid ice deposition during sample transfer by keeping the cryogenic specimen within an enclosed reservoir. It is fully compatible with Thermo Scientific cryo-TEMs that have an Autoloader system, including the Glacios 3 Cryo-TEM. This enables safe, easy sample transfer, thereby improving the overall success rate of workflows such as the transfer of SPA samples between cryo-TEMs or the transfer of cryo-ET lamellae from a cryo-focused ion beam (cryo-FIB).

Cryo-ET supported by TomoGrid compatibility

After a delicate cryogenic lamella is prepared with a cryo-FIB, it is essential that it is precisely aligned during sample loading into the cryo-TEM. The Glacios 3 Cryo-TEM supports TomoGrids, specialized sample carriers designed to maintain the correct orientation of the lamella axis relative to the TEM tilt axis.

Technical overview

Electron optics and components

Source options

- X-FEG (extreme-high-brightness field emission gun)
- E-CFEG (low-energy-spread cold FEG)

Accelerating voltage

- Flexible accelerating voltage from 80 to 200 kV

Lenses

- Automatic condenser, objective, and SA apertures
- Symmetric constant-power objective lens that minimizes image aberrations and lens hysteresis during mode switching
- Symmetric constant-power C-TWIN objective lens with wide-gap pole piece (11 mm)

Imaging

- Rotation-free imaging upon magnification changes

Stage

- Computerized 4-axis specimen stage with $\pm 70^\circ$ alpha tilt
- Cryo-stage with single-axis holder

Fringe-free imaging

- Automated beam centering routine for long-term data acquisition

Aberration-free image shift

- Fast data collection with high accuracy

Energy filters and detectors

Energy filter

- Optional Selectris or Selectris X Imaging Filter

Detector options

- Falcon 4i Direct Electron Detector
- Thermo Scientific™ Ceta™ D Camera
- Thermo Scientific™ Ceta™ 16M Camera
- HAADF STEM detectors*
- On-axis BF/DF detectors*

*STEM is not compatible with fringe-free imaging

Software, workflows, and data management

- CryoFlow Software for integrative data management
- Optional Smart EPU Software for automated single particle analysis
- Optional CryoTomo Software Suite for efficient cryo-ET
- Optional microED package

Remote access

- Optional KVM extender for remote operation from up to 300 m
- Optional additional workstation

Installation

Installation requirements

- Room temperature: 18-23°C
- Temperature stability: within 2°C peak to peak in 24 hours
- Door height: 2.3 m (can be optionally reduced to 1.96 m)
- Door width: 1.118 m
- Room size: 4.2 x 3.8 x 2.7 m (WxLxH)

READY System for built-in environmental protection

- Integrated protection against acoustic and temperature variance
- Optional protection against electromagnetic interference
- Optional protection against floor vibrations

Connected cryo workflows

- Cryo-Autoloader for automated and contamination-free loading of cassettes containing up to 12 AutoGrids
- Optional Vacuum Capsule for secure sample transfer



ACT Ecolabel: documentation of the instrument's environmental footprint, as assessed by My Green Lab, an independent non-profit organization.

Learn more at thermofisher.com/glacios

thermoscientific

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