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DATASHEET

Krios G4 Cryo-TEM

Highest productivity in the most compact design

The new Thermo Scientific™ Krios™ G4 Cryo-Transmission Electron Microscope (Cryo-TEM) is the most compact TEM in its class. Through a thorough redesign of the mechanical base frame and system enclosure, the microscope height has been reduced to below 3 meters, which allows for instrument installation in labs with a ceiling height below 3.04m (10 ft), thereby avoiding costly room renovations.

The Krios G4 Cryo-TEM has improved ergonomics for easier sample exchange. Data acquisition set up is easier and faster thanks to enhanced automation, systematic user guidance and advanced performance monitoring (APM), a built-in self-diagnostic function that ensures microscope alignments are optimal for acquiring high-resolution data.

Simultaneously, the system's productivity and high-resolution performance have been further enhanced through a combination of new optical modes, improved optical specifications and on-the-fly pre-processing.



Key benefits

Easier to fit into new or existing accommodation. Redesigned internal base frame and system enclosure reduce height (<3 m/<10 ft) while enhancing system performance and avoiding costly room renovations

Enhanced productivity:

- Improved drift performance allows for a 3x faster experiment start
- EPU automatic grid square clustering assists selection of best grid squares
- Powerful combination of fringe-free imaging (FFI), aberration-free image shift (AFIS) and (optional) Falcon 4 Detector enhances SPA throughput by up to 400%
- EPU Quality Monitor enables on-the-fly pre-processing of SPA data for data acquisition optimization
- Advanced performance monitoring (APM) ensures best optical starting point for automated single particle runs

Best image quality. Best in class optical performance – 0.12 nm information limit and linear distortion of <0.5%; Falcon 4 Direct Electron Detector: highest DQE in its class

Workflow connectivity. Designed-in exchangeability of the cassettes that contain cryo samples allows smooth transfer of specimen between Autoloader equipped instruments (e.g. Krios, Arctica, Glacios electron microscopes) – full connectivity throughout the screening and data collection workflow

For a further throughput increase, the Krios G4 Cryo-TEM can also be equipped with the new Thermo Scientific Falcon™ 4 Direct Electron Detector.

The latest generation of the award-winning Krios platform is now even further optimized for highly productive automated applications such as single particle analysis (SPA), cryo-tomography and micro-electron diffraction (MicroED), allowing every user to achieve the ultimate performance for every experiment.

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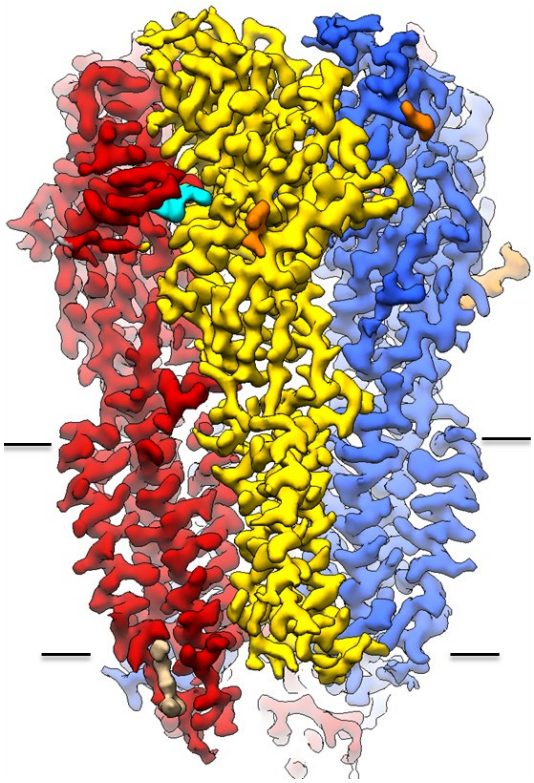


Figure 1. 3D reconstructions of the GABA receptor membrane protein in a nanodisk, bound to the drug Ro-15-4513. Displayed resolution is 2.75 Å. Data taken on a Krios Cryo-TEM with the Falcon 4 Detector in counting mode. *Images Courtesy of Simonas Masiulis, Radu Aricescu, MRC-LMB Cambridge and Evgenia Pechnikova, Abhay Kotecha, Thermo Fisher Scientific.*

Fits more easily into new and existing labs

Installing a high-end cryo electron microscope can be challenging and often requires significant room renovations because of instrument size. Thanks to its completely redesigned mechanical base frame and system enclosure, the Krios G4 Cryo-TEM now has a system height of <3 m, avoiding these costly and challenging renovations.

As part of the redesign, the system ergonomics have also been improved. Specifically, the sample loading area has been brought to a physically lower position, allowing convenient and safe access; there is no need to climb a ladder to load precious cryo-samples.

Close to the sample loading area, an interactive touch screen is available to indicate/control key microscope parameters, facilitating the sample loading process. This is especially beneficial when the operating room is remotely located.

Maximized productivity

The Krios G4 Cryo-TEM features a built-in self-diagnostic function (APM) which evaluates if microscope alignments are optimized for acquiring high-resolution data. Automated alignment routines allow the instrument to be tuned to its optimal starting point for SPA or cryo-electron tomography. Combined with the instrument's thermal and mechanical stability, APM can help ensure that ideal alignment is available for all users.

A typical SPA experiment starts with screening of vitrified sample for the best possible grid areas. Thermo Scientific EPU Software is the built-in tool for sample screening and SPA data acquisition. With full control over the Autoloader, all 12 grids in an Autoloader cassette can be automatically batch screened. After the creation of a grid atlas, grid squares are automatically clustered based on their ice quality (presence, thickness); this guides the selection of best grid squares. In combination with the improved stage stability of the single axis holder (resulting in reduced drift after sample insertion), these features enhance the efficiency of screening and data acquisition set up.

In preparation for high-resolution data acquisition, EPU Software has the abilility to automatically perform daily tuning of essential alignments such as focus, eucentricity correction, stigmation and coma correction.

The automated data acquisition itself is accelerated up to 4x through the use of image/beam shifts rather than a number of mechanical stage movements. This is possible due to aberration-free image shift (AFIS), a new optical mode which performs large beam shifts without off-axis coma and astigmatism, as well as collection of more images per foil hole with fringe-free imaging (FFI).

EPU Quality Monitor is an on-the-fly pre-processing tool (consisting of motion correction and CTF estimation, including derived parameters) that evaluates the acquired SPA data during the actual acquisition process.

This allows you to judge the quality of the acquired data, and consequently optimize the data acquisition, while it is happening. This way, the highest quality data can be acquired in the most efficient way.

Best image quality for high resolution 3D reconstruction

The Krios Cryo-TEM has a proven track record of high resolution imaging for a wide variety of particles: the vast majority (>95%) of

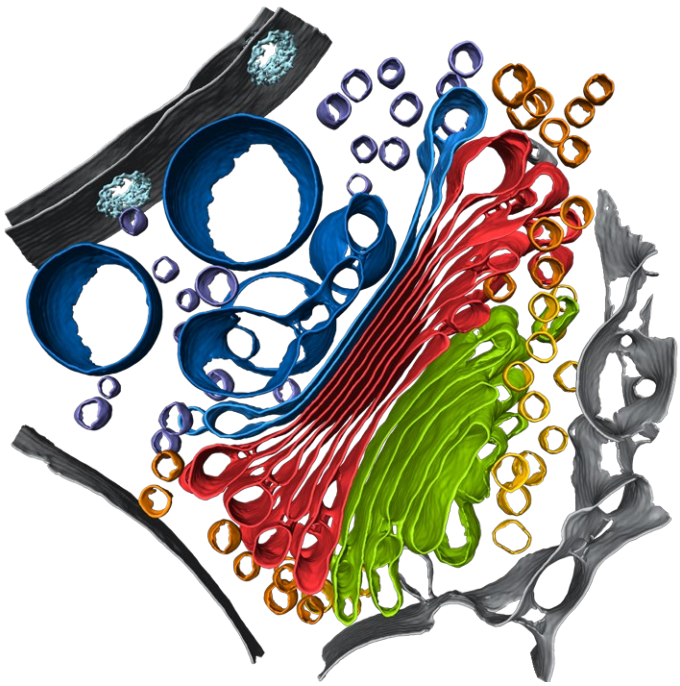


Figure 2. 3D visualization of a Golgi apparatus from the green alga *Chlamydomonas reinhardtii.* The unicellular alga was flash-frozen without any artificial stains or fixatives. Prior to imaging with cryo-ET, a thin cryo-lamella sample was prepared from the vitrified cell by cryo-focused ion beam (cryo-FIB) milling with the Thermo Scientific Aquilos™ Cryo-FIB. Data segmentation and visualization by Thermo Scientific Amira™ Software. *Data courtesy of Dr. Benjamin Engel, Department of Molecular Structural Biology, Max Planck Institute for Biochemistry, Martinsried, Germany.*

published structures at or below 4 Å have been determined using Thermo Fisher Scientific Cryo-TEMs[1]. To allow reconstruction of increasingly smaller molecules at increasingly higher resolutions, the improved information limit (0.12 nm) and linear distortion below 0.5% ensure the best possible boundary conditions for ultimate high-resolution imaging.

Furthermore, the Krios G4 Cryo-TEM can be equipped with the new Falcon 4 Detector (faster and more sensitive than its predecessors) and the Thermo Scientific Phase Plate Solution.

Workflow connectivity

Sample screening is an essential component of a successful cryo-EM workflow, allowing verification of sample quality in terms of both biochemistry and vitrification. The Krios G4 Cryo-TEM fits seamlessly into SPA and cryo-electron tomography workflows, with convenient and contamination-risk-free sample transfer throughout the workflow.

For SPA, the designed-in connectivity of the Autoloader capsule and cassette systems ensure a robust and contamination-free transfer of multiple samples between Thermo Scientific Glacios™, Talos™ Arctica and Krios Cryo-TEMs without the need for manipulation of individual grids.

Similarly, for cryo-electron tomography, samples can be transferred from sample fabrication (in the Thermo Scientific Aquilos™ Cryo-FIB) to tomography data collection in the Krios G4.

Besides optimal mechanical connectivity, the newly introduced EPU Data Management (powered by Thermo Scientific Athena™ Software) ensures the best connectivity for reproducible operation and storage of acquired data.

[1] Determined via analysis of EMDB data. February, 2019.

Technical Highlights	Optional Configurations
Extreme high-brightness field emission gun (X-FEG)	Thermo Scientific Falcon 3 or Falcon 4 Direct Electron Detector
Flexible accelerating voltage from 80-300 kV	Gatan BioQuantum energy filter
Cryo-Autoloader for automated and contamination-free loading of cassettes, containing up to 12 Autogrids	Thermo Scientific Ceta™ or Ceta D 16Mpix CMOS Camera
Temperature management software, including liquid nitrogen autofill and scheduling of cool down after cryo cycle	Cs Image Corrector
Automatic condenser, objective and SA apertures	Thermo Scientific Phase Plate Solution
Three-condenser lens system for automated, continuous parallel sample illumination	HAADF STEM detectors
Computerized 4-axis specimen stage with ±70 degree alpha tilt	On-axis BF/DF detectors
Cryo-stage with single axis holder for optimized stability and drift performance	Thermo Scientific Vitrobot System
Constant power lens design; minimizes lens hysteresis and image aberrations during mode switching (imaging modes and diffraction)	Accelerate Integrated Service and Applications Support Packages to accelerate customer innovation and enhance productivity
Symmetric constant power C-TWIN objective lens with wide-gap pole piece (11 mm)	
Rotation-free imaging upon changing magnification	
Advanced Performance Monitoring: self-assessment of microscope status, combined with automated alignments, ensuring optimal experimental conditions	
AFIS: Aberration-free image shift between grid holes for shorter relaxation times.	
FFI: Fringe-free imaging for multiple image acquisitions per grid hole	
Thermo Scientific EPU 2 Software for automated SPA screening and data acquisition	
Primary control unit including two 30” monitors and hand panels to be placed within 15 meters from the column and the option to extend up to 300 meters from the column	
Windows® 10 Operating System	
Environmental enclosure	

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Notes

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