



# Glacios 2 Cryo-TEM

Transforming structural biology at 200 kV  
with up to 1.5 Å resolution using C-EFEG

# Solve your challenges with record-breaking resolution

The Thermo Scientific™ Glacios™ 2 Cryo-Transmission Electron Microscope (Cryo-TEM) is a powerful tool that can help answer some of the most challenging research and drug discovery questions by providing structural determination of complex proteins and macromolecules at routinely high resolution ( $<3 \text{ \AA}$ ) with improved efficiency, throughput, and ease of use. This flexible platform is ideal for multiple applications, including single particle analysis (SPA), cryo-electron tomography (cryo-ET), and micro-electron diffraction (MicroED).

This next-generation Glacios 2 Cryo-TEM offers many improvements over the flagship instrument. The combination of the Thermo Scientific™ Falcon™ 4i Direct Electron Detector, a low-energy-spread cold field emission gun (E-CFEG), fringe-free imaging (FFI), a newly designed enclosure, and innovative Thermo Scientific™ Smart EPU Software work together to provide an intuitive user experience and record-breaking resolution at 200 kV, enabling both new and experienced users to get the best possible results from their samples.

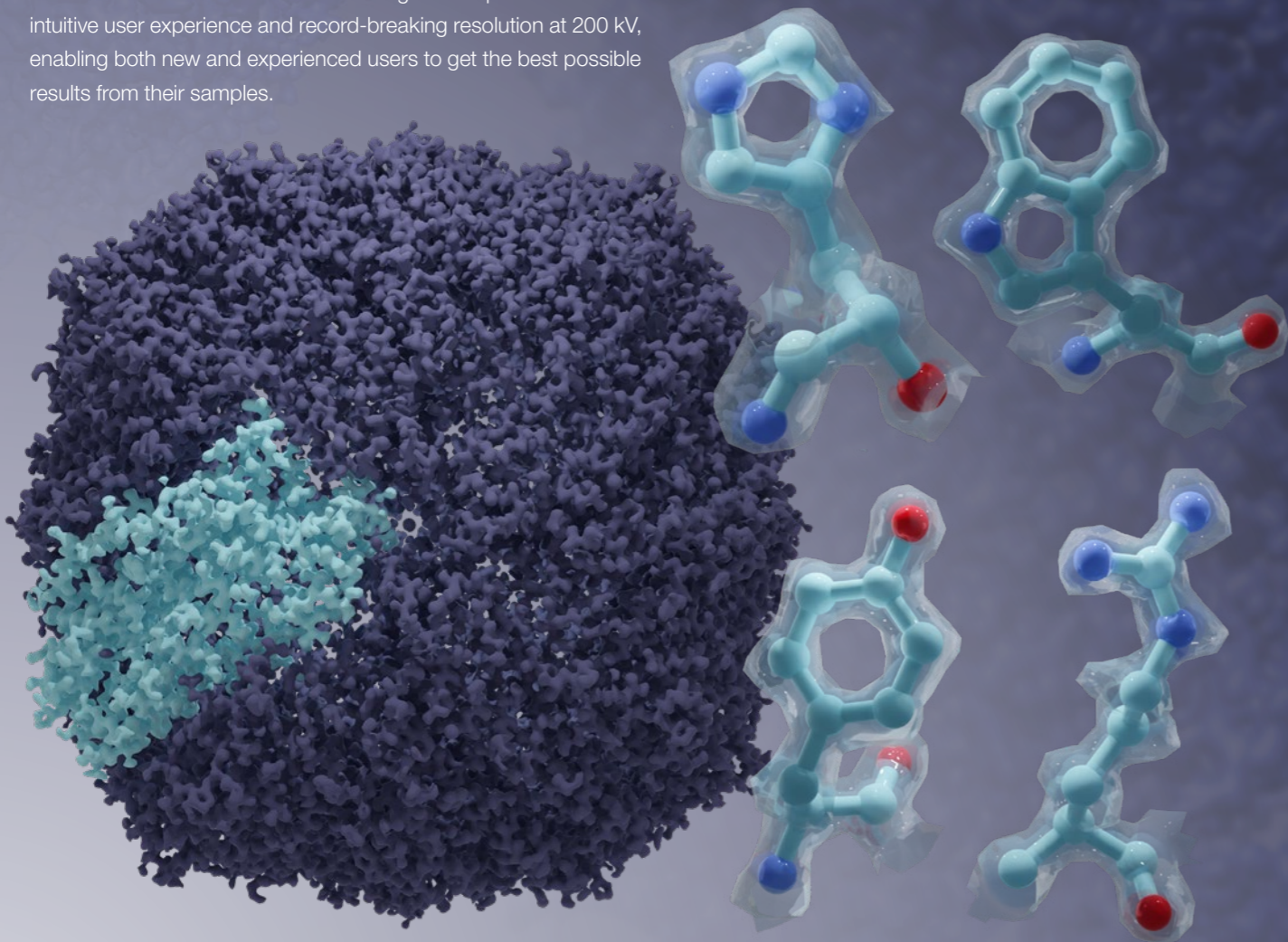


Figure 1. A reconstruction of apoferritin at 1.5 Å resolution from data collected over 11 hours using the Glacios 2 Cryo-TEM with E-CFEG, Falcon 4i Direct Electron Detector, Selectris Imaging Filter, and FFI.

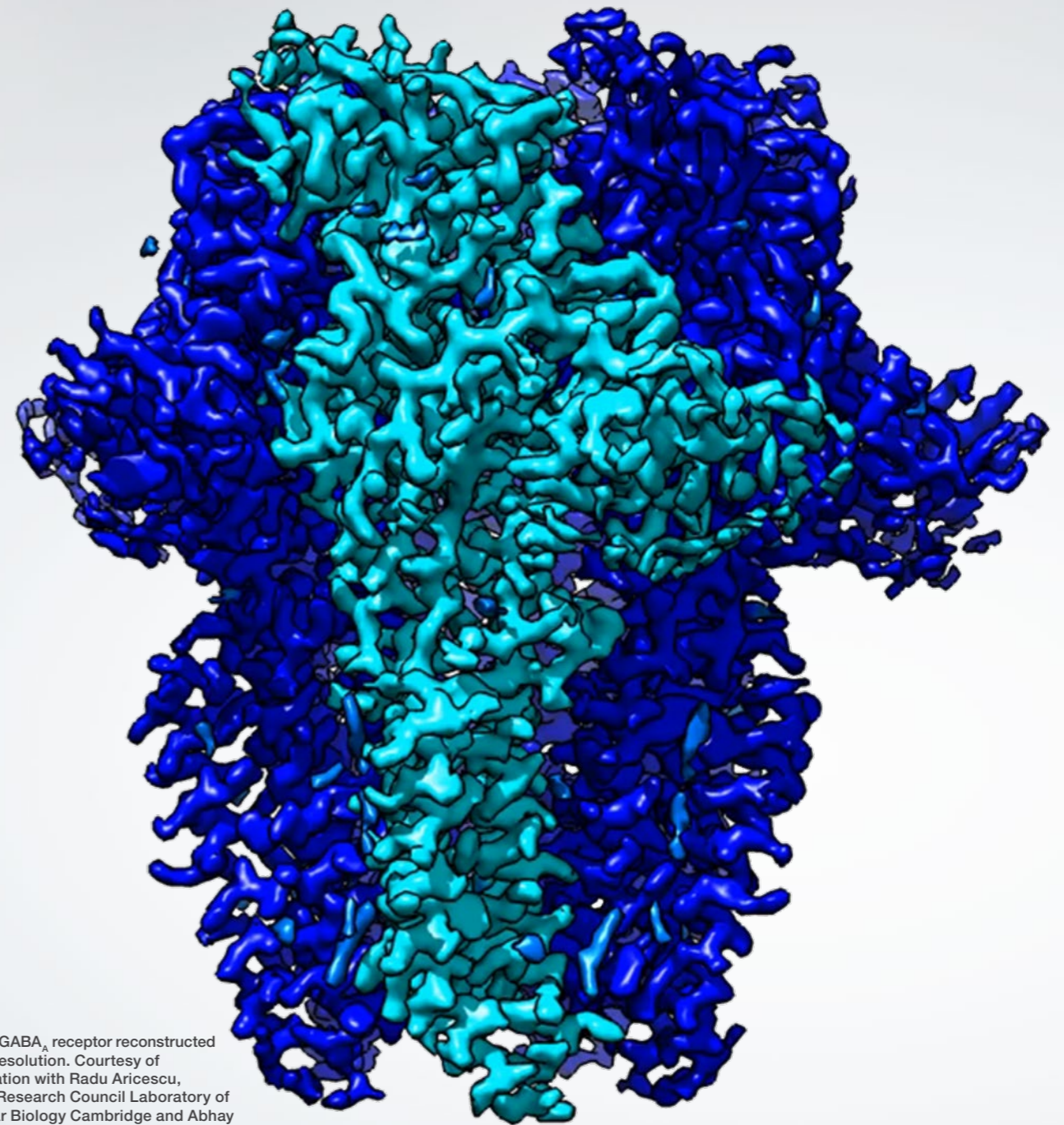


Figure 2. GABA<sub>A</sub> receptor reconstructed at 2.4 Å resolution. Courtesy of collaboration with Radu Aricescu, Medical Research Council Laboratory of Molecular Biology Cambridge and Abhay Kotecha, Thermo Fisher Scientific.

## Gain near-atomic insights into protein structure

With its high-resolution capabilities, the Glacios 2 Cryo-TEM is ideal for single particle analysis, enabling near-atomic structural determination of challenging proteins without the need for crystallization. Samples can be studied directly in solution. High-quality data collection is possible thanks to hardware improvements such as E-CFEG and the integration of innovative Thermo Scientific Smart EPU software.

# Transform drug discovery and development

Cryo-EM has become an invaluable tool for drug discovery and has underpinned success for many small molecule and biologics programs that have reached clinical stages of development and beyond. The Glacios 2 Cryo-TEM couples high-resolution with high-throughput to provide valuable structural insights to identify promising targets.

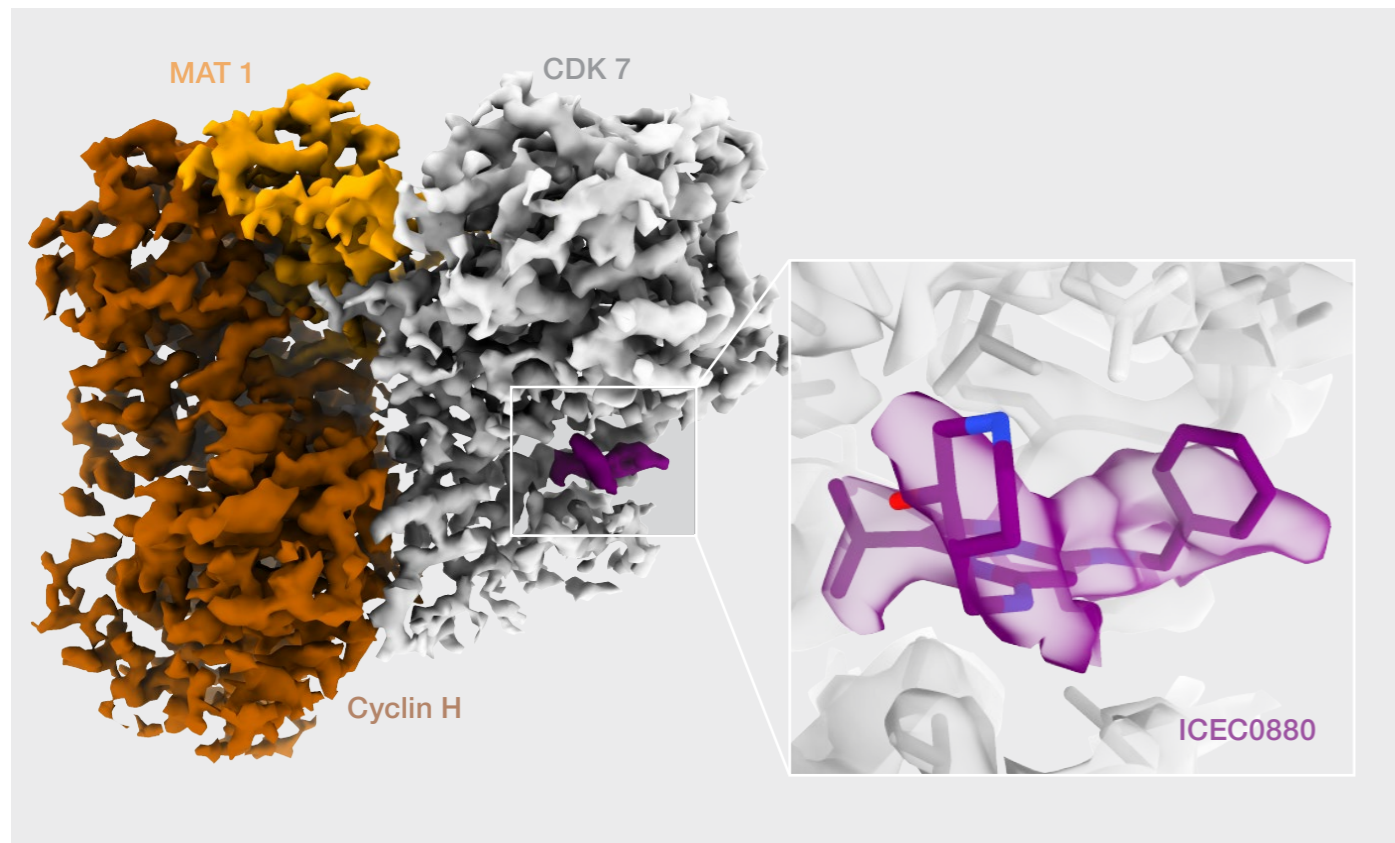


Figure 3. CDK-activating kinase (CAK) complex structures solved on a Glacios 2 Cryo-TEM. Drug binding occupancy on this complex was analyzed following a fast-screening strategy of only a few hours of data collection per sample. A large dataset enabled a 2.3 Å structure in less than a day where an atomic model could be built unambiguously. This project was a collaboration with Basil Greber from Institute of Cancer Research, London, and Professors Simak Ali and Matthew J. Fuchter from Imperial College, London.



"Using the Glacios 2 Cryo-TEM, we developed a workflow that enables us to determine structures of small, asymmetric complexes at high resolution and with high throughput. Uncovering such structures provides us with detailed insight into inhibitor binding and suggests a mechanism for target selectivity in cancer therapeutics that we are currently testing."

—Basil Greber  
Institute of Cancer Research, London, UK

# Explore the interactions of proteins and complexes

The Glacios 2 Cryo-TEM offers excellent cryo-electron tomography (cryo-ET) capabilities, providing nanometer-scale imaging of a cell's interior in 3D and the visualization of protein complexes within their physiological environments.

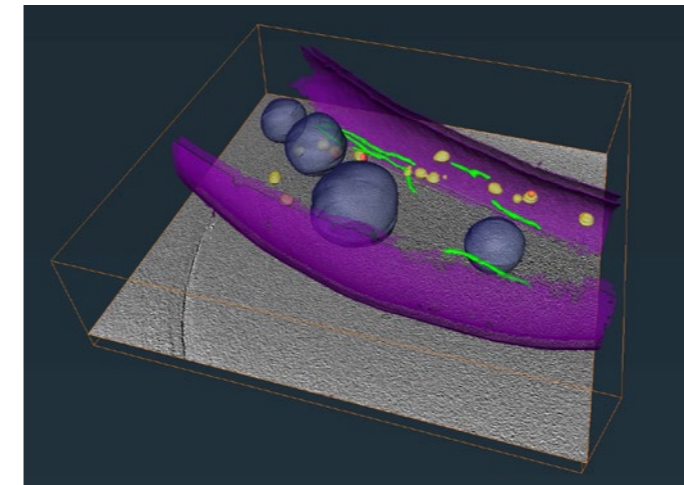


Figure 4. 3D visualization of cell membrane, liposomes and filaments from the bacteria Magnetospirillum gryppiswaldense (courtesy of Dirk Schüler, Uni Bayreuth) using the Glacios 2 Cryo-TEM from a sample that was prepared with the Thermo Scientific™ Vitrobot™ Mark IV System. Data segmentation and visualization by Thermo Scientific™ Amira™ Software.

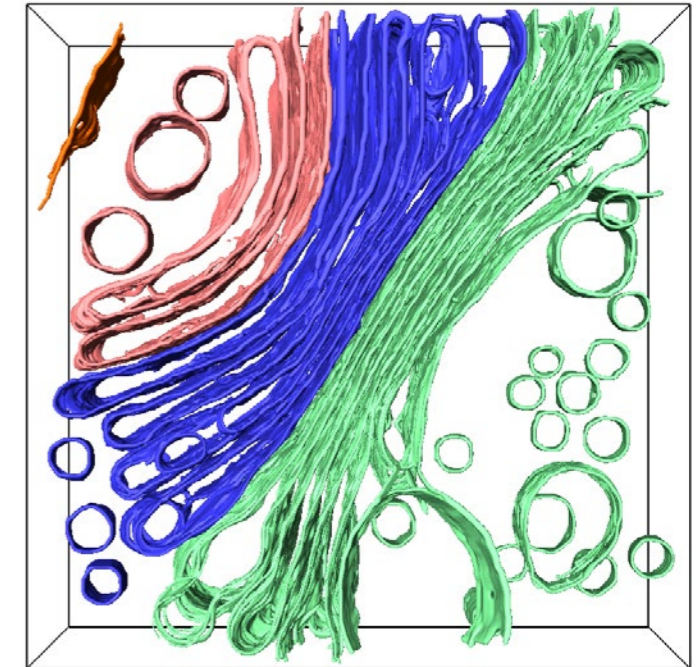
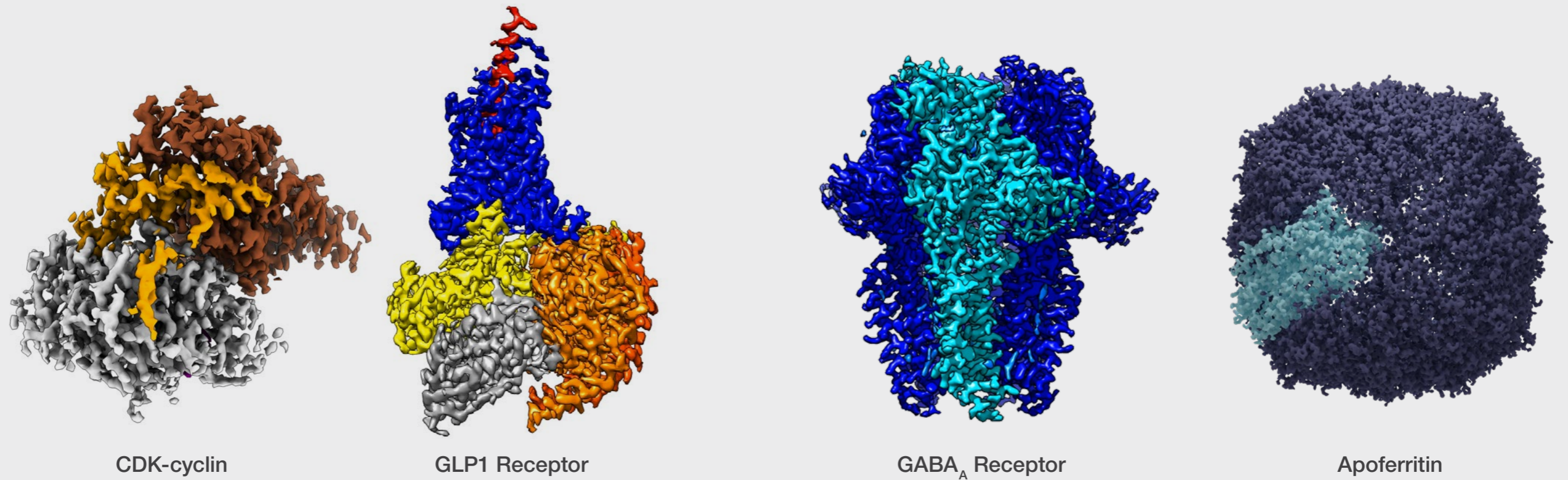


Figure 5. 3D visualization of a Golgi apparatus from the green alga Chlamydomonas reinhardtii using the Glacios 2 Cryo-TEM from a sample that was prepared with the Thermo Scientific™ Aquilos™ Cryo-FIB. Data segmentation and visualization by Thermo Scientific™ Amira™ Software.

# Overcome the challenges of visualizing small molecules

The structural determination of small molecules and proteins can be challenging using standard methods such as X-ray crystallography. Scientists have turned to new techniques such as microcrystal electron diffraction (MicroED). The Glacios 2 Cryo-TEM enables fast, high-resolution imaging using MicroED, where atomic details can be extracted from individual nanocrystals (<200 nm in size), even in a heterogeneous mixture.



Molecular weight	85 kDa	150 kDa	210 kDa	450 kDa
Acquisition time (data collection)	~22 hours	~20 hours	~12 hours	~11 hours
Resolution	2.3 Å	2.6 Å	2.4 Å	1.5 Å*

\* Apoferritin resolved using E-CFEG.

## Improved resolution and throughput

Speed and resolution can be further improved when the Glacios 2 Cryo-TEM is configured with the Thermo Scientific™ Selectris™ X Imaging Filter and E-CFEG. The hardware improvements and new full enclosure minimize the influence of environmental factors and maximize system stability. These enhancements improve performance, raise the information limit to 2.1 Å, and reduce transmission loss to 2% in 24 hours to help you collect high-quality images. FFI also contributes to better image quality due to less charging from smaller illumination.

The Falcon 4i Direct Electron Detector, with optical and throughput enhancement modes in combination with fringe free imaging (FFI), accelerates automated data acquisition. FFI eliminates Fresnel fringes at the edge of the beam and its implementation alone allows for the collection of more images per foil hole, accelerating SPA throughput significantly. The E-CFEG option provides a low energy spread  $\leq 0.3$  eV and enables higher contrast at high resolutions ( $\leq 2.0$  Å); improved contrast at high spatial frequencies to reach higher resolutions in less time. When configured with the Selectris X Imaging Filter, it's possible to use a very stable narrow slit width ( $< 10$  eV), which provides an additional boost in contrast for single particle cryo-EM and cryo-ET, improves resolution, and delivers results faster with less data, maximizing your resolution efforts.

Thermo Scientific™ EPU Software is embedded on the Glacios 2 Cryo-TEM for single particle acquisition. Its simplified user interface, advanced automation, and screening capabilities provide user guidance to increase throughput and deliver reproducible results.

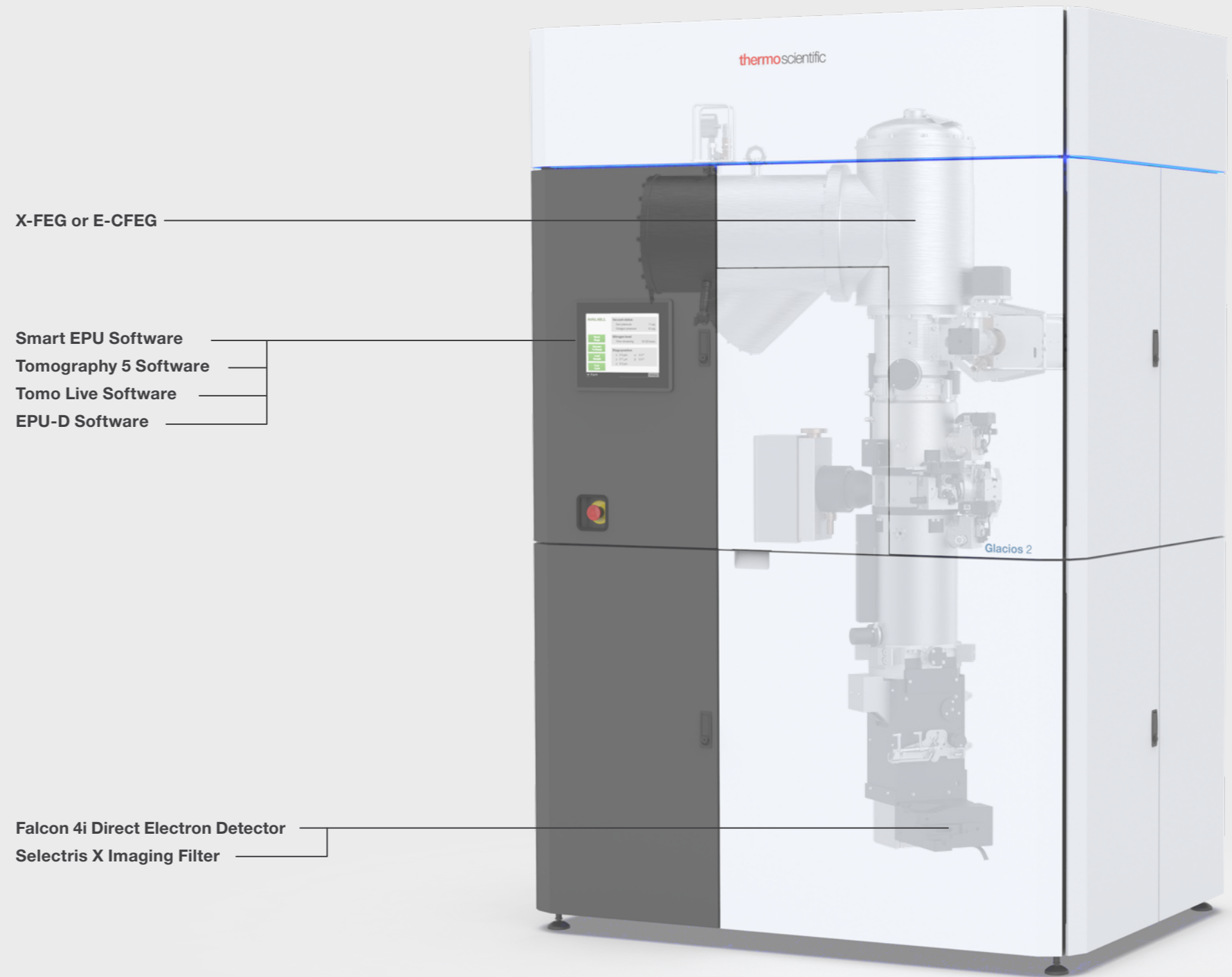
Thermo Scientific™ EPU Multigrid Software is another add-on that can set up unattended and multi-day data collection runs, maximizing microscope efficiency by establishing a queue of automated acquisitions across multiple grids.

Thermo Scientific™ Tomography 5 Software is available as an add-on for cryo-tomography, enabling the acquisition of valuable 3D data, even on challenging vitrified samples. Tomography 5 Software also connects with Thermo Scientific™ Tomo Live Software for automatic on-the-fly data reconstruction and review in any browser. In addition, Thermo Scientific™ EPU-D software, as part of a comprehensive MicroED package, enables quick switching between imaging and diffraction, and guides optimal low-dose setup, and drives the constant speed continuous tilt for MicroED data collection.

# Record-breaking resolution and throughput at 200 kV

Discover cryo-EM that is accessible and versatile with improved ease-of-use and productivity for both new and experienced users.

Obtain the highest resolution and throughput available at 200 kV by combining the Glacios 2 Cryo-TEM with E-CFEG, Falcon 4i Direct Electron Detector, Selectris X Imaging Filter, and FFI.



Technical highlights	
Source	X-FEG (extreme high-brightness field emission gun) or E-CFEG (low-energy-spread cold FEG)
Accelerating voltage	Flexible accelerating voltage from 80 to 200 kV
Cryo-Autoloader	Cryo-Autoloader for automated and contamination-free loading of cassettes containing up to 12 AutoGrids
Lenses	<ul style="list-style-type: none"> <li>Automatic condenser, objective, and SA apertures</li> <li>Symmetric constant power objective lens (minimize image aberrations and lens hysteresis during mode switching)</li> <li>Symmetric constant power C-TWIN objective lens with wide-gap pole piece (11 mm)</li> </ul>
Imaging	Rotation-free imaging upon magnification changes
Stage	<ul style="list-style-type: none"> <li>Computerized 4-axis specimen stage with <math>\pm 70^\circ</math> alpha tilt</li> <li>Cryo-stage with single-axis holder</li> </ul>
Installation requirement highlights	<ul style="list-style-type: none"> <li>Environmental temperature: 18°C to 23°C</li> <li>Door height: 2.32 m (optionally reduced to 2.0 m)</li> <li>Door width: 0.99 m</li> <li>Ceiling height: 2.80 m</li> </ul>
AFIS (aberration-free image shift)	Enhancing throughput with shorter relaxation times when moving coma-free between grid holes
FFI (fringe-free imaging)	For multiple image acquisitions per grid hole
Smart EPU Software	<ul style="list-style-type: none"> <li>Automated sample screening and data acquisition</li> <li>Open application programming (API) interface</li> <li>EPU MultiGrid functionality (optional)</li> <li>Smart EPU Software with EPU Quality Monitor (EQM) (optional)</li> <li>Smart EPU Software with Embedded CryoSPARC Live (optional)</li> </ul>
Tomography software (optional)	<ul style="list-style-type: none"> <li>Tomography 5 Software</li> <li>Tomo Live Software</li> <li>Thermo Scientific Inspect 3D Software</li> </ul>
MicroED package (optional)	<ul style="list-style-type: none"> <li>Thermo Scientific EPU-D Software</li> <li>Modified beam stop, optimized for MicroED</li> <li>Optimized C2/SA aperture set</li> <li>MicroED lens series</li> <li>90° rotation projection system</li> <li>Thermo Scientific Ceta-D Camera <ul style="list-style-type: none"> <li>Optimized for diffraction application: increased accuracy and sensitivity</li> <li>Compatible with single-particle-analysis screening requirements</li> <li>Compatible with bottom-mount filter (retractable)</li> </ul> </li> </ul>
Additional components	Primary control unit including two 24" monitors to be placed within 10 m of the column
Detectors (optional)	<ul style="list-style-type: none"> <li>Falcon 4i Direct Electron Detector</li> <li>Ceta-D Camera</li> <li>Ceta-M Camera</li> <li>HAADF STEM detectors*</li> <li>On-axis BF/DF detectors*</li> </ul>
Energy filter (optional)	<ul style="list-style-type: none"> <li>Selectris Imaging Filter</li> <li>Selectris X Imaging Filter</li> </ul>

\* STEM is not compatible with FFI

## Additional resources



Our [Dedicated Support Network](#) is committed to your success when you purchase our cutting-edge cryo-electron microscopes with complete end-to-end workflow solutions

- Remote fleet monitoring for maximum uptime
- Local technical experts just a call away
- Financing to meet changing needs, including construction and innovation
- Dedicated Program Manager to ensure success
- Full remote operation from any site

The [Electron Microscopy Funding Support Center](#) offers technical content, resources, and proposal writing tools to help you acquire the research instrument you need.





### [Getting Started with Cryo-EM eBook](#)

Cryo-EM is easier to adopt and more affordable than ever before. Explore how cryo-EM can overcome the current limitations of traditional techniques such as X-ray crystallography (XRD). Learn about key methods, including single particle analysis, microcrystal electron diffraction (MicroED), and cryo-tomography, and how these techniques are used to answer important scientific questions.



### [Structural virology with cryo-EM eBook](#)

Cryo-EM technology is helping researchers overcome challenges related to virus purification and protein homogeneity and revolutionizing antiviral drug discovery and vaccine design. Learn more about how cryo-EM can help solve structural puzzles in virology.



### [Understanding the complexity of cancer with cryo-EM eBook](#)

Leverage structural insights to better understand the conditions for cancer-cell growth and identify new ways to treat cancer. Learn how cryo-EM is revolutionizing cancer research.



### [Untangling neurodegeneration with cryo-EM eBook](#)

Cryo-EM technology is used to uncover the atomic structures of numerous misfolded proteins and their aggregates, including tau filaments,  $\alpha$ -synuclein fibrils, and amyloid- $\beta$  aggregates, as well as small-molecule drug candidates that bind to these proteins. Learn how cryo-EM can enable the structure-based classification of tauopathies.



### [Revolutionizing cell biology with cryo-electron tomography ebook](#)

Access the inner workings of cells through 3D sample reconstruction at unprecedented nanoscale resolution. Results from this technique are having profound effects on our understanding of cell biology, revealing native cellular architecture with molecular clarity. Explore a curated collection of publications highlighting the use of cryo-ET.