

# Krios 5 Cryo-TEM

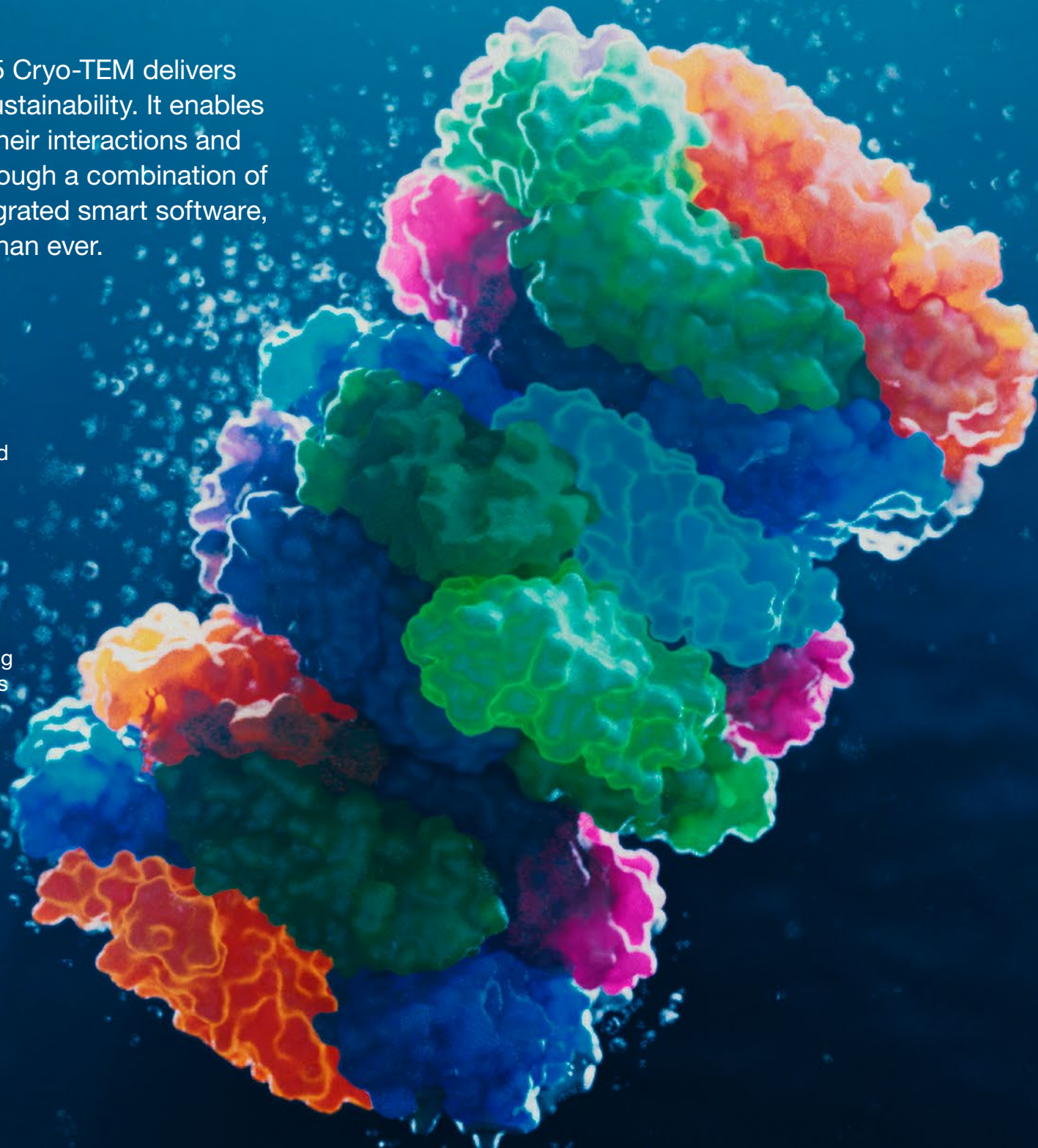
Reveal the intricacies of life with  
unprecedented fidelity and throughput



# Pushing the boundaries of cryo-electron microscopy. Again.

The 300 kV Thermo Scientific™ Krios™ 5 Cryo-TEM delivers exceptional fidelity, productivity, and sustainability. It enables 3D visualization of proteins as well as their interactions and dynamics within the biological cell. Through a combination of advanced hardware and powerful, integrated smart software, the Krios 5 Cryo-TEM is easier to use than ever.

- **Higher quality results plus faster single particle analysis and tomography** thanks to the high DQE of the proven Thermo Scientific™ Falcon™ 4i Direct Electron Detector
- **Faster high-quality data collection and hassle-free data processing** with automated daily alignments and magnification precision better than 1%
- **High workflow efficiency for tomography and single particle analysis** through robust workflow connectivity, as well as faster setup and interpretation of experiments
- **Built-in sustainability** provides energy-saving Eco modes with fast wake up scheduling, plus environmental impact certification with the My Green Lab® ACT® Ecolabel
- **Our highest resolution and contrast** with the Thermo Scientific™ Selectris™ X Imaging Filter and Thermo Scientific E-CFEG cold field emission source



Phycobilisome protein complex (PDB 7SC8)  
Harvesting light in blue-green algae

## **Fidelity and throughput**

The Krios 5 Cryo-TEM offers an optimized balance of power and usability through full automation of routine alignments, optical precision, and advanced software.

## **High workflow efficiency for cryo-electron tomography and single particle analysis**

With the Vacuum Capsule, you can easily transfer FIB-prepared cryo-lamellae between the Thermo Scientific™ Arctis™ Cryo-PFIB and the Krios 5 Cryo-TEM. This ensures robust and contamination-free sample transfer, preserving the entire surface of the lamellae for data acquisition.

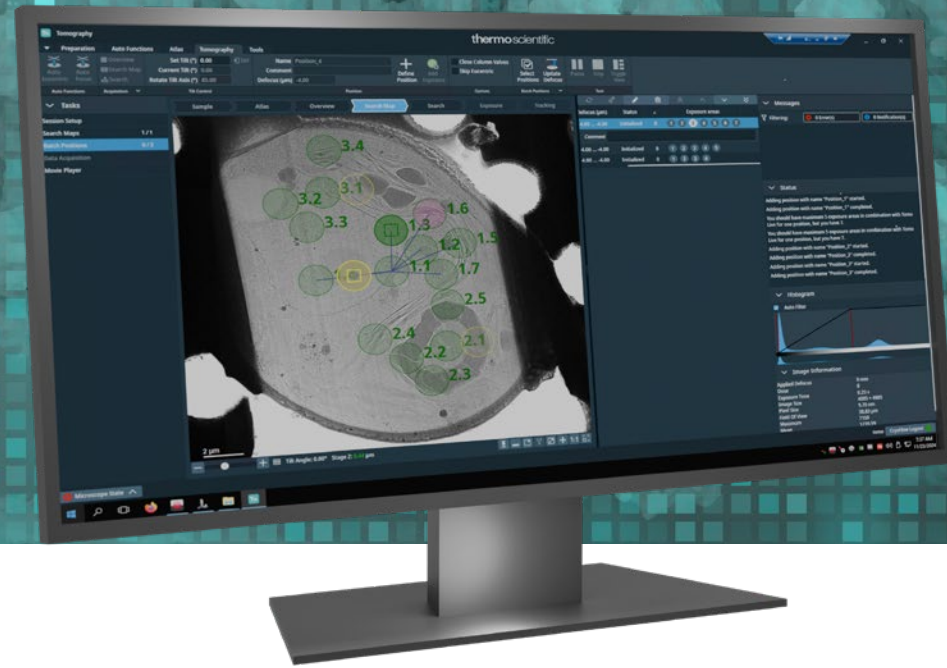
## **Seamless software integration for increased automation and productivity**

New AI-based Thermo Scientific Smart EPU Plugins enhance the screening process for single particle analysis. Smart grid square selection, ice thickness estimation, and location of the right foil holes help you acquire high-quality data efficiently and conveniently. For cryo-tomography, Thermo Scientific Tomography 5 Software allows you to set up multigrid acquisitions across multiple tomography grids in the Autoloader cassette for overnight data collection sessions, similar to Thermo Scientific EPU Multigrid Software for single particle analysis.

## **Falcon 4i Direct Electron Detector for more productive single particle analysis and tomography**

Direct electron detectors boost the productivity and performance of cryo-EM, enabling observations down to atomic resolution, especially when coupled with a Selectris Imaging Filter and E-CFEG cold field emission source. Unlock detective quantum efficiency beyond the Nyquist frequency with Electron Event Representation (EER) 8k decoding and on-the-fly motion correction, enabling either higher resolutions or larger field of views for cryo-electron tomography.



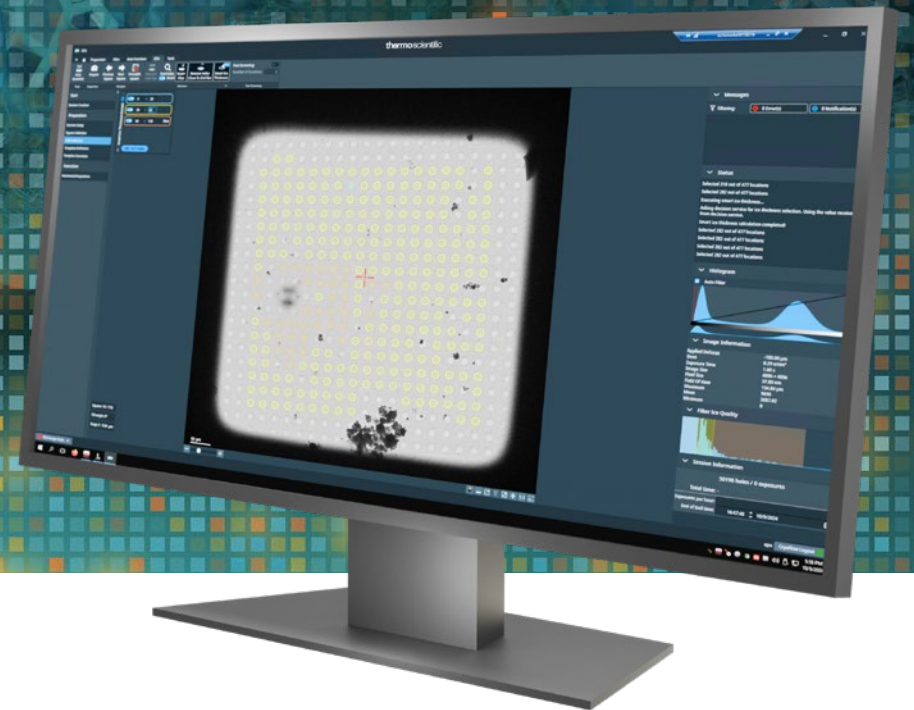


## Integrated software solution for cryo-electron tomography workflows

Experience outstanding efficiency in cryo-electron tomography with the Thermo Scientific CryoTomo Software Suite. Installed on a Krios 5 Cryo-TEM, the suite helps streamline tilt series acquisition and 3D analysis with connected tools, user-friendly batch acquisition, and advanced motion correction. Integrated Thermo Scientific™ CryoFlow™ Software shows real-time results and facilitates data access through a web portal.

### The CryoTomo Software Suite can help you:

- Seamlessly schedule long data acquisitions for multiple grids without interrupting ongoing collection
- Easily achieve high-throughput with parallelization along with multi-site, multi-shot, and multi-grid batch tomography
- Evaluate sample quality with parameter-free, on-the-fly reconstruction, EER decoding up to 8k, and visualization of tomograms
- Filter and export pre-processed data in a number of image formats for focused analysis in commonly used cryo-EM post-processing programs
- Simultaneously view and work on the same project in real time with other users, increasing collaboration regardless of location

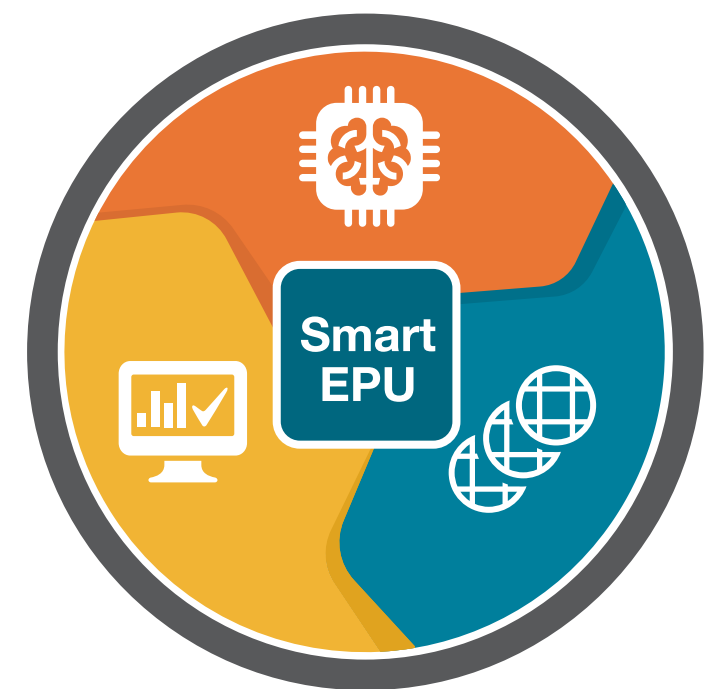


## Acquire single particle data faster and easier than ever

Imaging on the Krios 5 Cryo-TEM is controlled through Thermo Scientific Smart EPU Software, which uses intelligent components that work together to automate single particle data acquisition and analysis. The software's EPU plugins can be combined with EPU Multigrid, EPU Quality Monitor, or Embedded CryoSPARC Live™ Software to guide you seamlessly from experiment setup to data processing and visualization.

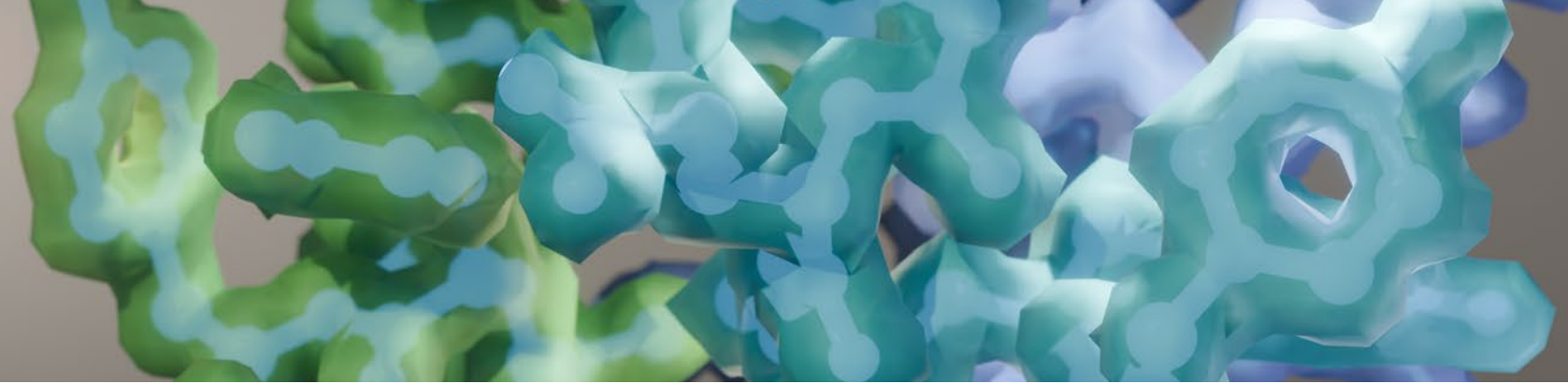
### Smart EPU Software makes it easy to:

- Set up imaging sessions in one day, even remotely, with a simplified interface and training
- Automatically set up and screen grids using AI plugins
- Schedule and run multiple unattended particle screening sessions
- Automatically adjust imaging parameters on the fly and receive real-time feedback on sample quality
- Filter and export only quality data through full integration with [Thermo Scientific CryoFlow Software](#)





# Moving single particle analysis forward

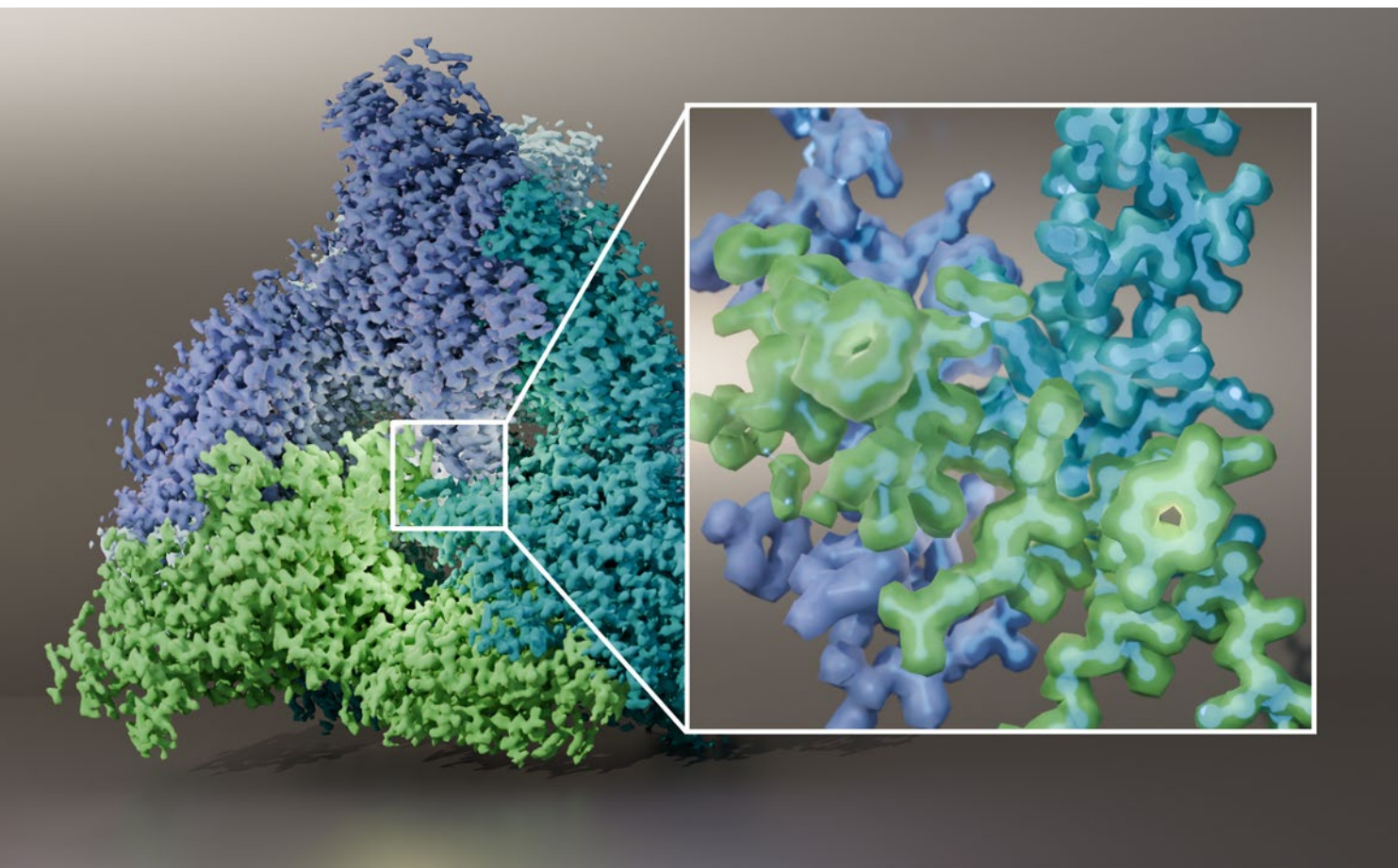


Single particle analysis (SPA) cryo-EM continues to be an invaluable tool in the structural determination of biomolecules at up to atomic resolution, providing a window into dynamic biological processes and the structure of biomolecular complexes/assemblies.

Through a combination of innovative hardware and software, including extended aberration-free image shift (AFIS), magnification calibration accuracy within 1%, and AI-powered Smart EPU Plugins, the Krios 5 Cryo-TEM can deliver higher data fidelity for an up to 25% increase in throughput relative to the previous generation of Krios Cryo-TEM.

## Exceptional SPA throughput and productivity

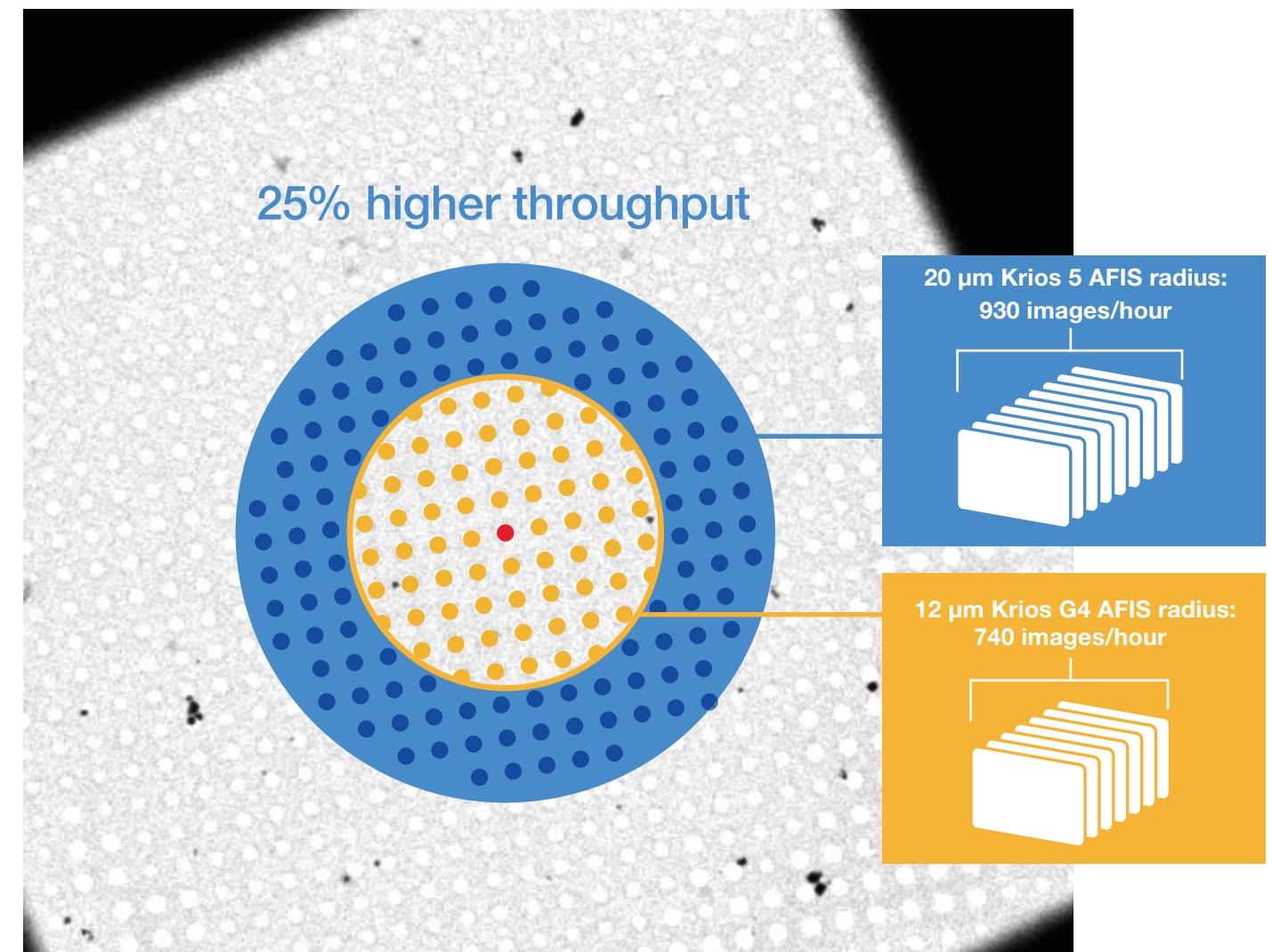
Extending the range of AFIS from 12 to 20  $\mu\text{m}$  enables the acquisition of large datasets with less mechanical stage movements. In the case of LAI (bottom left), 25% more images could be collected per hour without sacrificing image quality, resulting in a 15% reduction in experimental runtime.



L-arabinose isomerase structure at 1.52 Å resolution, determined with the Krios 5 Cryo-TEM. Data courtesy of University of BRIN, Indonesia.

L-arabinose isomerase (LAI) is a catalyst for the biotransformation of L-arabinose to L-ribulose and D-galactose to D-tagatose. This is valuable in both the development of sugar substitutes as well as the synthesis of antiviral drugs and other potential therapeutics, as arabinose is a synthesis precursor for these molecules.

The structure of the LAI protein (336 kDa) was determined to a record 1.52 Å resolution with the Krios 5 Cryo-TEM equipped with an E-CFEG, Selectris X Imaging Filter, Falcon 4i Direct Electron Detector, and Smart EPU Software. This is a substantial advancement over the highest resolution X-ray crystallography structure determined at 2.25 Å.



The evolution from standard mechanical stage movement (red circle, Krios G3i Cryo-TEM) to AFIS (Krios G4 Cryo-TEM) and extended AFIS (Krios 5 Cryo-TEM). This has dramatically increased throughput while maintaining image quality.



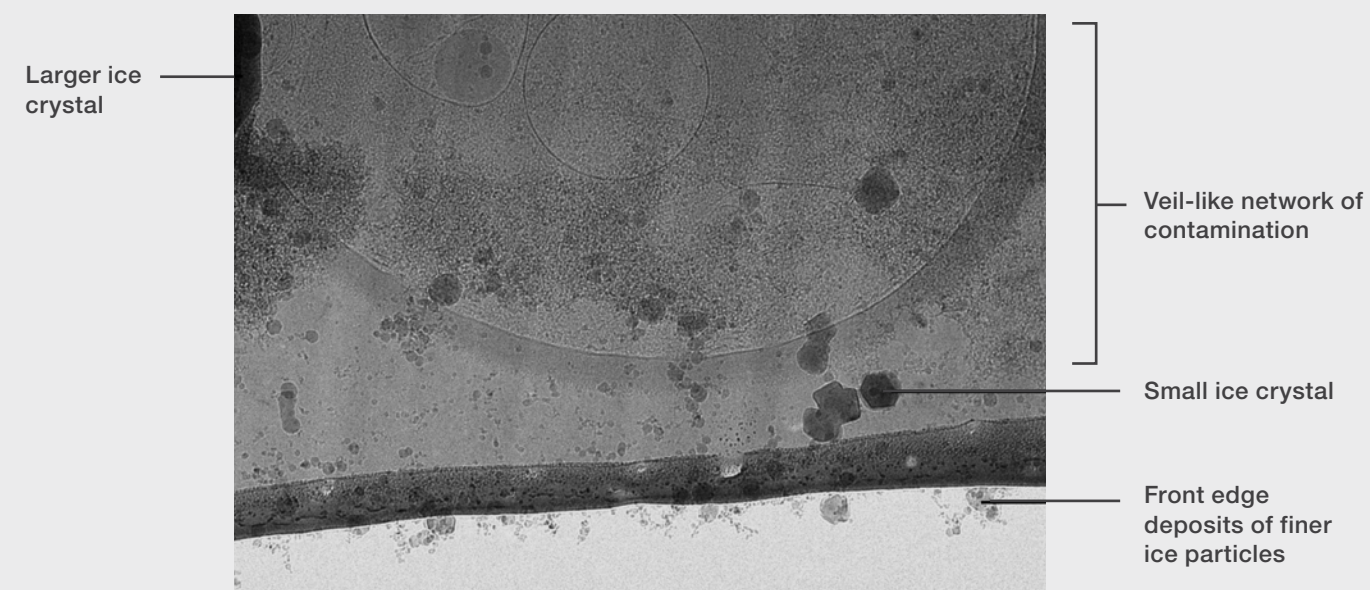
# An efficient, connected cryo-tomography workflow

Cellular cryo-electron tomography (cryo-ET) is a transformative technique that allows you to visualize the 3D structures of macromolecular complexes within their native cellular environments. This detailed structural information is crucial for understanding the molecular mechanisms underlying various biological processes and diseases. The Krios 5 Cryo-TEM brings significant improvements to the cryo-ET workflow by directly addressing image blurring caused by sample motion, as well as variable lamellae quality and throughput.

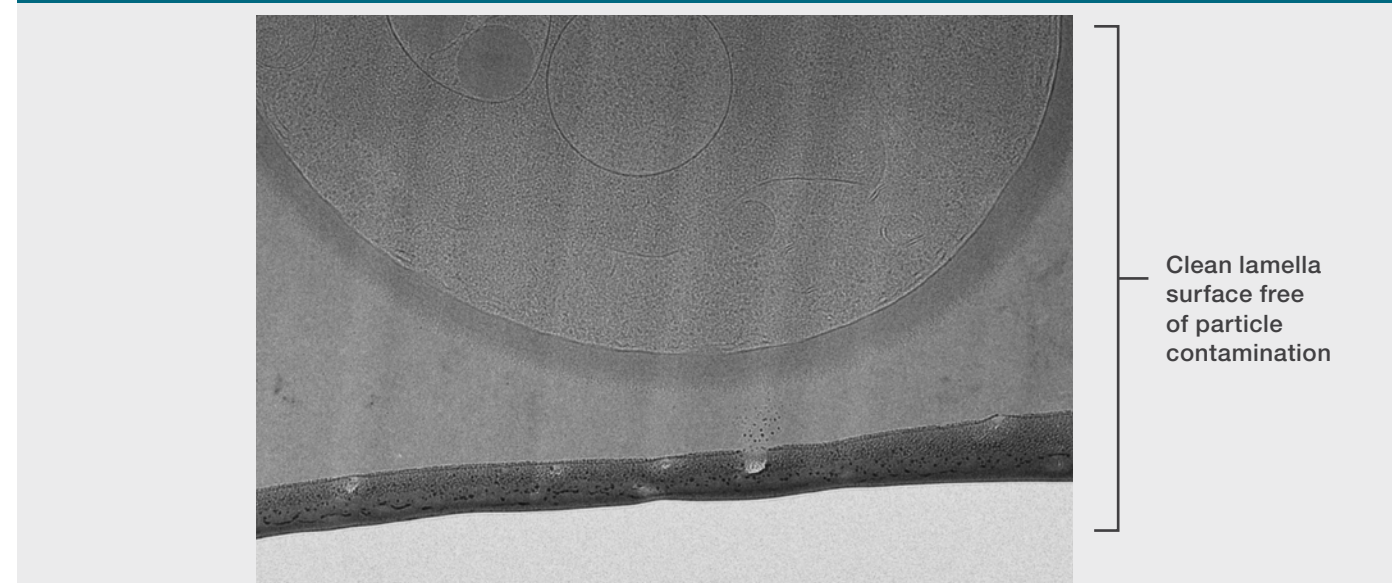
- On-the-fly motion correction is automated in the CryoTomo Software Suite along with Electron Event Representation (EER) 8K decoding for higher resolutions or larger fields of view
- The new Thermo Scientific Vacuum Capsule enables seamless shuttling between the Autoloaders of the Arctis Cryo-PFIB and the Krios 5 Cryo-TEM, ensuring a contamination-free environment for the transfer of freshly prepared lamellae and the preservation of sample integrity
- Fast set-up and interpretation of experiments thanks to end-to-end software and new features designed for tomography like multigrid acquisitions, task parallelization, and Discovery Viewer as part of CryoFlow Software



## After liquid nitrogen exposure



## With Vacuum Capsule





FIB-prepared cryo-lamellae are transferred between the Arctis Cryo-PFIB and Krios 5 Cryo-TEM using the new Vacuum Capsule.



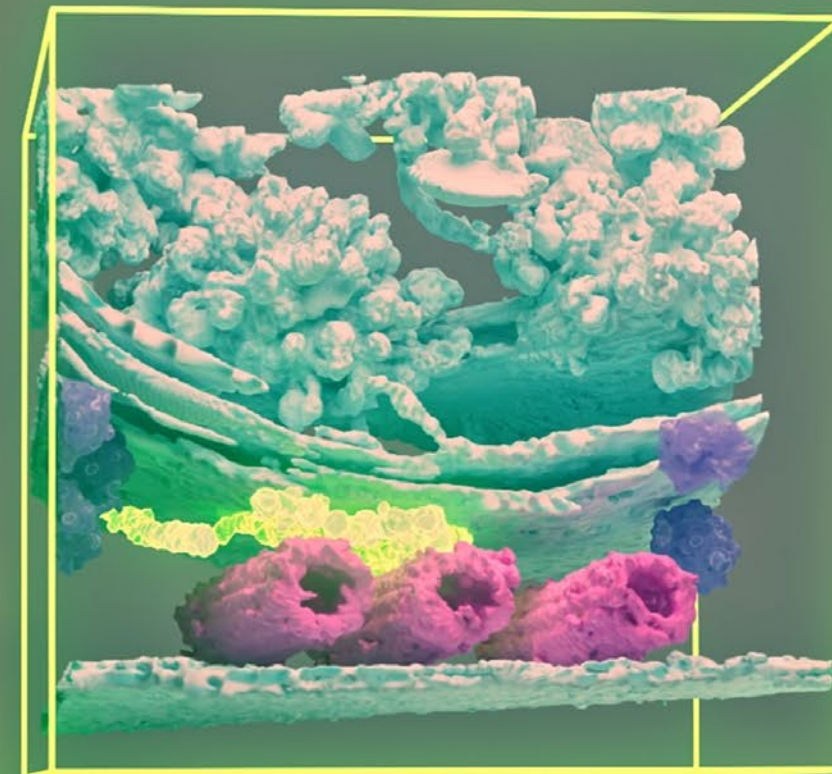
Thermo Scientific Vitrobot™ System



Vacuum Capsule Thermo Scientific Arctis Cryo-Plasma-FIB



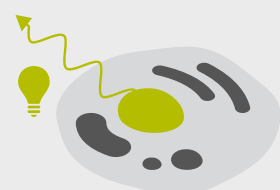
Thermo Scientific Krios Cryo-TEM



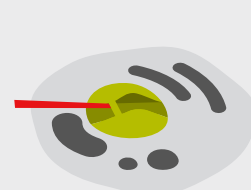
Cell culture



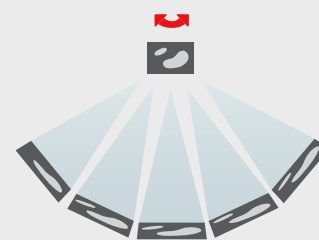
Vitrification



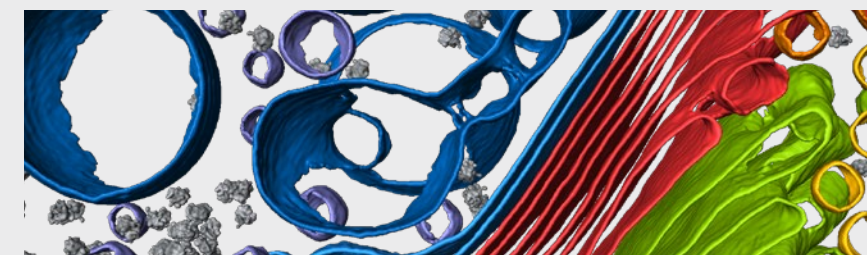
Localization by fluorescence



Thinning by milling



Imaging



Reconstruction and visualization

Arctis Web UI



Tomography 5 Software



Tomo Live Software

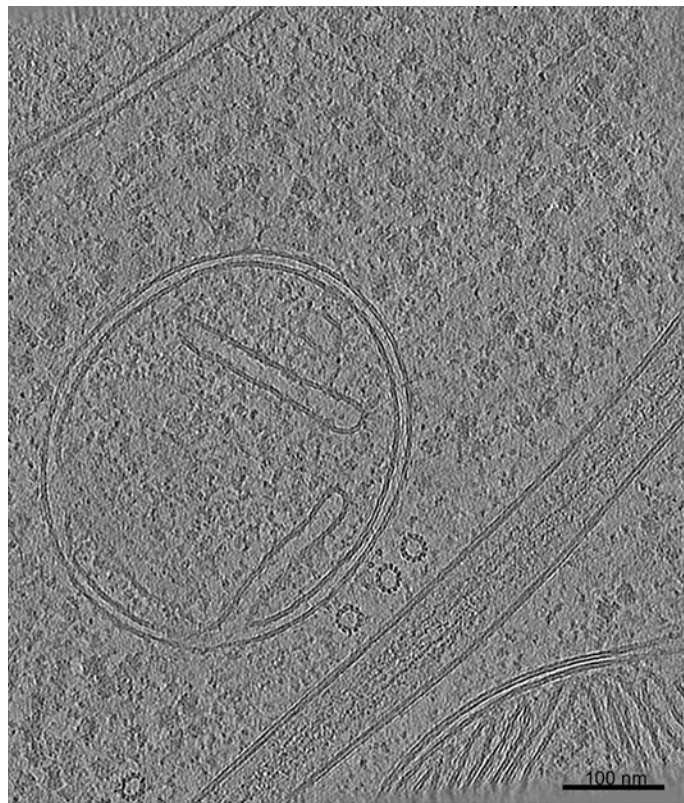
Amira Software



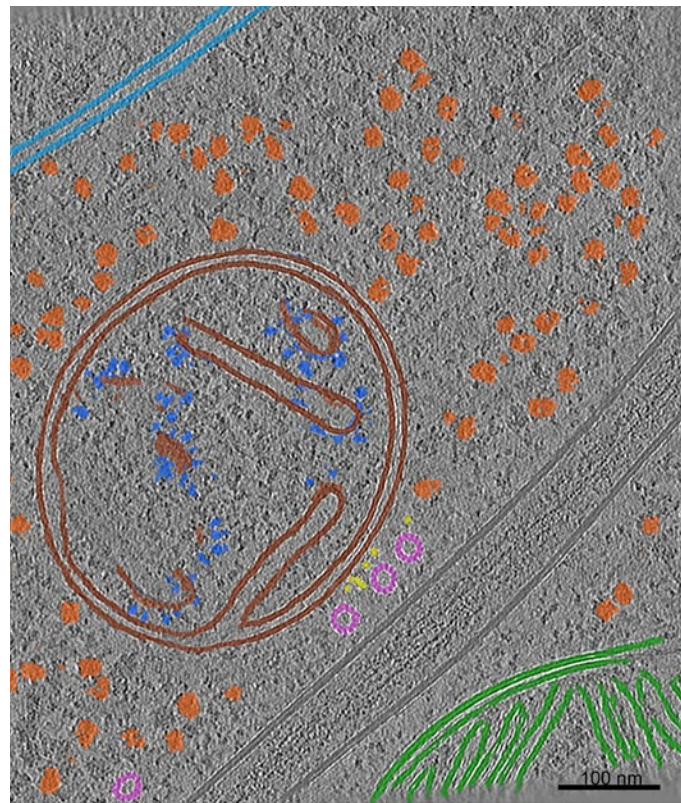


## Open clear windows into the cell

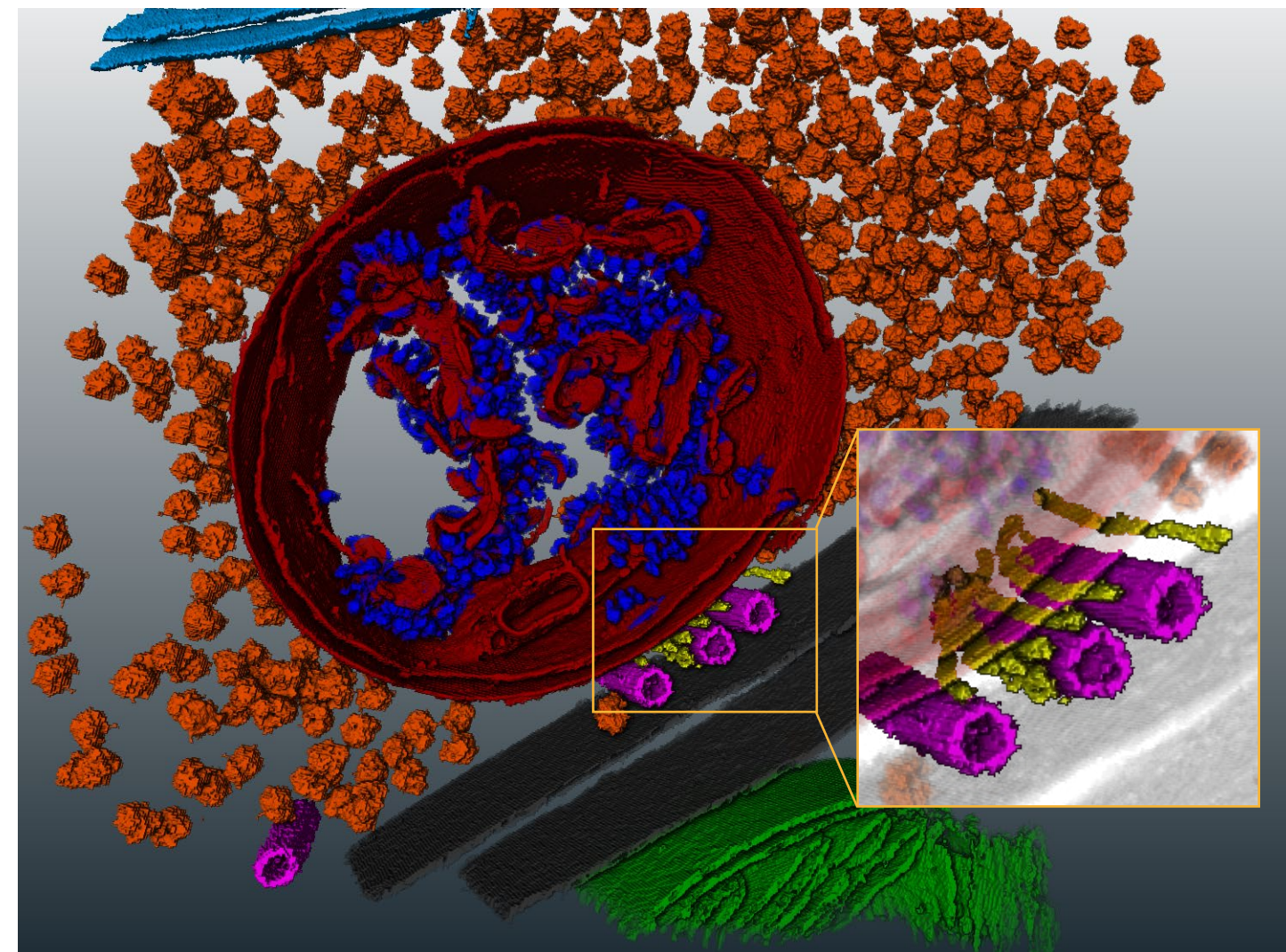
Cryo-electron tomography delivers structural information on individual proteins along with their spatial arrangements within the cell, providing enormous potential for cell biology as it bridges the gap between light microscopy and atomic-level SPA.



High-resolution tomograms produced by the Krios Cryo-TEM show details of the cellular architecture within *Chlamydomonas reinhardtii*.



When segmented, the 2D image shows precise delineation of cellular components, which is made possible by the exceptional quality of the tomogram data.

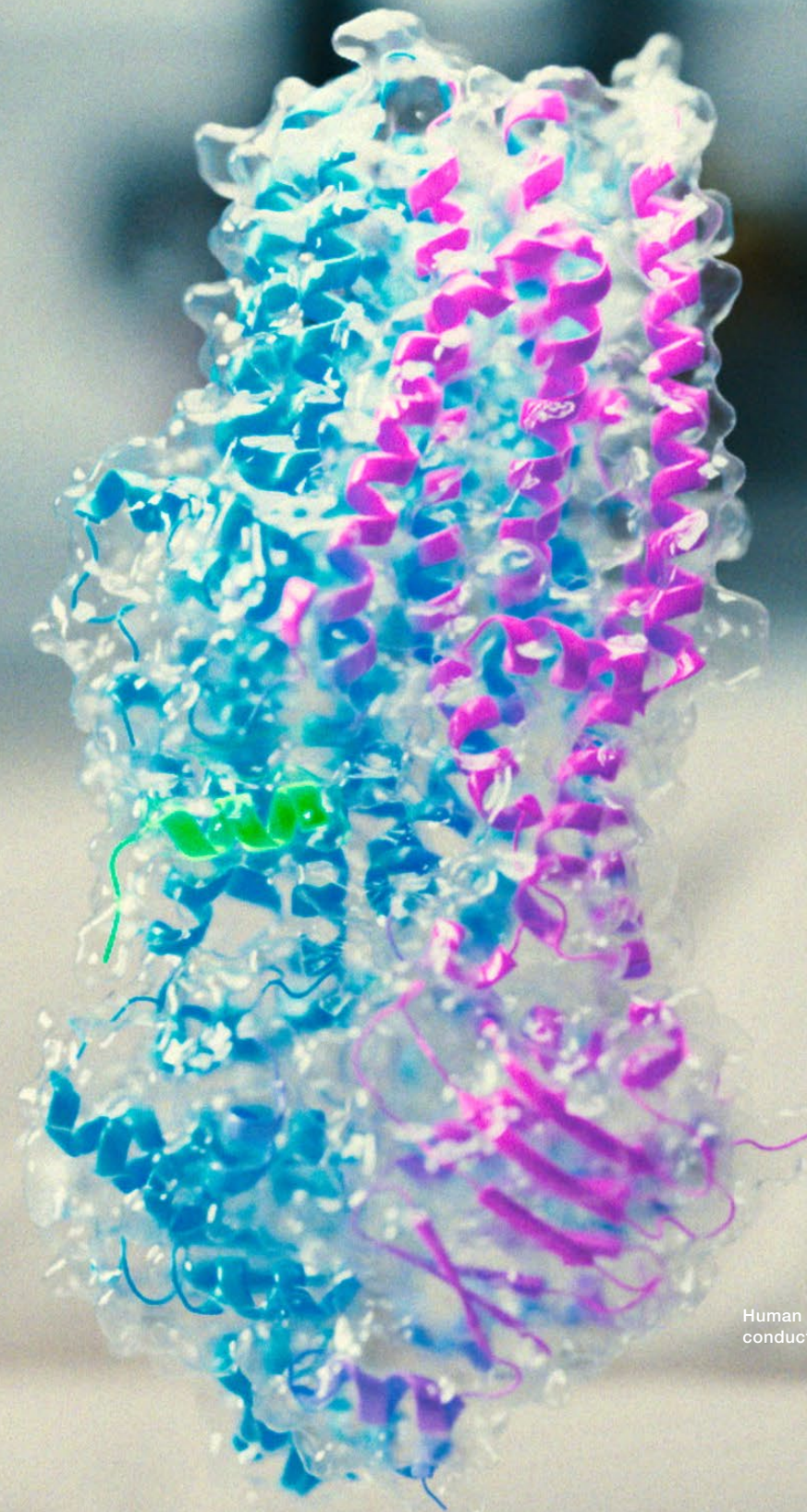


3D reconstruction and segmentation, produced with Thermo Scientific™ Amira™ Software, reveals thin filaments of unknown identity at the interface between the mitochondrion and microtubules (inset zoom). These observations have the potential to reveal exciting new aspects of cellular biology.



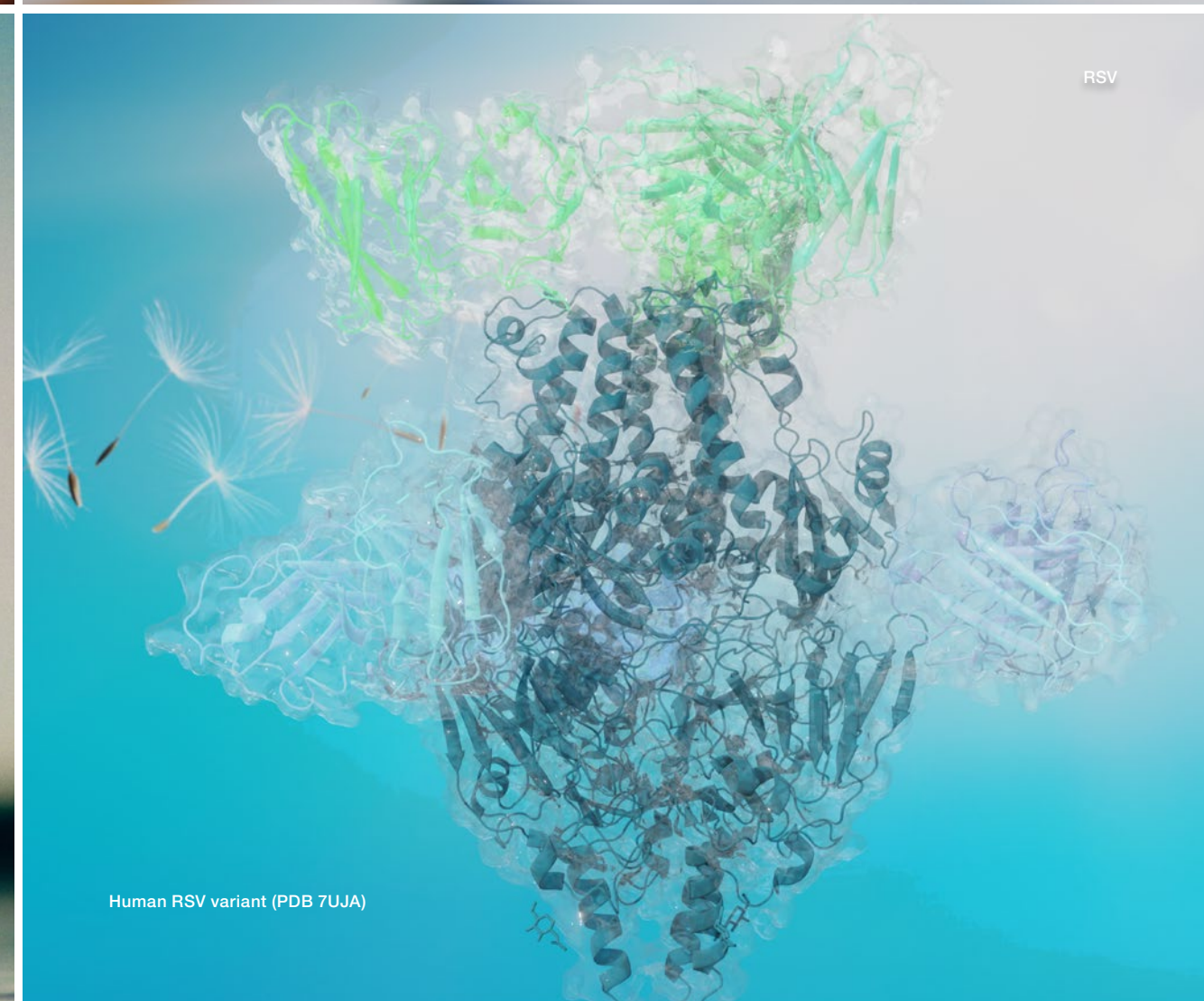
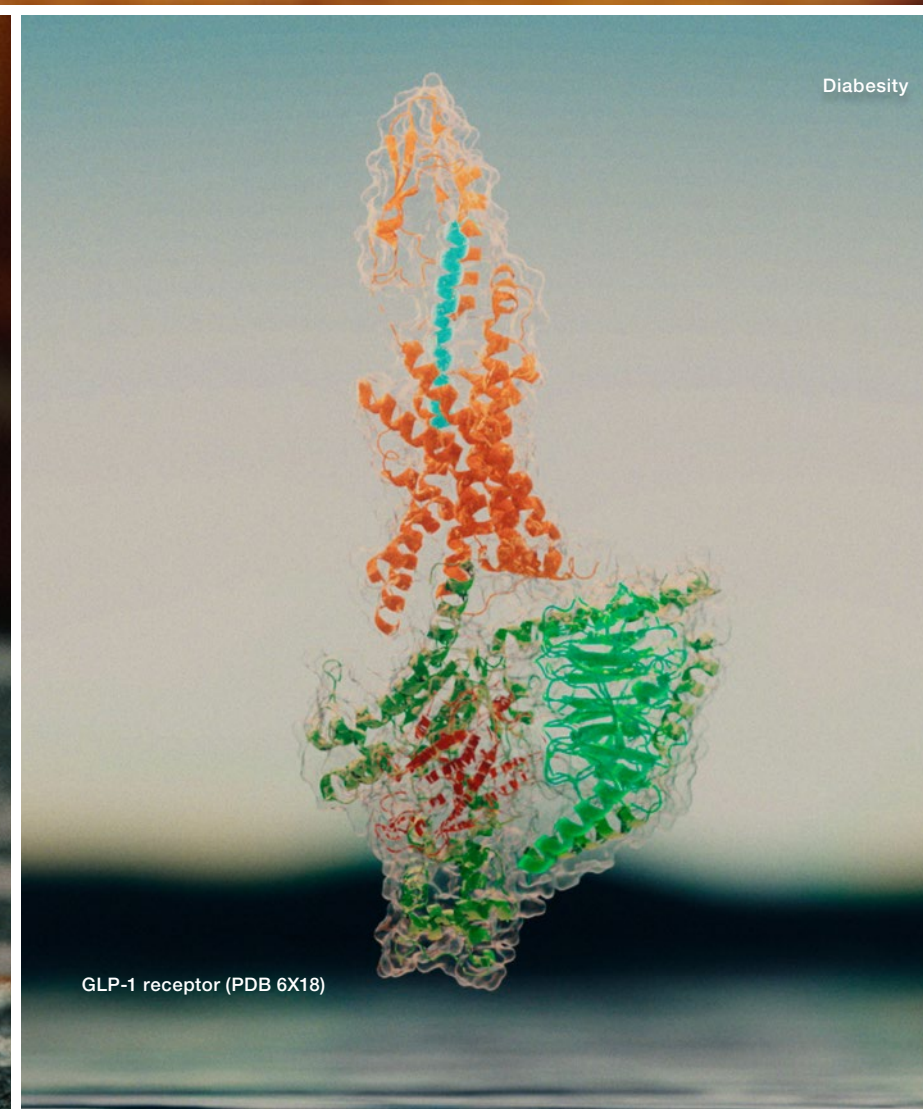
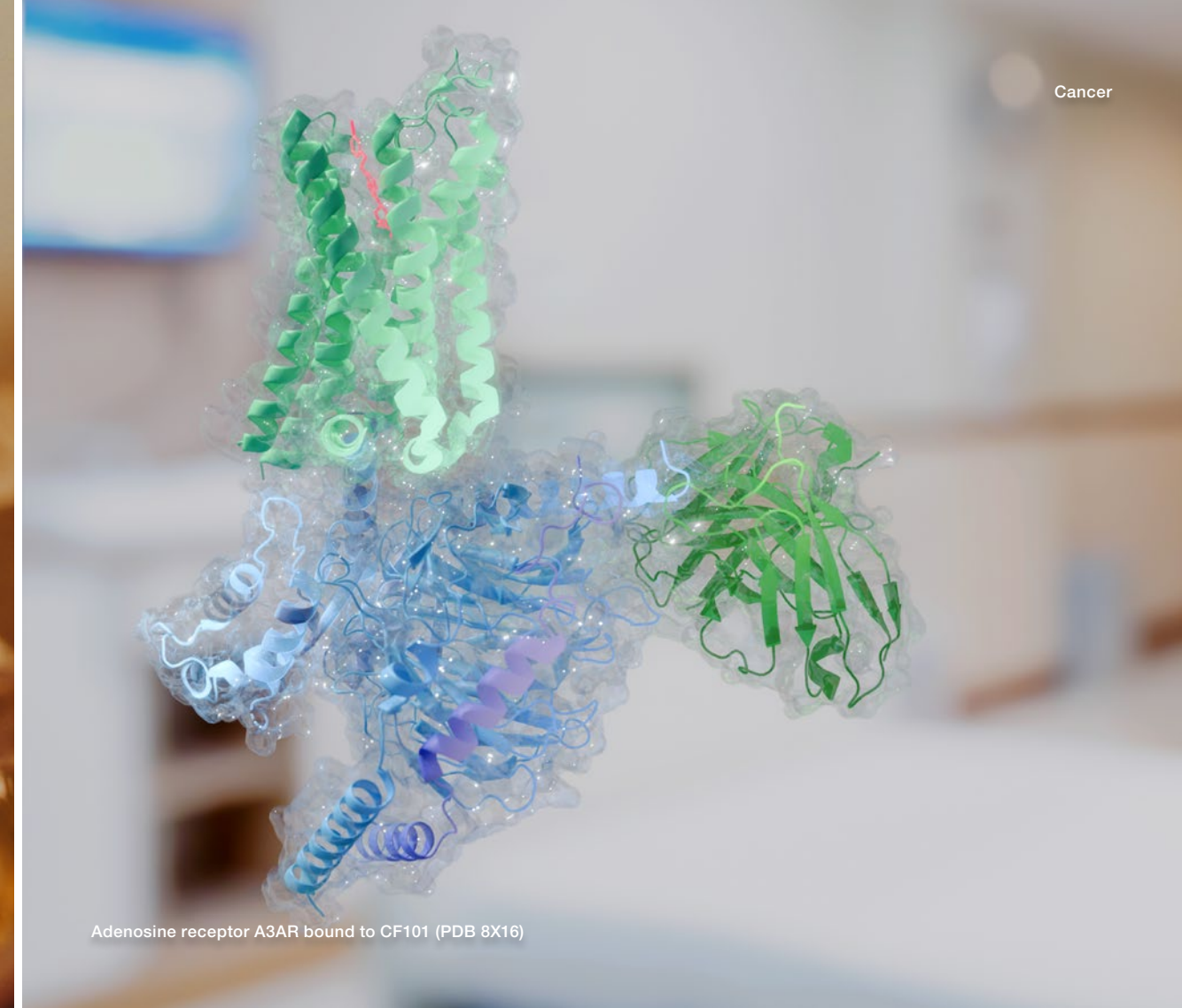
# Every Krios Cryo-TEM has a story in the fight against disease

Cryo-EM single particle analysis has become the go-to method for scientists around the world, helping to generate breakthroughs in the research of infectious and neurodegenerative diseases, cancer, and more. Krios Cryo-TEMs have continued to deliver critical structural insights that support powerful breakthroughs in drug discovery on a variety of targets, many of which were once considered intractable.



Human cystic fibrosis transmembrane  
conductance regulator (PDB 8GLS)





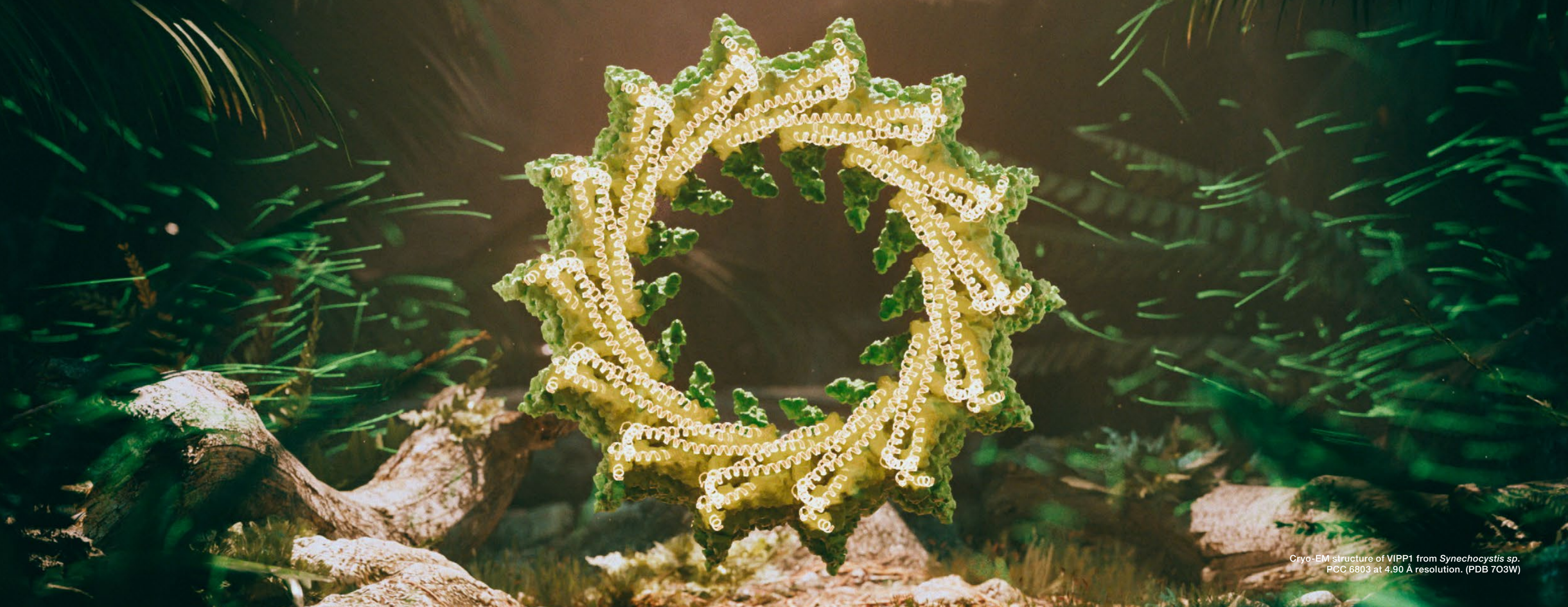


# Making the world healthier

A review of notable public disclosures for clinical stage assets reveals the impact that cryo-EM is having on the development of a diverse range of small molecule drugs and biotherapeutics.







Cryo-EM structure of VIPP1 from *Synechocystis sp.* PCC 6803 at 4.90 Å resolution. (PDB 7O3W)

## Designed for sustainability and the environment

At Thermo Fisher Scientific, sustainable product design is our priority, and we believe all greener product claims should be transparently documented. That's why the Krios 5 Cryo-TEM is the world's first cryo-electron microscope to receive an ACT Ecolabel from My Green Lab.

The Krios 5 Cryo-TEM features low-power Eco modes that not only wake quickly but also translate to **reduced power consumption and reduced operating costs.**



Created by the non-profit organization My Green Lab to help consumers make smart, more sustainable product choices, the virtual ACT Ecolabel provides environmental accountability, consistency, and transparency. The score is based on the product's impact through manufacturing practices, energy and water use, and end-of-life disposal.

 Learn more about our commitment to environmental responsibility at [thermofisher.com/actlabel](https://thermofisher.com/actlabel)



**E-CFEG**

Cold field emission gun optimized for low energy spread ( $\leq 0.3$  eV) enables high contrast and resolution ( $\leq 2.0$  Å) in a short time frame

**Autoloader**

Samples can be retrieved and transferred contamination-free to another Autoloader equipped microscope for re-investigation, optimizing tool connectivity

**Vacuum Capsule**

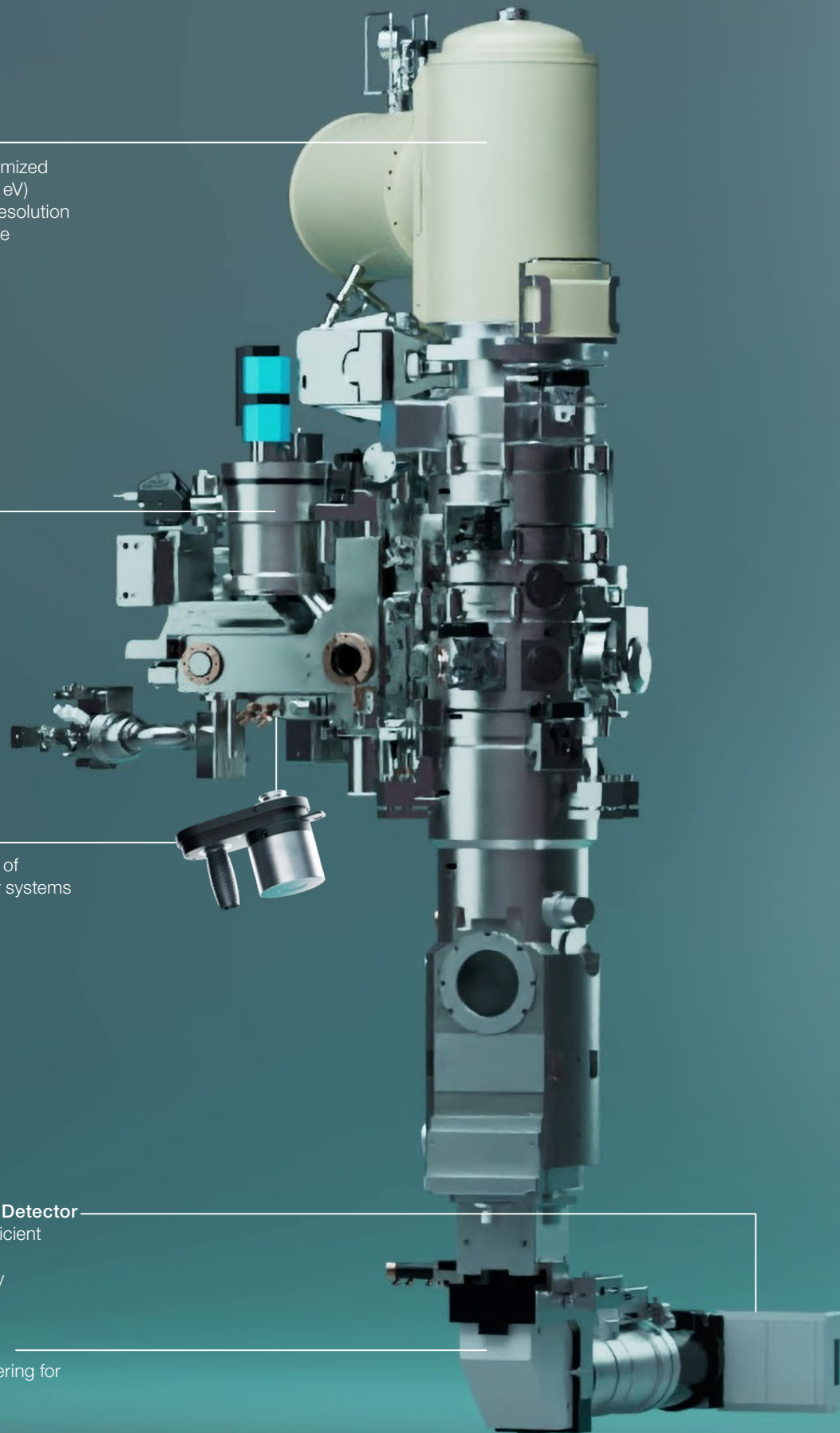
Contamination-free transfer of lamellae between Autoloader systems

**Falcon 4i Direct Electron Detector**

Speed, productivity, and efficient data compression without compromising image quality

**Selectris X Imaging Filter**

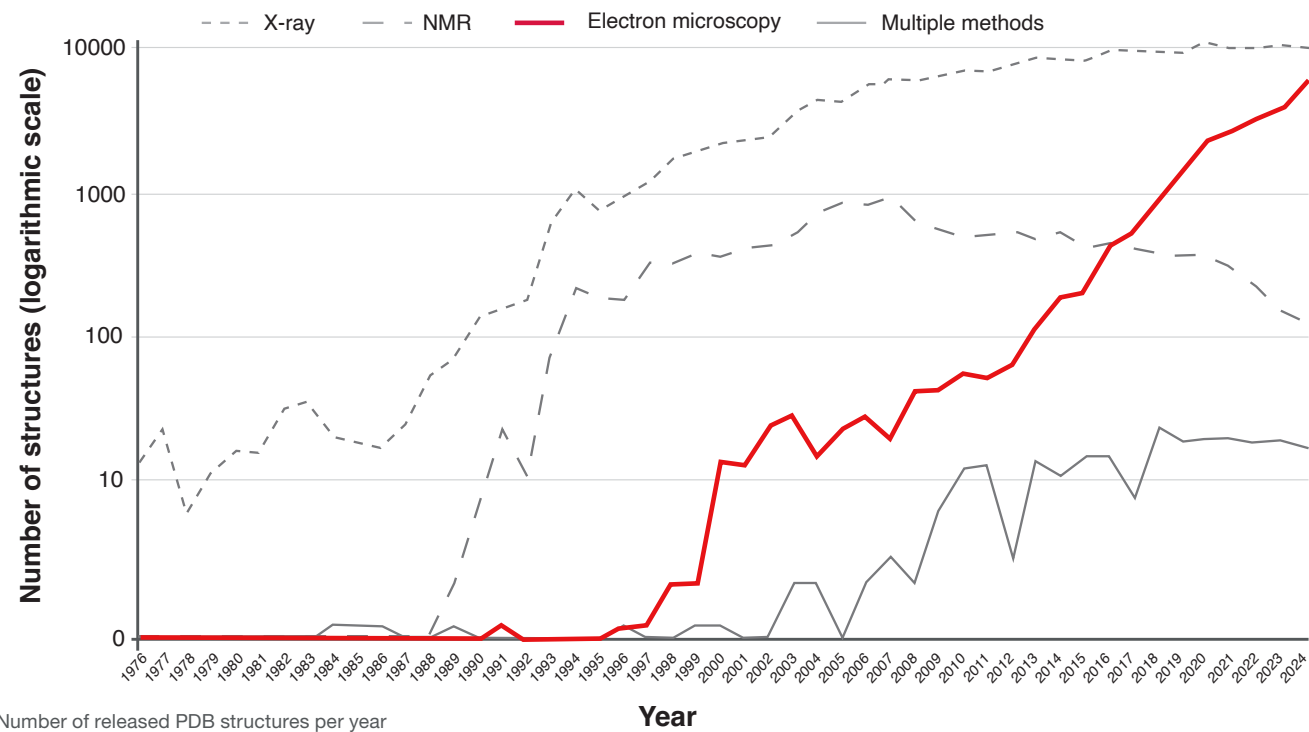
Stable, zero-loss energy filtering for atomic-resolution cryo-EM



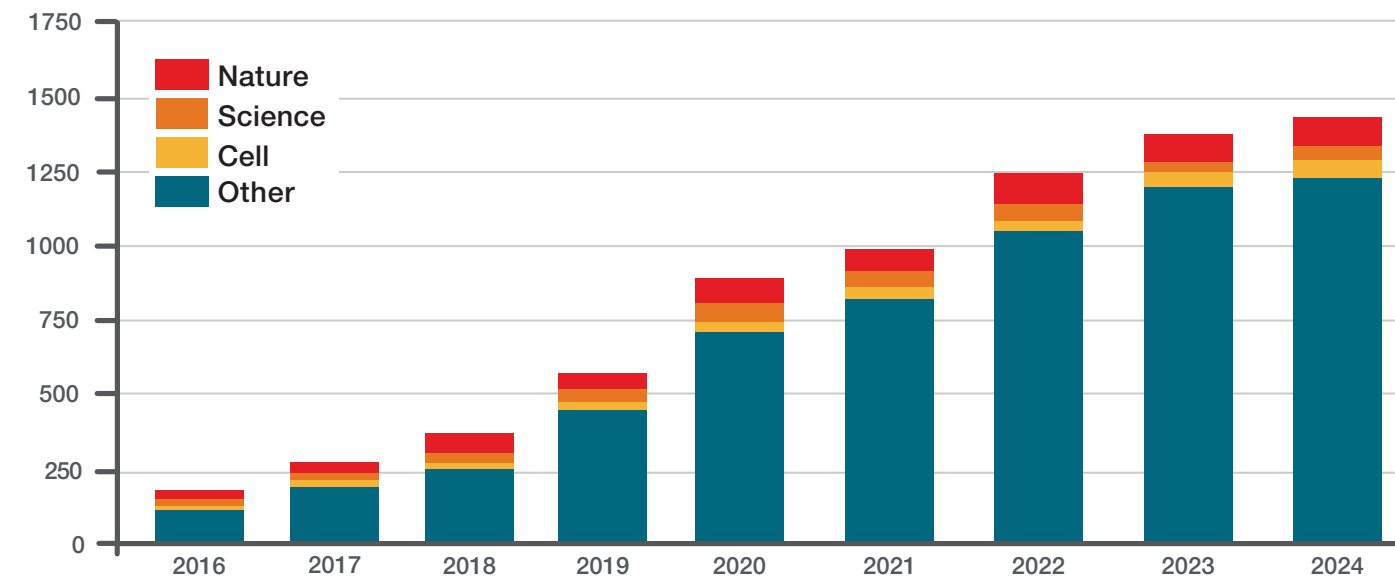


# Proven and trusted by scientists around the world

As of January 2025, 24,091 structures solved using EM have been deposited into the protein data bank. The volume of publications using Cryo-EM has increased year over year since 2016.



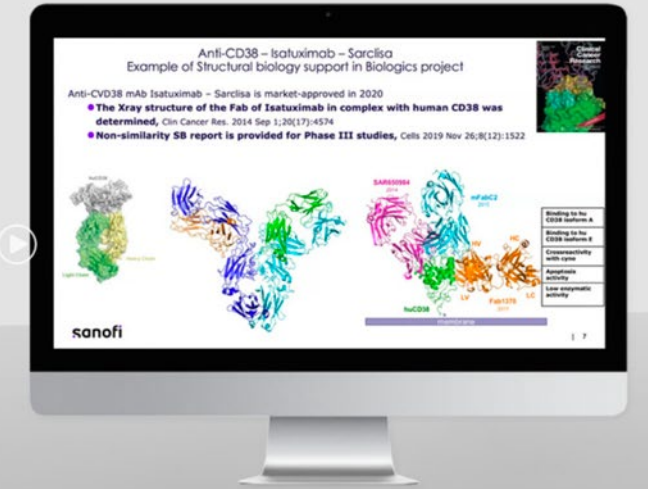
Number of released PDB structures per year



Thermo Scientific Krios Cryo-TEM publications associated with released maps  
Source: EMDDB database Jan 10 2025

## Cryo-electron microscopy is revolutionizing rational drug discovery pipelines

Presented by  
Alexey Rak, Sanofi



### Cryo-electron microscopy is revolutionizing rational drug discovery pipelines

Rational design leveraging routine, high-resolution protein structure determination is driving the discovery and development of diverse biologic and small molecule therapies. In this webinar, hear how experts from Sanofi are utilizing cryo-EM to enhance their drug discovery pipelines.



“ We have the highest-end possible microscope **on this planet** and that is the Krios Cryo-TEM. ”

– Alexey Rak, Head of Biostructure and Biophysics, Integrated Drug Discovery, Sanofi

To explore more resources on rational drug design and its impact on drug discovery pipelines, visit [thermofisher.com/sbdd](https://thermofisher.com/sbdd)



# Resources

## Technical highlights

### Source

- Low-energy-spread cold field-emission gun (E-CFEG) (<0.3 eV)

### Accelerating voltage

- 80–300 kV

### Cryo-Autoloader

- Automated and contamination-free loading of cassettes (up to 12 grids)
- Compatible with Vacuum Capsule for contamination-free transfer of grids

### Temperature management software

- Features liquid nitrogen autofill and scheduling of cool down after cryo-cycles

### Lenses

- Automatic condenser, objective, and SA apertures
- Three-condenser-lens system for automated, continuous, and parallel sample illumination
- Symmetric constant power C-TWIN objective lens with wide-gap pole piece (11 mm)
- Constant power lens design minimizes lens hysteresis and image aberrations during mode switching between imaging modes and diffraction

### Stage

- Computerized 4-axis specimen stage with  $\pm 70$ -degree alpha tilt
- Cryo-stage with single axis holder for optimized stability and drift performance

### Imaging

- Rotation-free imaging with changing magnification

### Advanced performance monitoring

- Highly precise magnification calibration over the full SA range (<1%)
- Self-assessment of optical microscope status, combined with automated alignments, ensures ideal experimental conditions
- Automated user alignments including Center Beam, Center C2 Aperture, and Falcon 4i Detector gain reference collection through Microscope Companion Software
- Optimized optics including the center objective aperture, AutoComa, AutoStigmat, and filter tuning in Thermo Scientific EPU and Tomography Software

### Room size requirements

- 17' x 22' x 10' (L x W x H)

### AFIS (aberration-free image shift)

- Enhanced throughput with short relaxation times when moving coma-free between grid holes
- Extended AFIS range (up to 20  $\mu\text{m}$ ) allows for quick data collection without compromising quality

### FFI (fringe-free imaging)

- Enhanced throughput with multiple image acquisitions per grid hole

### Smart EPU Software

- Automated sample screening and data acquisition
- EPU Multigrid functionality

### Additional components

- Three 24" monitors
- Hand panels to be placed within 15 meters of the column; can be extended up to 300 meters from the column (optional)
- Windows 11 Operating System

### Energy savings mode

- Eco mode designed for sustainability, including scheduling capabilities for rapid wake up

### Detectors (optional)

- Falcon 4i Direct Electron Detector
- EPU-D Camera package for microcrystal electron diffraction (MicroED)
- Thermo Scientific™ Ceta™ D Camera
- Thermo Scientific™ Ceta™ 16M Camera
- HAADF STEM detectors
- On-axis Thermo Scientific Panther BF/DF STEM Detectors

### Energy filter (optional)

- Selectris X Energy Filter
- Selectris Energy Filter
- Gatan BioContinuum Energy Filter

### Software (optional)

- Smart EPU Software with all available AI plugins
- Smart EPU Software with Embedded CryoSparc Live
- CryoTomo Software Suite
- CryoFlow Software for data management

### Other options

- 60°C heat decontamination solution for installation in higher biosafety-level containment facilities (e.g., BSL-3)
- Cs Image Corrector
- Thermo Scientific Phase Plate Solution
- Accelerate and Advance Integrated Service and Applications Support Packages for Drug Discovery, Single Particle Analysis, and Cryo-Tomography



## Electron microscopy resource library

Our life science electron microscopy resource library offers a wealth of information from how to get started with cryo-EM, to research case studies, webinars, and more.

Learn more at [thermofisher.com/emresourceLibrary](https://thermofisher.com/emresourceLibrary)


## Drug discovery resources

Hear from industry leaders about the impact that cryo-EM has had on their biologics and small molecule drug discovery pipelines. Discover how cryo-EM can help your research with our curated white papers, blogs, posters, and on-demand webinars.

Learn more at [thermofisher.com/sbdd-resources](https://thermofisher.com/sbdd-resources)





 Discover more about the Krios 5 Cryo-TEM at [thermofisher.com/krios](https://thermofisher.com/krios)