

# Krios G4

Explore the hidden  
side of life





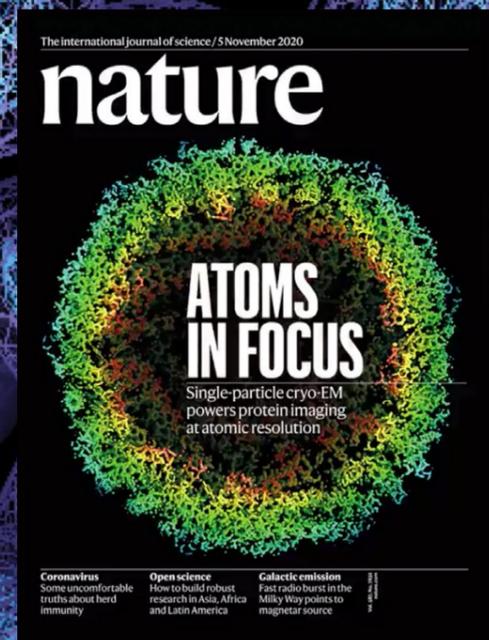
## Insights into protein function only cryo-EM can provide

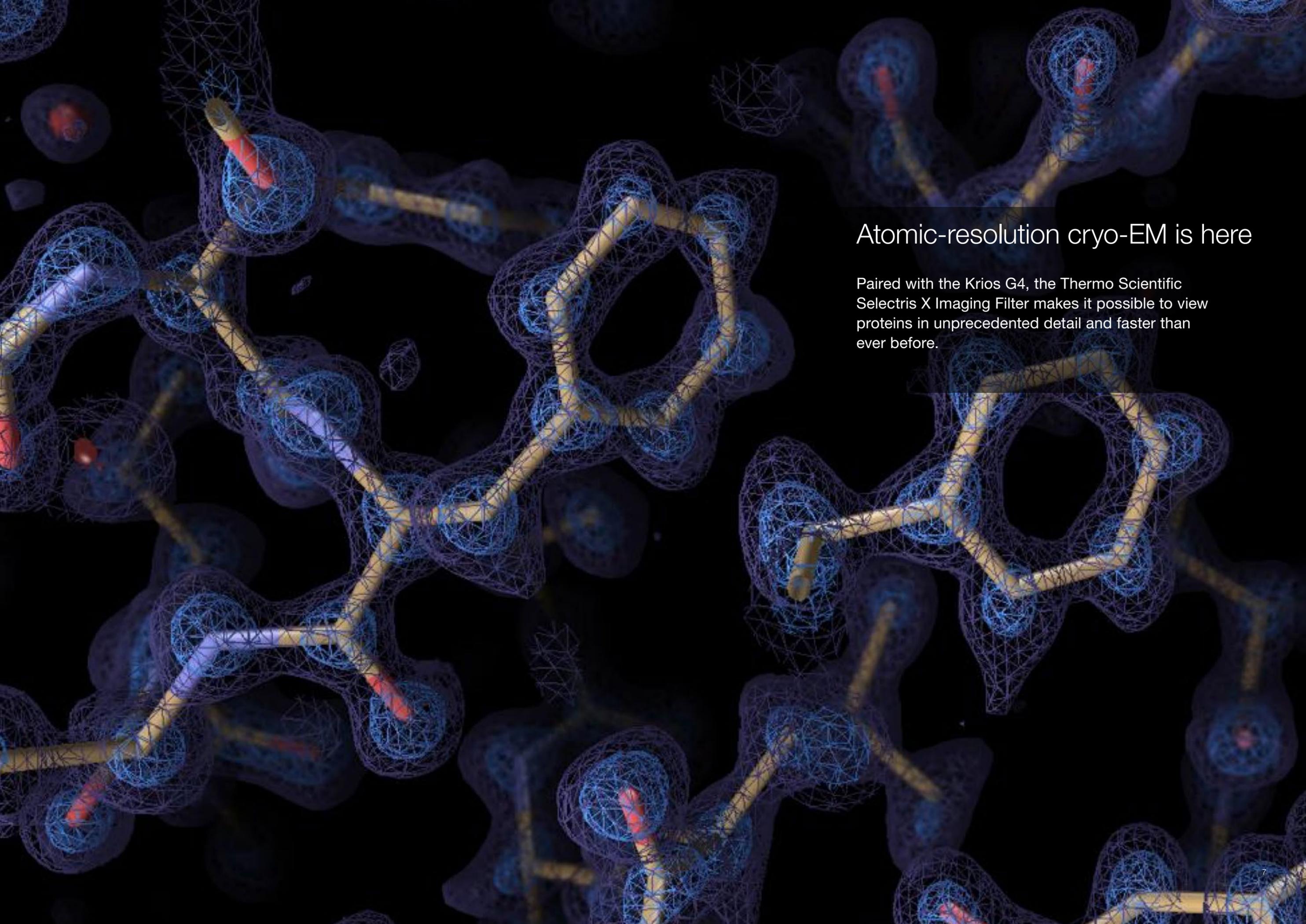
The award-winning Thermo Scientific Krios G4 is a 300 kV cryo-transmission electron microscope (cryo-TEM) engineered to enable 3D visualization of proteins and molecular machines, their localization, and dynamics within the architecture of the biological cell for unmatched biological insights.

Atomic-resolution cryo-EM map of the protein apoferritin resolved at 1.2 Å.  
Image courtesy P. Emsley, MRC LMB, Cambridge

# What will you discover with atomic-resolution cryo-EM?

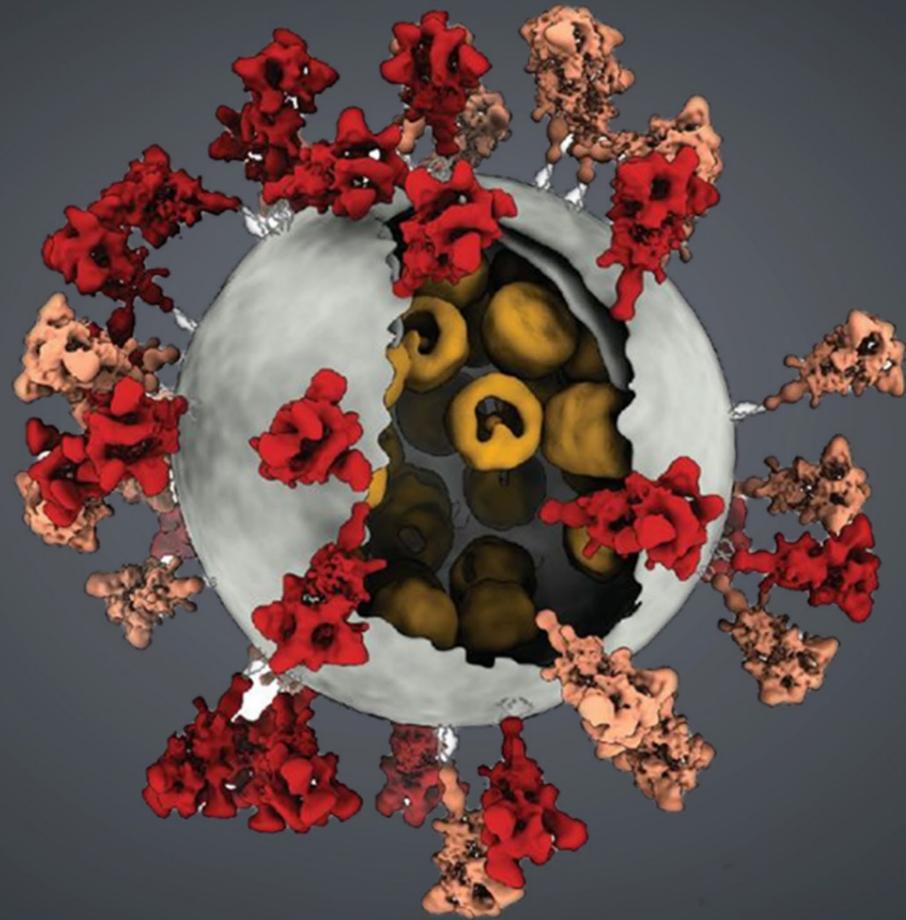
Knowing the 3D structure of molecular machines is crucial to understanding molecular processes. With the Krios G4 Cryo-TEM, there are no longer boundaries to push—only discoveries to be made.





## Atomic-resolution cryo-EM is here

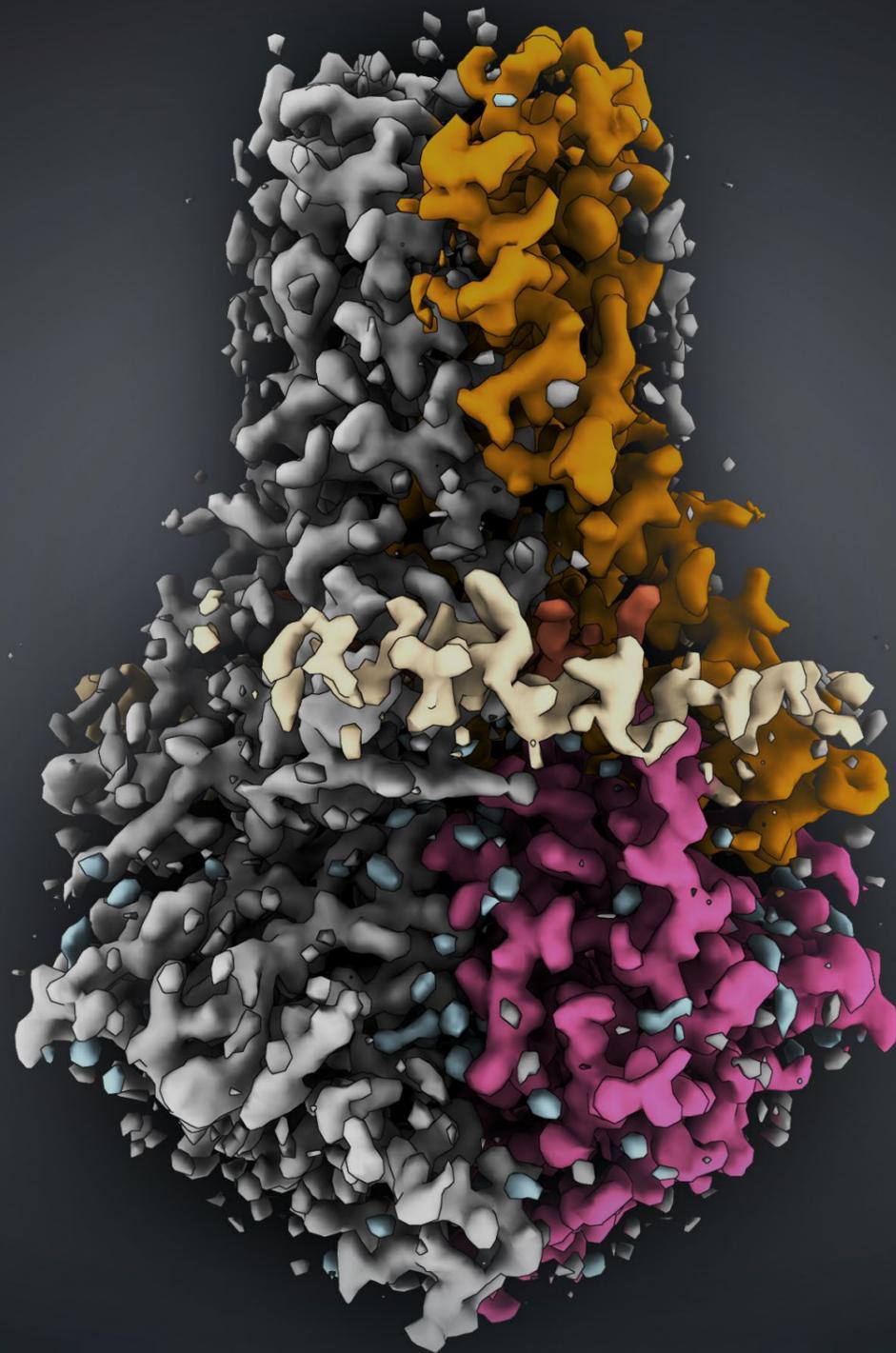
Paired with the Krios G4, the Thermo Scientific Selectris X Imaging Filter makes it possible to view proteins in unprecedented detail and faster than ever before.



## Every Krios has a story

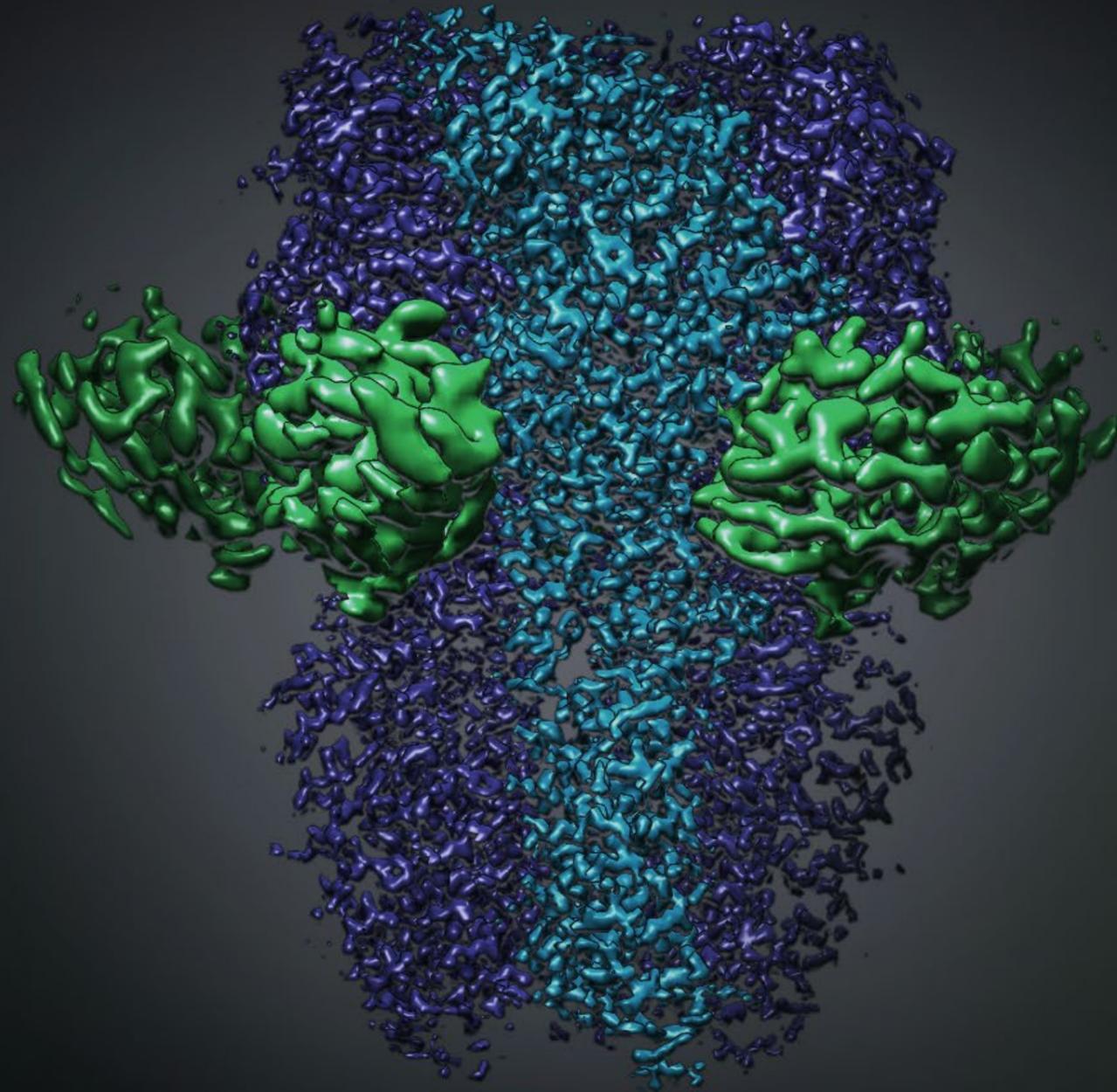
For generations, biological scientists have sought to unlock the mysteries of life -- aging, curing disease, and enhancing health. Whether working on cancer, HIV, neurodegenerative diseases or drug discovery research, scientists need a deep understanding of cell behavior, functionality, and structure.

Cryo-electron tomography image of SARS-CoV-2. Courtesy of Sai Li.  
Yao, C. Molecular Architecture of the SARS-CoV-2 Virus, *Cell*, 183: 730-739, 2020.  
Zimmer, Carl. "The Coronavirus Unveiled," *New York Times* 9 Oct 2020.



In February 2020, cryo-EM researchers determined the structure of the SARS-CoV-2 spike protein and its cellular receptor during infection and made their cryo-EM structures publicly available. Researchers used these results to develop an mRNA vaccine that entered phase 1 clinical trials in March 2020. The vaccine was approved for emergency use in December 2020. Research groups around the world continue to use cryo-EM to gain a detailed understanding of SARS-CoV-2 and its variants to aid in the development of vaccines, antivirals, and neutralizing antibodies.

Cryo-EM structure of the SARS-CoV-2 3a ion channel in lipid nanodiscs at 2.1 Å nominal resolution viewed from the membrane plane. Courtesy of S. Brohawn.



GABA<sub>A</sub> human membrane proteins are primary target sites for a range of clinically relevant drugs like general anesthetics and neuroactive steroids. With the Selectris X Imaging Filter, details of the binding pocket were observed, like histamine coordination with surrounding water molecules. For structure-based drug design, this shows how a drug could displace water molecules, potentially resulting in safer and more effective drugs.

Courtesy of A. Sente and R. Aricescu.  
Nakane, Single-particle cryo-EM at atomic resolution, *Nature*, 587, 152–156, 2020.

**E-CFEG**  
Cold field emission gun optimized for low energy spread ( $\leq 0.3$  eV) enables higher contrast at highest resolutions ( $\leq 2.0$  Å) in a shorter time

**Autoloader**  
Samples can be retrieved and transferred contamination free to another autoloader equipped microscope for re-investigation – optimal tool connectivity

**Falcon 4 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

## Designed for true atomic resolution and speed

Advance cryo-EM discovery beyond what you thought possible with unprecedented resolution, speed, and ease of use by pairing the Krios G4 Cryo-TEM with any or all of our add-ons designed to help scientists achieve a specific resolution with much less data.

### Increase your productivity

#### Aberration-free imaging shift (AFIS)

Most movements can be done with image beam shift, which is faster and does not create any stage-movement induced sample drift

#### Fringe-free imaging (FFI)

Eliminate fringes at the edge of the beam so users acquire more usable images per foil hole to enhance overall throughput

#### EPU 2

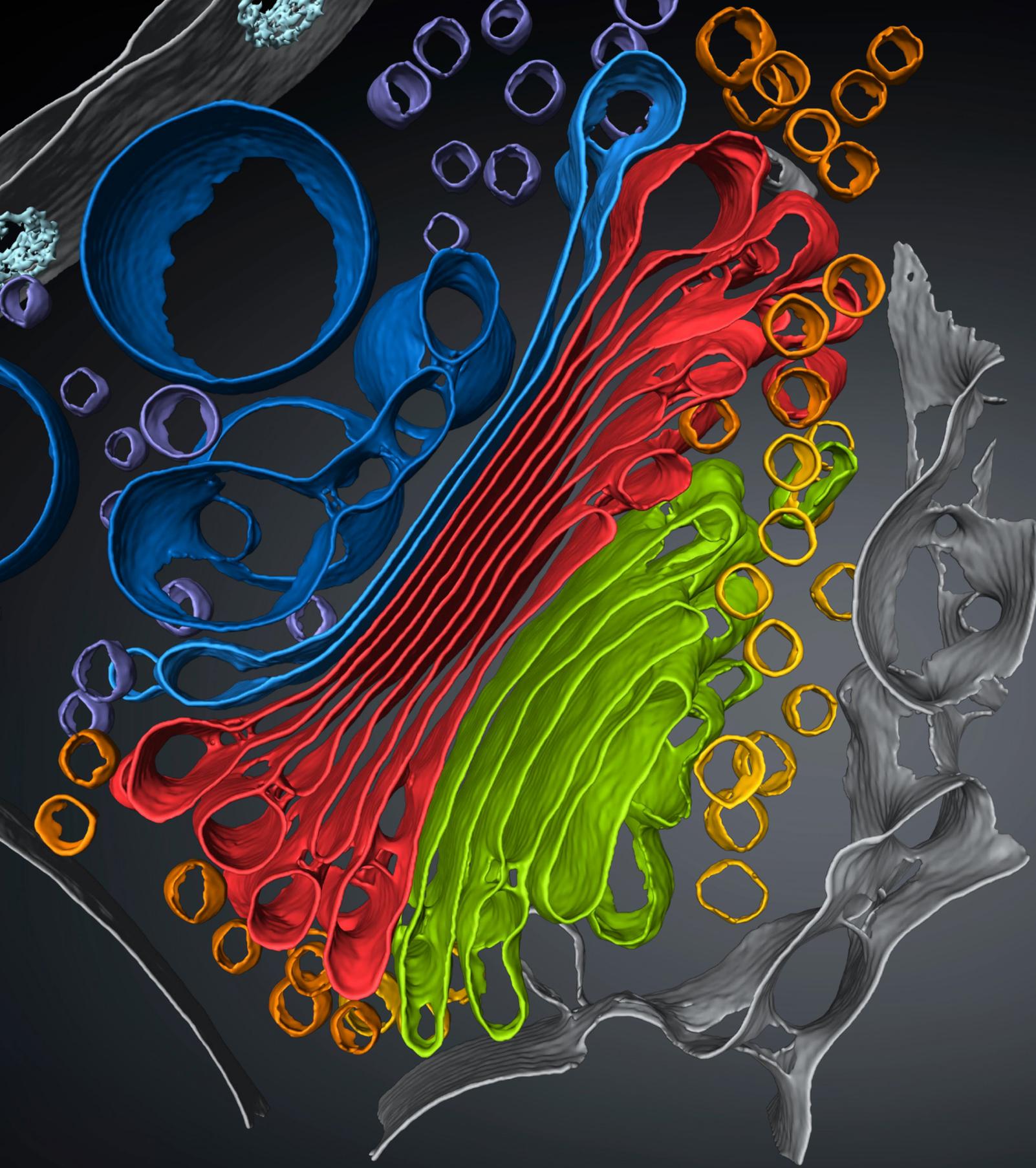
Microscope-embedded SPA software solution for automated grid screening and data acquisition with systematic user guidance, automated alignments, automation of tasks

#### EPU Multigrid

Enables automated single-particle analysis data acquisition on multiple grids

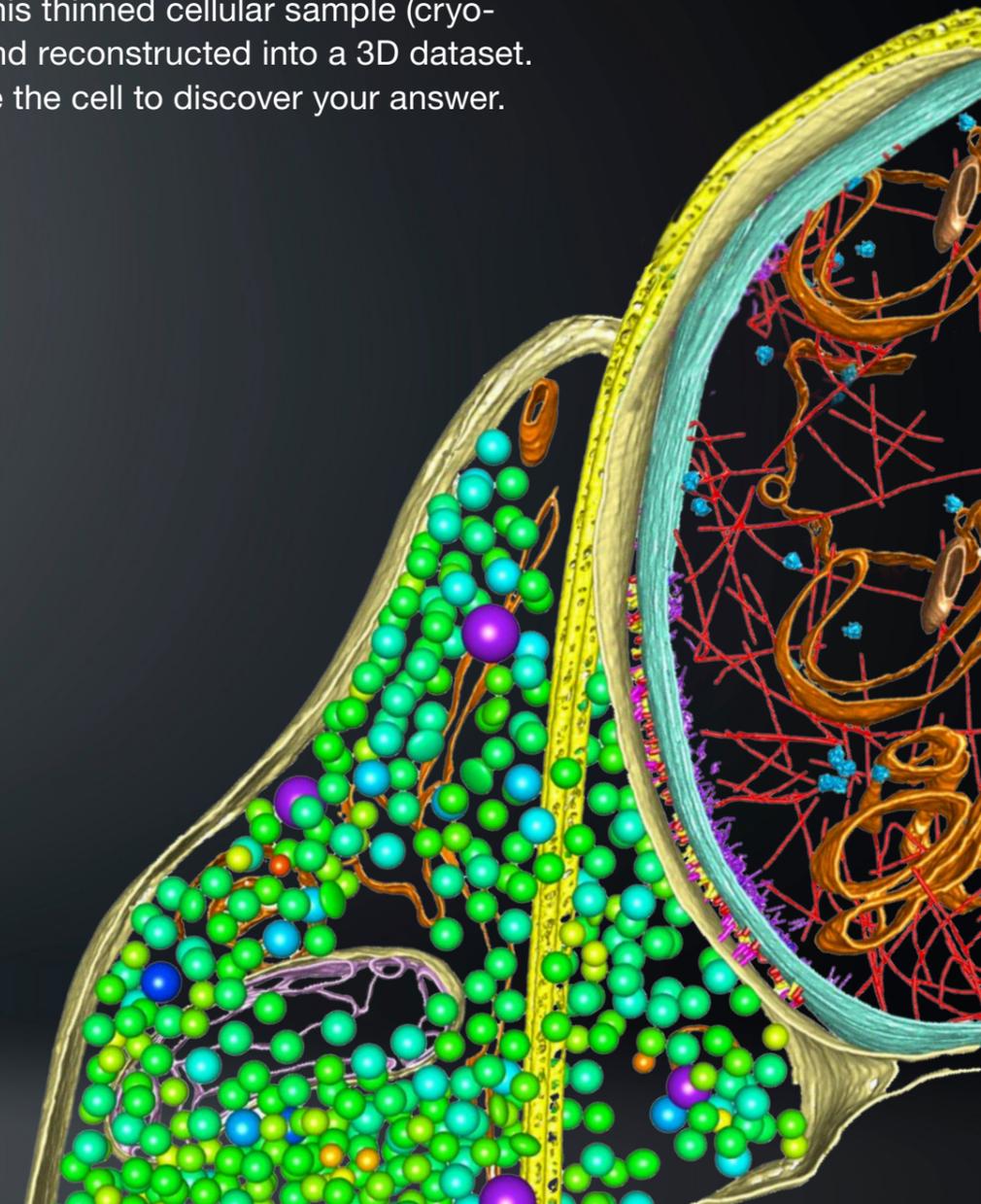
#### Tomography 5 Software

Automated 3D data acquisition for multi-site batch tomography and automatic cassette mapping for grid quality assessment and lamella identification



## Explore every hidden corner of a cell

Cellular cryo-electron tomography is a label-free cryogenic imaging technique that provides 3D datasets of organelles and protein complexes at nanometer resolution. This is done by opening windows into the cell with focused ion beam milling of a cryogenically frozen (vitrified) cell. A series of 2D images is taken of this thinned cellular sample (cryo-lamella) and reconstructed into a 3D dataset. See inside the cell to discover your answer.

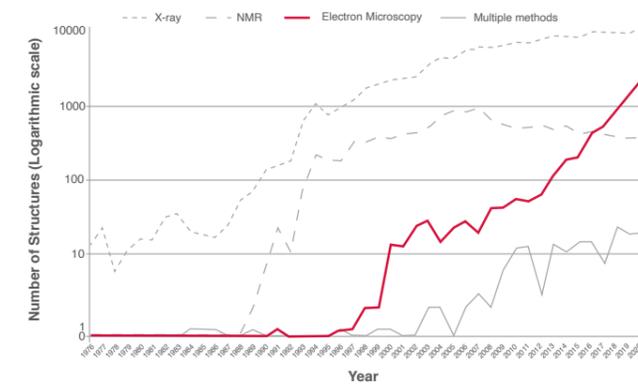


Left: Molecular architecture of the Chlamydomonas Golgi apparatus. Courtesy of B. Engel. Right: Excitatory synapse of hippocampal neuron. Courtesy of G. Bi and H. Zhou. Data segmentation and visualization by Thermo Scientific Amira Software.

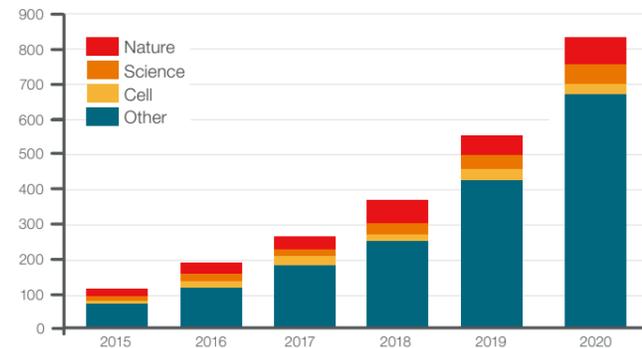
# Global Thermo Fisher Cryo-EM Network

The Krios stands out as the preferred cryo-TEM of leading researchers around the world. Since 2012, there have been more than 4,000 scientific articles published citing the Krios, and as of January 2021, 2,500 of these are associated with the Electron Microscopy Data Bank, a public repository for electron microscopy density maps of macromolecular complexes and subcellular.

Scientists are releasing their published structures in an effort to create the kind of collaborative environment essential to advancing science. Of these, 98% were solved using Thermo Scientific instruments. In recognition, the Krios G3i received the 2018 Edison Award in Molecular Analysis.



Number of Released PDB Structures per Year



Thermo Scientific Krios Cryo-TEM publications associated with released maps  
Source: EMDB database Jan 20, 2021

## Must Reads

Kühlbrandt, W. The Resolution Revolution. *Science* (2014) doi: [10.1126/science.1251652](https://doi.org/10.1126/science.1251652)

Nakane, T., Kotecha, A., et al. Single-particle cryo-EM at atomic resolution. *Nature* (2020) doi: [10.1038/s41586-020-2829-0](https://doi.org/10.1038/s41586-020-2829-0)

We're impressed with the stability of both the hardware and the software. Due to the enhanced performance and stability, all our COVID-19 work is now done on the Selectris X Imaging Filter. We routinely collect 5 eV tomograms, which was previously impossible.

**Alistair Siebert**  
Principal Electron Microscopist for the electron Bio-Imaging Centre (eBIC), Diamond Light Source

The Krios G4 is much more than an upgrade. The state is more stable and accurate – tomography should be a joy! I definitely get better results on the G4 and I don't think there is much contamination. This would put the G4 on par with the best materials science microscopes.

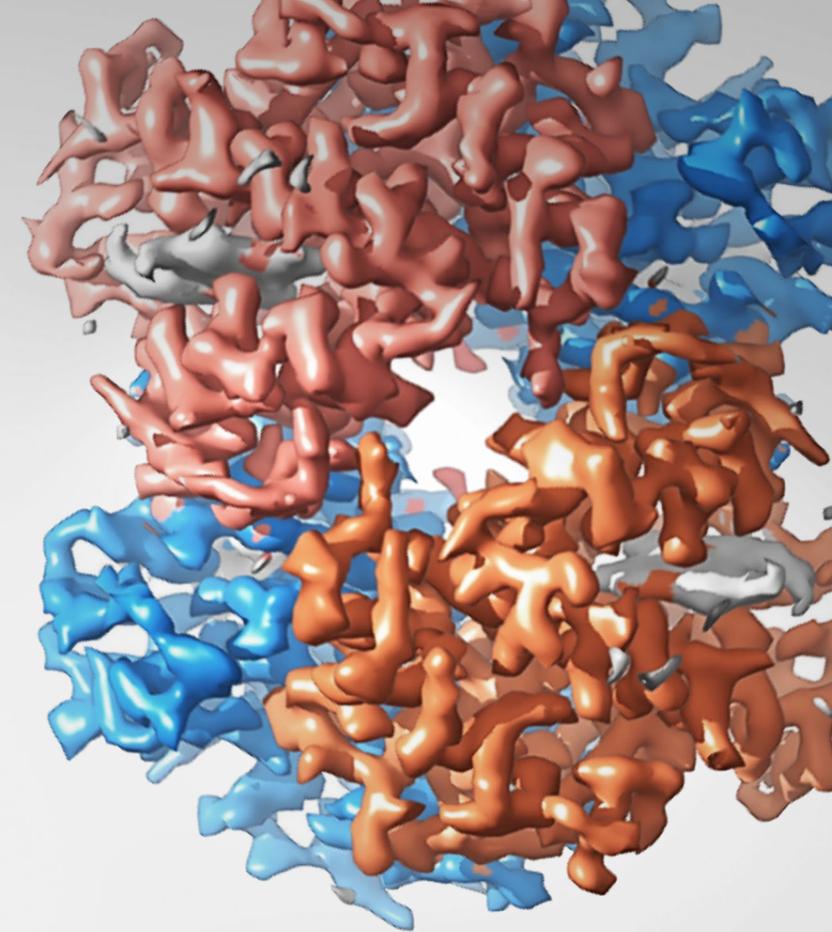
**Rado Danev**  
Professor, University of Tokyo



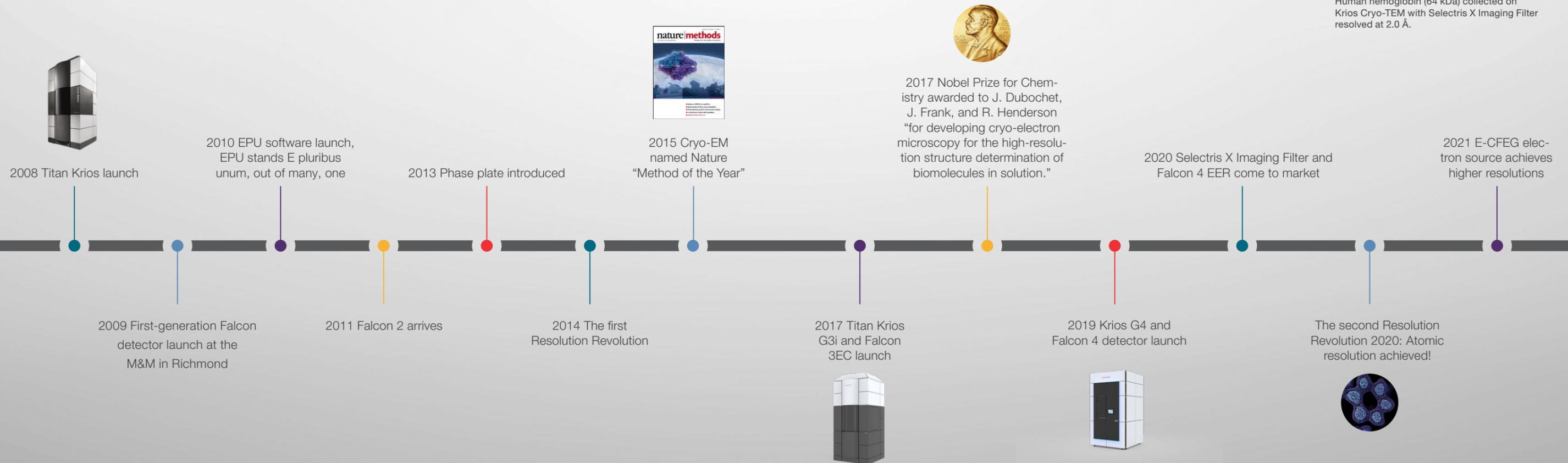
# Making history again and again

The first-generation Titan Krios demystified the complexity of cryo-EM through the introduction of the Autoloader, which fully automated the process of loading frozen hydrated samples into the microscope and changed microscopy forever.

We strive to be pioneers in cryo-EM, to forge a path for our customers with deep imagination and innovation to explore the hidden side of life.



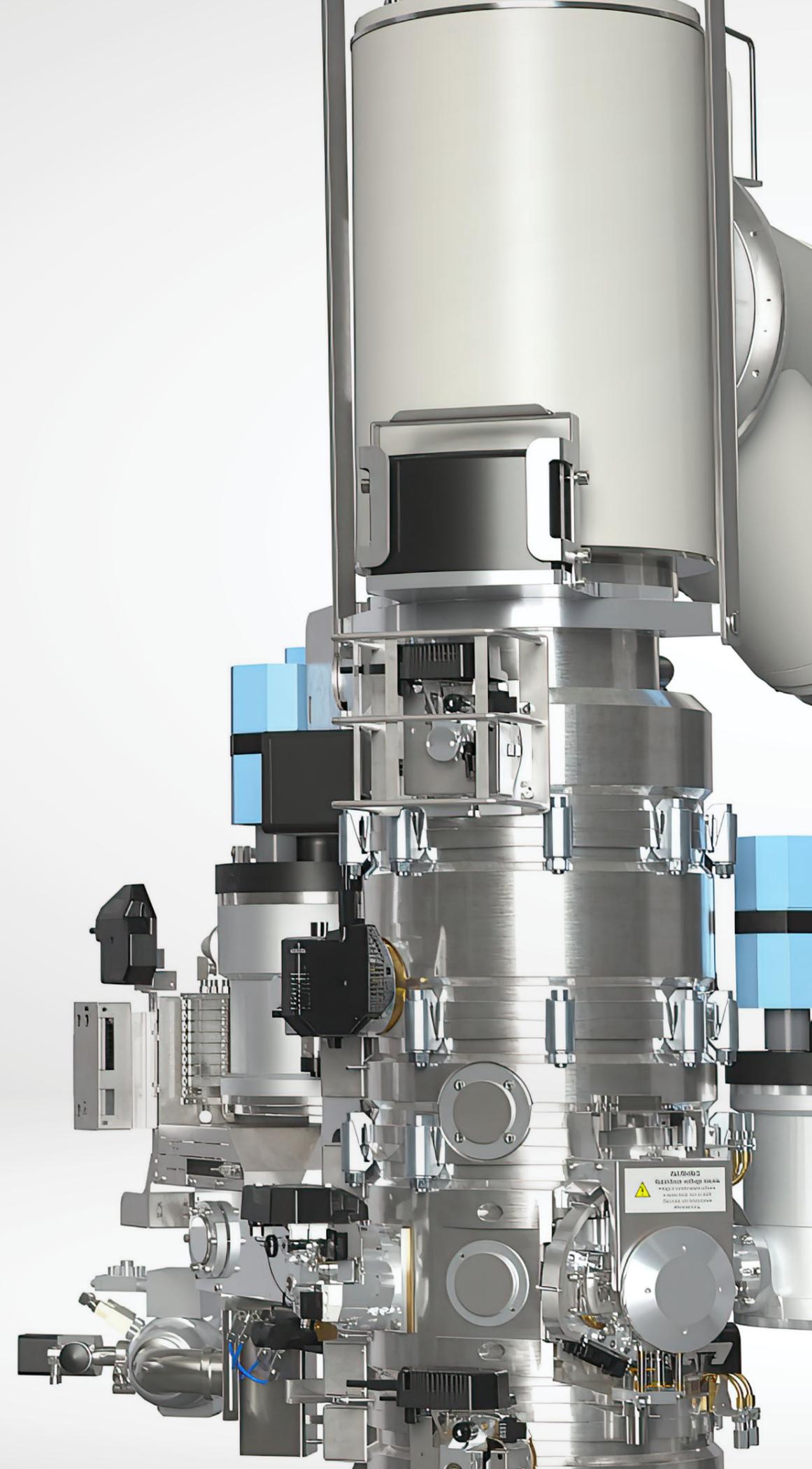
Human hemoglobin (64 kDa) collected on Krios Cryo-TEM with Selectris X Imaging Filter resolved at 2.0 Å.





## Technical Highlights

<b>Source</b>	X-FEG (extreme high-brightness field emission gun) or low-energy-spread cold FEG (E-CFEG)
<b>Accelerating voltage</b>	80–300 kV
<b>Cryo-autoloader</b>	Automated and contamination-free loading of cassettes (up to 12 grids)
<b>Temperature management software</b>	Includes liquid nitrogen autofill and cool down scheduling
<b>Lenses</b>	<ul style="list-style-type: none"> <li>• Automatic condenser, objective and SA apertures</li> <li>• Three-condenser-lens system for automated, continuous, and parallel sample illumination</li> <li>• Symmetric constant power C-TWIN objective lens with wide-gap pole piece (11 mm)</li> </ul>
<b>Stage</b>	<ul style="list-style-type: none"> <li>• Computerized 4-axis specimen stage with <math>\pm 70</math>-degree alpha tilt</li> <li>• Cryo-stage with single axis holder for optimized stability and drift performance</li> </ul>
<b>Imaging</b>	Rotation-free imaging with changing magnification
<b>Advanced performance monitoring</b>	Self-assessment of optical microscope status, combined with automated alignments, ensures ideal experimental conditions
<b>Room size requirements (L x W x H)</b>	17' x 22' x 10'
<b>AFIS (aberration-free image shift)</b>	Enhancing throughput with shorter relaxation times when moving coma-free between grid holes
<b>FFI (fringe-free imaging)</b>	Enhanced throughput with multiple image acquisitions per grid hole
<b>Thermo Scientific EPU 2 Software</b>	<ul style="list-style-type: none"> <li>• Automated sample screening and data acquisition</li> <li>• EPU Multigrid functionality</li> </ul>
<b>Additional components</b>	<ul style="list-style-type: none"> <li>• Three 24" monitors</li> <li>• Hand panels to be placed within 15 meters of the column, or extend up to 300 meters from the column (optional)</li> </ul>
<b>Detectors (optional)</b>	<ul style="list-style-type: none"> <li>• Falcon 4 Direct Electron Detector</li> <li>• Thermo Scientific Ceta™ D Camera</li> <li>• Thermo Scientific Ceta 16M Camera</li> <li>• HAADF STEM detectors</li> <li>• On-axis BF/DF detectors</li> </ul>
<b>Energy filter (optional)</b>	<ul style="list-style-type: none"> <li>• Selectris Imaging Filter</li> <li>• Selectris X Imaging Filter</li> <li>• Gatan BioContinuum Energy Filter</li> </ul>
<b>Other options</b>	<ul style="list-style-type: none"> <li>• Cs Image Corrector</li> <li>• Thermo Scientific Phase Plate Solution</li> </ul>



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

**thermo** scientific