Tundra Cryo-TEM

Unravel complex proteins with simplified cryo-EM

Dedicated structural determination solution that provides more accessible single-particle cryo-electron microscopy (cryo-EM) to scientists who are new to the technique.

Harness the power of cryo-EM technology

In order to fully understand biological processes and diseases, it is vital to obtain structural information for the relevant biological machinery. Notably, it is becoming increasingly apparent that proteins, the key biological players in fundamental biology and disease mechanisms, often adopt multiple conformations or act in complexes with other proteins. These large and/or dynamic systems present a challenge to traditional methods of 3D structural determination. Cryo-EM techniques, particularly single particle analysis (SPA), have emerged as a valuable tool for the determination of native protein function and the dynamics of complex biological systems.

In cryo-EM, specimens are rapidly frozen (vitrified) so that their biologically relevant native states are preserved. SPA can then obtain structural details of the samples at atomic resolution. This technique has transformed the field of structural biology, leading to new insight into numerous biological processes. SPA validates biochemical methods by directly showing details such as: protein-protein interactions in heteromeric complexes, conformational changes of flexible proteins, and mechanisms of large macromolecular machines such as viruses, ribosomes, and proteasomes.

The Thermo Scientific™ Tundra™ Cryo-TEM is a cryo-transmission electron microscope optimized for SPA, bringing this powerful technique to every biochemistry laboratory. The Tundra Cryo-TEM is especially designed for new users who are not experts in electron microscopy. It is easier to use than typical cryo-TEM instruments and is priced to meet a range of grant programs globally. In combination with the Thermo Scientific™ Falcon™ C Direct Electron Detector (DED), the Tundra Cryo-TEM provides improved resolution, offering deeper structural insights into challenging proteins.

Key features

- **Structural information** at biologically relevant resolution
- **Ideal for sample and grid selection** for analysis on higher resolution platforms
- **Easy, iterative loading** and imaging for rapid sample-viability determination
- **Loader technology** mitigates common biochemistry optimization problems
- **AI-guided automation** with results displayed progressively
- **User-friendly interface** with pre-defined settings to streamline data collection
- **Unique AI algorithms** allow the microscope to learn over time to improve decision making

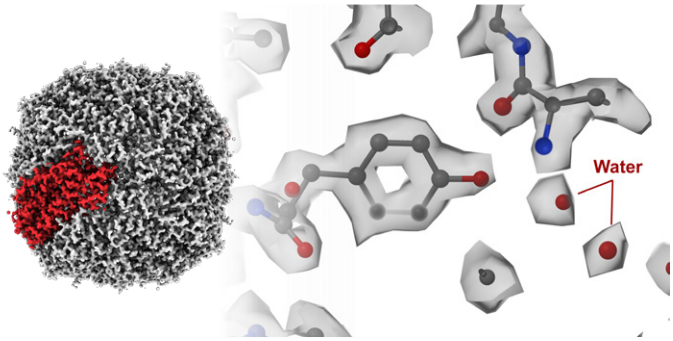

Figure 1. Apoferritin at ~2.1 Å; data collected with the Tundra Cryo-TEM and Falcon C Direct Electron Detector.

For example, ~2.1 Å resolution can be achieved for benchmark proteins such as apoferritin, which are rigid and optimized for cryo-EM (Figure 1). Such high-resolution maps allow for *de novo* model building; the protein backbone can be clearly traced, side chains can be easily modeled, and water networks in active sites are now visible. Atomic models can help you understand how proteins function, how to modify genes, and how to design drugs accordingly.

The Tundra Cryo-TEM.

Answer key biological questions

3D structures can provide you with new information on your samples, generating highly valuable, revolutionary insights. For example, Transthyretin (TTR), a highly conserved 55 kDa protein, transports the thyroid hormone thyroxine and the retinol-binding protein bound to retinol (vitamin A). TTR is present in blood as a stable tetramer with four identical subunits that form a symmetrical structure Mutations in TTR are associated with ATTR amyloidosis, a progressive and fatal disease.

With cryo-EM, this structure can be visually resolved, and the Tundra Cryo-TEM can easily produce a 3D structure at ~3.5 Å resolution. These structural insights allow researchers to gain a better understand of TTR misfolding and aggregation in order to develop TTR stabilizing therapeutics. (Figure 2).

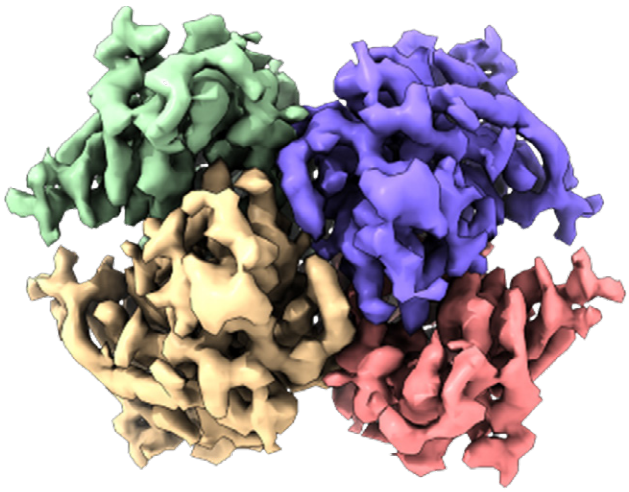

Figure 2. Transthyretin determined at 3.5 Å resolution using the Falcon C Detector. Sample courtesy of Gabrial Lander, Scripps Research Institute, CA.

Simplify sample analysis

Iteration is often a necessary part of the journey from gene expression and sample preparation to the final 3D reconstruction needed to answer your research questions. Biology is inherently complex, and while the sample requirements for cryo-EM are not as rigorous as they are for traditional techniques such as X-ray crystallography, the sample still needs to be optimized to provide the best possible structural information. Electron microscopy can be a straightforward method for the quality assessment of purified biological specimens at the microscopic scale.

The Tundra Cryo-TEM can visualize the impact of biochemical adjustments to samples faster than other technologies. Each iteration is also extremely efficient due to the instrument's unique sample-loading technology. It only takes a few minutes to load a new cryo-sample into the microscope, allowing for rapid sample condition optimization. The process is automated without risk of sample damage or vacuum leak from the microscope. Notably, this technology is designed so that even new users are capable of doing this procedure without extensive training. The instantaneous feedback of the Tundra Cryo-TEM significantly shortens the time required for biochemical sample optimization.

Access improved resolution

The Tundra Cryo-TEM can be configured with either the Falcon C Detector or the Thermo Scientific Ceta-F CMOS Camera. The Falcon C Detector has been designed specifically for this platform. It provides higher resolution capabilities than the Ceta-F Camera, with a unique combination of high image quality, high throughput, and efficient lossless data compression through electron-event representation (EER). The Falcon C Detector also streamlines data management and quality monitoring, providing an overall productivity and performance boost compared to the standard Ceta-F Camera (Figure 3).

The Ceta-F Camera is equipped with a dose-fractionation mode and offloading functionality for high-resolution protein reconstruction. Acquisition of dose-fractions can reduce the sample drift and motion caused by beam induced movement.

Protein	Molecular weight (kDa)	Falcon C Detector	Ceta-F Camera
		Highest resolution (Å)	Highest resolution (Å)
Hemoglobin	64	5.0	8.1
Apoferritin	450	2.1	2.6
T20S proteosome	700	2.7	3.0

Table 1. Comparison of the highest resolution achieved for three protein structures using two different detector options.

Focus on science with an intelligent microscope

The Tundra Cryo-TEM comes with a complete suite of automation software for the efficient optimization of your samples' biochemistry and structural determination. This includes user-friendly SPA data acquisition software, Thermo Scientific EPU 3 Software, guided day-to-day operation, a traffic light UI element that indicates the microscope's status, and predefined templates for typical use cases, allowing for high-resolution data collection in only a few clicks. Additionally, the Tundra Cryo-TEM is integrated with Thermo Scientific Smart EPU Software, an AI-enabled software solution that is capable of analyzing intermediate results, providing instant feedback, and steering data collection on the fly. The AI algorithms are based on years of cryo-EM knowledge, replacing decisions that experts need to make upfront and ensuring that the instrument is working at optimal conditions.

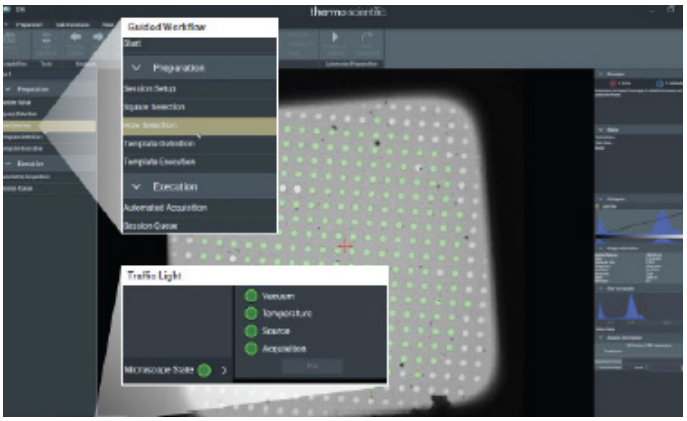

Figure 3. Screenshot of the Thermo Scientific EPU Software user interface.

Utilize room temperature screening

The Tundra Cryo-TEM can be utilized for negative-stain electron microscopy, an easy and cost-effective method for the quality assessment of purified biological specimens at room temperature (Figure 4). In addition, room-temperature sections of resin-embedded cells and tissues (Figure 5), or isolated particles of protein complexes and viral assemblies, can be visualized with the Tundra Cryo-TEM.

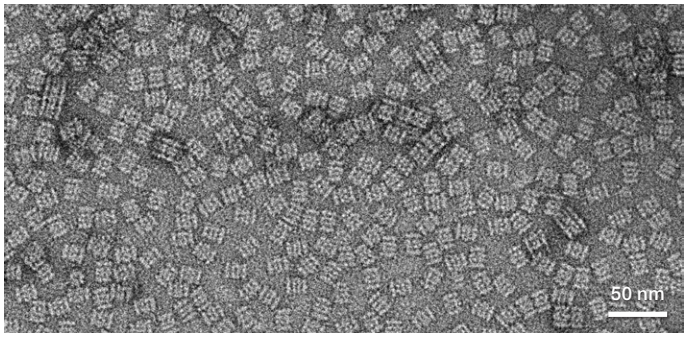

Figure 4. Negative-stain TEM image of T20S proteasome in uranyl formate (2%). Sample courtesy of the New York Structural Biology Institute.

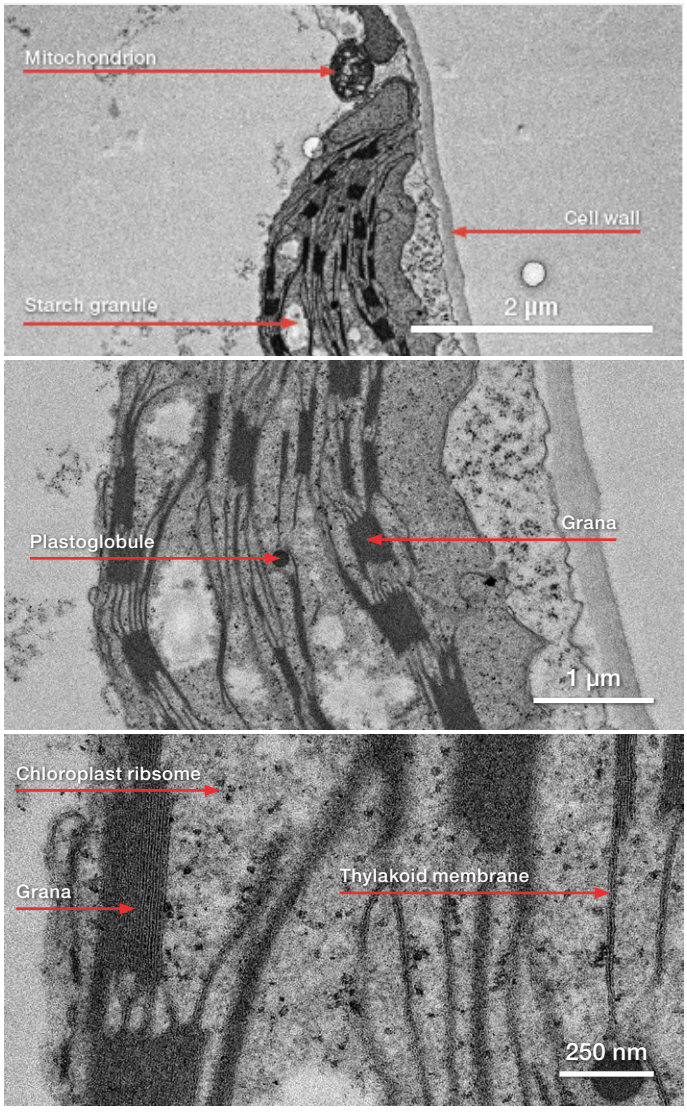

Figure 5. TEM image of resin-embedded tobacco leaf tissue, produced with the Ceta-F CMOS Camera. Sample courtesy of Sarah Powers, Doug Allen Lab, Janithri Wickramanayake, and Kirk Czymmek, Danforth Plant Science Center.

Technical highlights of the Tundra Cryo-TEM

- 2.1 Å apoferritin structure determination in 18 hours using the Falcon C Detector
- High-brightness X-FEG (extreme field emission gun)
- Fixed accelerating voltage of 100 kV
- Semi-automated sample loading
- Cryo-preparation station, allowing for contamination-free sample exchange
- Sample transfer device for transferring single AutoGrids to the microscope, with a fixed cryo-box that keeps the sample contamination-free for 72 hours
- Computerized specimen cryo-stage
- High-resolution objective lens optimized for SPA
- Two detector options:
  - High-performance Falcon C Direct Electron Detector for improved resolution capabilities
  - Standard Ceta-F Camera with dose fractionation, optimized for low-dose imaging
- Smart EPU Software: an AI-enabled software solution that provides feedback for data collection. Includes:
  - EPU 3.0 Software, which controls the microscope and runs automated data collection
  - Data management platform (DMP)
  - EPU Quality Data Monitor (EQM), which enables on-the-fly quality monitoring
  - Smart Plugins, which actively provide feedback from the image quality assessment to EPU Software during automated data collection

Floor plan and installation requirements

- Environmental temperature: 18–23°C
- Temperature stability: 1°C per 24 hours
- The enclosure can handle any temperature variation time within this bandwidth
- Relative humidity: <60 %
- All-in-one room dimensions: 4.20 x 4.00 m (13.8 x 13.1 ft)
- Dimensions, with cryo-loading station in neighboring room: 4.00 x 3.80 m (13.1 x 12.5 ft)
- Ceiling height: 2.74 m (8.99 ft)
- Door height: 2.30 m (7.55 ft)
  - Can be optionally reduced to 1.97 m (6.5 ft)
- Door width: 1.00 m (3.28 ft)
- Weight distribution maximum: 700 kg/m2
- Double earth connection
- Frequency: 50 or 60 Hz (±3%)
- Compressed air supply with a pressure range of 5–7 bar
- Sulfur hexafluoride (SF6) gas in properly ventilated room
- LAN connection for Thermo Scientific RAPID Service (Remote Access Program for Interactive Diagnosis)

Learn more at **thermofisher.com/tundra**