Tundra Cryo-TEM

Introducing a more cost-effective, easy-to-use cryo-transmission electron microscope for single particle analysis (SPA)

Dedicated structure determination solution that is easy to install, maintain and operate for both experts and non-experts.

Cryo-EM technology

In order to fully understand biological processes, and how they fail in disease, 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 or 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. Fortunately, cryo-electron microscopy (Cryo-EM) techniques, particularly single particle analysis (SPA), have emerged as a well-suited approach 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 specimen at atomic resolution. This technique has transformed the field of structural biology, leading to new insight into numerous biological processes. SPA validates your biochemistry work 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 dedicated to SPA, bringing this powerful technique to every biochemistry laboratory. The Tundra Cryo-TEM is specially designed for new users who are not experts in electron microscopy. It is easier to use than typical cryo-TEM instruments and matches grant mechanisms and funding opportunities globally. The Tundra Cryo-TEM is a powerful tool that can help answer your most challenging research questions, offering structural determination at biologically relevant resolutions.

Key Benefits
Structural information at biologically relevant resolution
Cost effective and space efficient
Easy, iterative loading and imaging for rapid sample-viability determination
Common biochemistry optimization problems addressed with new loader technology
AI-guided automation with results displayed progressively
A user-friendly interface with pre-defined settings to streamline data collection
Unique AI algorithms allow the microscope to learn over time so that you can stay focused on the science

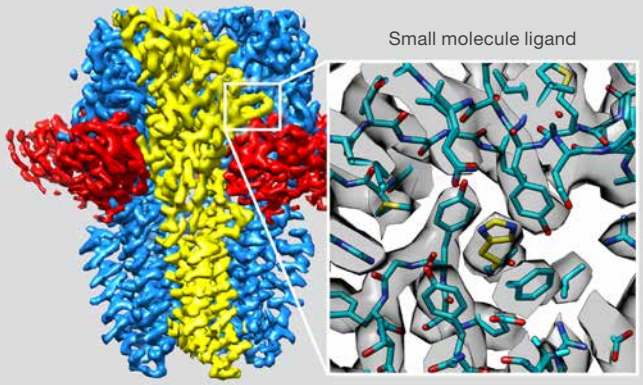


Figure 1. $GABA_A$ receptor in a lipid nanodisc. Its structure was determined with Tundra Cryo-TEM to a 3.4 Å resolution. ***Image courtesy of Radu Aricescu, Medical Research Council Laboratory of Molecular Biology, Cambridge, as well as Dimple Karia and Abhay Kotecha, Thermo Fisher Scientific.***

Answer your biological questions

3D structures provide researchers with new information on their samples, generating highly valuable, revolutionary insights. For example, the human GABAA (gamma-aminobutyric acid type A) receptor is a small membrane protein and ligand-gated chloride-ion channel that mediates inhibitory neurotransmission. GABAA receptors are an important therapeutic target, so it is vital to understand the molecular mechanism by which these receptors mediate neurotransmission. However, even with decades of effort, only non-physiological forms of GABAA receptors have been crystallized and structurally resolved; the physiological forms are needed to explain the receptors' mechanism of action. With Cryo-EM, these structures can be visually resolved and the Tundra Cryo-TEM can easily produce a 3D structure at ~4–5 Å resolution.

At this level of detail, scientists can visualize the stable conformation of the GABAA receptor channel within nanodisks or detergent micelles, as well as nanobody binding. Generally, many important biological details can be visualized at this resolution, such as the binding of antibodies or nanobodies (critical for epitope mapping), the molecular details of protein-protein complex formation and interaction, or virus-receptor interactions.

With benchmark proteins such as apoferritin, which are rigid and optimized for cryo-EM workflow, ~3 Å resolution can be achieved with Tundra Cryo-TEM. Such high-resolution maps allow de novo model building; the protein backbone can easily be traced, and major side chains become clearly visible. Such atomic models help scientists to understand how proteins function, how to modify genes, and how to design drugs accordingly.

Biochemical sample optimization with the Tundra Cryo-TEM

Iteration is often a necessary part of the journey from gene expression and sample preparation to the final 3D reconstruction that you need 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 structural information. Luckily, electron microscopy is also 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, since you do not need to go through the lengthy process of crystal growth. Each iteration is also extremely efficient due to the instrument's unique sample-loading technology (patent pending). It takes a few minutes to load a new cryo-sample into the microscope, allowing you to optimize sample conditions quickly. 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.

Focus on your science with an intelligent microscope

The Tundra Cryo-TEM comes with a complete suite of automation software for the efficient optimization of your

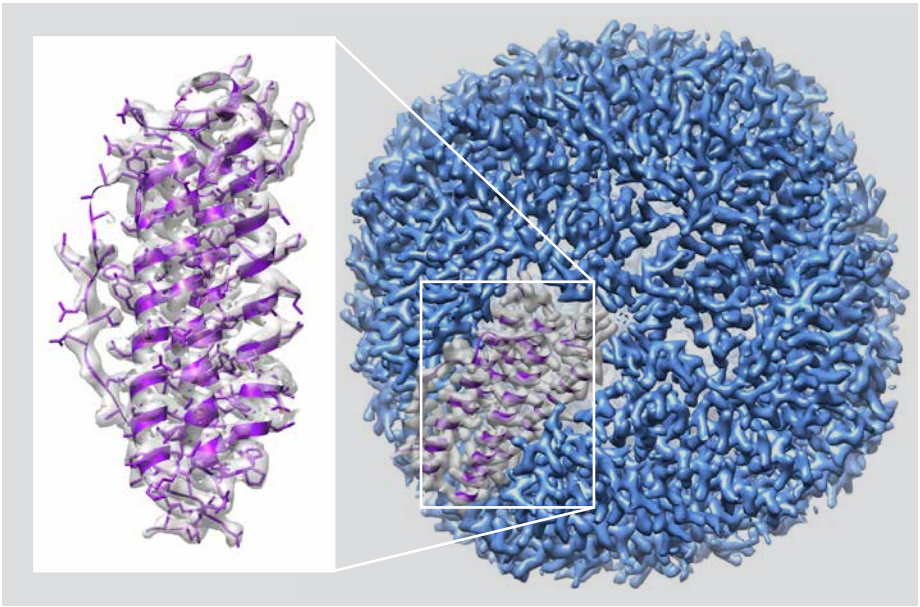


Figure 2. Apoferritin electron density map determined with cryo-TEM.

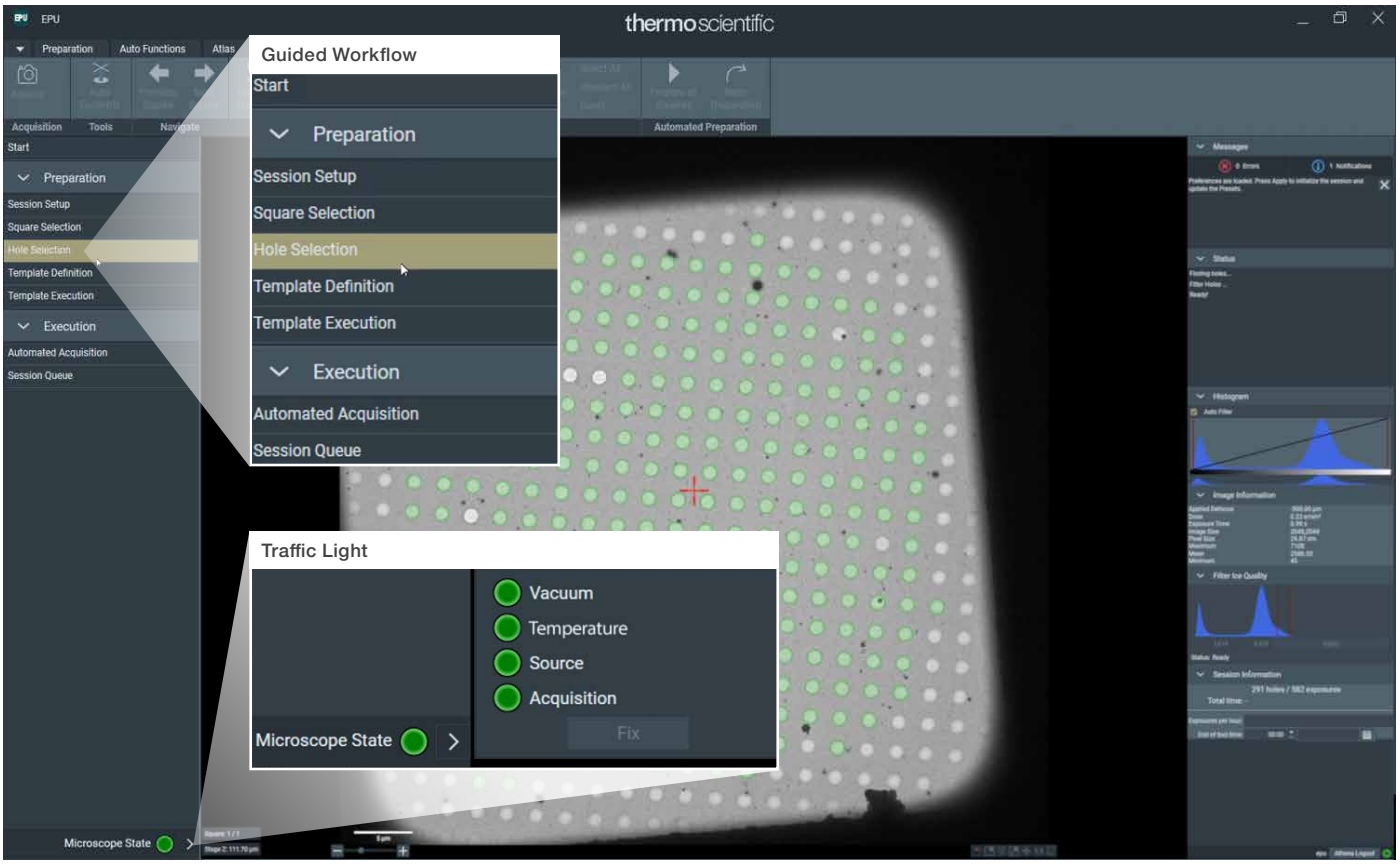


Figure 3. Screenshot of the Thermo Scientific EPU 2 Software user interface.

samples' biochemistry and determination of its structure. This includes user-friendly SPA data acquisition software, Thermo Scientific EPU 2 Software, guided day-to-day operation, a traffic-light UI element that indicates the microscope's status, and pre-defined templates for typical use cases that allow you to begin collecting high-resolution data with only a few clicks. Additionally, the Tundra Cryo-TEM is the debut of 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. Our AI algorithms are based on years of cryo-EM knowledge, replace decisions that experts need to make upfront, and ensure that your instrument is working at optimal conditions, allowing you to focus on the science rather than on fine-tuning the microscope.

Cryo-EM within your reach

The new hardware architecture of the Tundra Cryo-TEM has been purposefully designed with a smaller footprint and an easier access path without sacrificing performance. In many cases, this allows you to avoid the additional investment and unwanted downtime that comes with modification of your existing laboratory infrastructure (or even the need for a new, purposely built lab) to accommodate the instrument.

Additionally, a wide range of funding and instrumentation grants were considered when designing the Tundra Cryo-TEM so that its price falls within the reach of most instrumentation grants.

Enabling your success

In addition to state-of-the-art hardware, our comprehensive service enables your success on the Tundra Cryo-TEM. With the Accelerate service portfolio, which runs through the warranty period, we will validate your workflow and provide application support to make sure your users are trained in all aspects of your workflow. Our Customer Success Manager will work with you closely to ensure you are achieving your desired results.

Keep resources at your fingertips with the step-by-step Scientific Workflows App. You can also view system health and performance metrics through the secure Connected Care portal. Our technical team will monitor your system's performance and respond on-site if maintenance is needed.

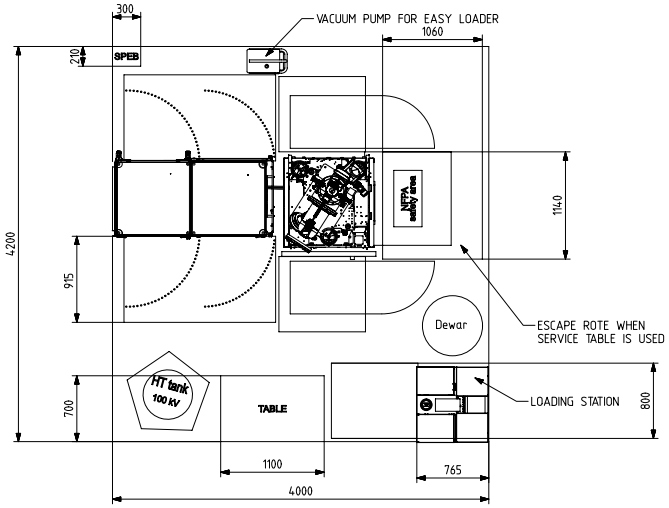
We created Accelerate services for customers with a range of budgets and buying cycles. You can feel confident that our team will give you the training, tools and resources to be successful using the Tundra Cryo-TEM.

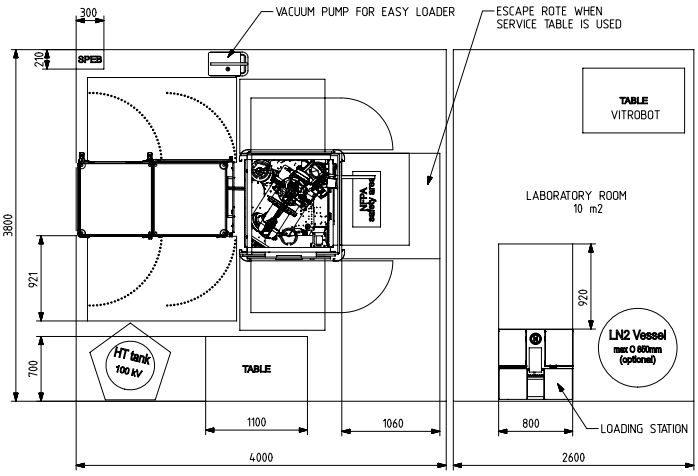
Technical highlights of the Tundra Cryo-TEM

- 3.5 Å apoferritin structure determination in 24–72 hours
- High-brightness X-FEG (extreme field emission gun)
- Fixed accelerating voltage of 100 kV
- Semi-automated sample loading
- Cryo-preparation station allowing contamination free sample exchange
- Sample transfer device for transferring single AutoGrids to the microscope, with fixed cryo-box that keeps sample contamination-free for 72 hours
- Computerized specimen cryo-stage
- High-resolution objective lens optimized for SPA
- High-performance Thermo Scientific Ceta™ Camera with dose fractionation, optimized for low dose imaging
- Smart EPU Software: an AI-enabled software solution that provides feedback into 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; and Smart Plugins, which actively provide feedback from the image quality assessment to the 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/m^2
- Double earth connection
- Frequency: 50 or 60 Hz (±3%)
- Compressed air supply with a pressure range of 5–7 bar
- Sulfur hexafluoride (SF_6) gas in properly ventilated room
- LAN connection for Thermo Scientific RAPID Service (Remote Access Program for Interactive Diagnosis)





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

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