

2023 / CASE STUDY

Collaboration results in new, more powerful camera for cryo-electron microscopy

With rapid advancements being made in structural biology comes an industry-wide need for equally innovative technologies that enable breakthrough scientific discoveries at atomic resolution. That's why Prodrive Technologies worked with Thermo Fisher Scientific, the world leader in serving science, to develop a camera for cryo-electron microscopes that offers enhanced resolution, speed, and user experience.

World-class microscopes need world-class cameras

Structural biologists who use a cryo-transmission electron microscopy (cryo-TEM) to investigate proteins have two main requirements: they want their results fast and with even more detailed information.

Prodrive Technologies develops and manufactures high-precision mechanics, electronics, and mechatronic sub-systems. To further enable ground-breaking developments in cryo-EM specifically, Prodrive Technologies collaborated with Thermo Fisher Scientific to develop a new and improved camera for cryo-TEMs.

By working with Prodrive Technologies on this camera, Thermo Fisher was able to bring everything under one roof from development to production, including qualification, testing, and life cycle management.



Thermo Scientific™ Krios™ G4 Cryo-Transmission Electron Microscope (Cryo-TEM) with enhanced productivity and user experience

In partnership with:



This camera along with other technological improvements has enabled scientists to visualize individual atoms in proteins, including the encapsulating water molecules (H₂O) surrounding the protein. Images with such detail allow a better understanding of the protein's role in biological processes, helping scientists to improve patient health through diagnostics, life-changing therapies, and vaccines or gathering other new life science insights. The camera's six-fold speed improvement also helps scientists to finish their projects faster.

To enable this, the new cryo-TEM camera leverages a newly developed sensor that was developed by Thermo Fisher, which records the image by capturing electrons. The very high-end and delicate custom silicon sensor is only a few tens of μm thick.

Prodrive integrates the new sensor in the camera using a hightech, two-step technology process. The sensor is first packaged at Prodrive's facilities, which includes placing the silicon die onto a substrate with very high accuracy and making interconnection with a PCBA through wire bonds. For the sensor in this camera, 900 wire bonds were used. The sensor is then integrated into a camera system that is also developed at Prodrive Technologies. The camera operates in an ultra-high vacuum where samples are exposed to the electron beam. Active cooling via heat exchangers, cooled by water to extract the heat generated in vacuum conditions, is applied to ensure a high image quality.

In addition to the unprecedented performance, the camera is designed to improve the end-user experience. Each camera has high reliability as it lasts for more than 10 years. The insert and retraction of the camera in and out of the vacuum chamber has proven to withstand well over the specified minimum of 50,000 cycles. Additionally, the camera shape is unchanged compared to prior generation making it possible to integrate it and its latest technological advancements into an existing cryo-electron microscope.

“We are exceptionally happy with the new camera. The improved image quality and faster data acquisition allow us to determine high-resolution structures quickly, getting data for two or three new protein samples each week. This exciting technology promises to increase both the quality and quantity of data that our microscope produces.”

- John Rubinstein

Senior Scientist at the Hospital for Sick Children, Toronto, Canada.

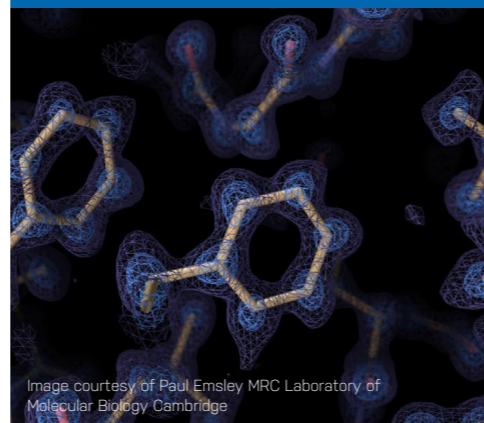


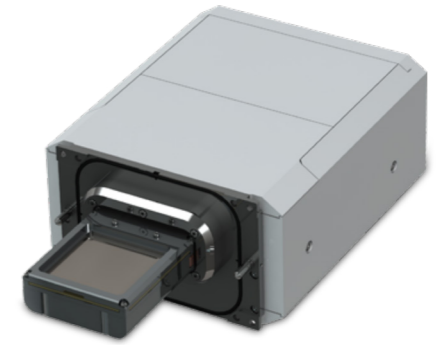
Image courtesy of Paul Emsley MRC Laboratory of Molecular Biology Cambridge

Apoferritin reconstruction at 1.2 Å resolution

When a joint effort results in breakthrough innovation

During the post-project evaluation, the main conclusion was that the open and efficient collaboration resulted in a camera that brings cryo-electron microscopy to the next level.

Thermo Fisher focused on the development of the sensor and provided clear product and end-user requirements needed to build a cryo-electron microscope to push science and technology a step beyond, while Prodrive led the sensor integration and camera development. An impressive example of collaboration and combined expertise leading to exciting new capabilities.

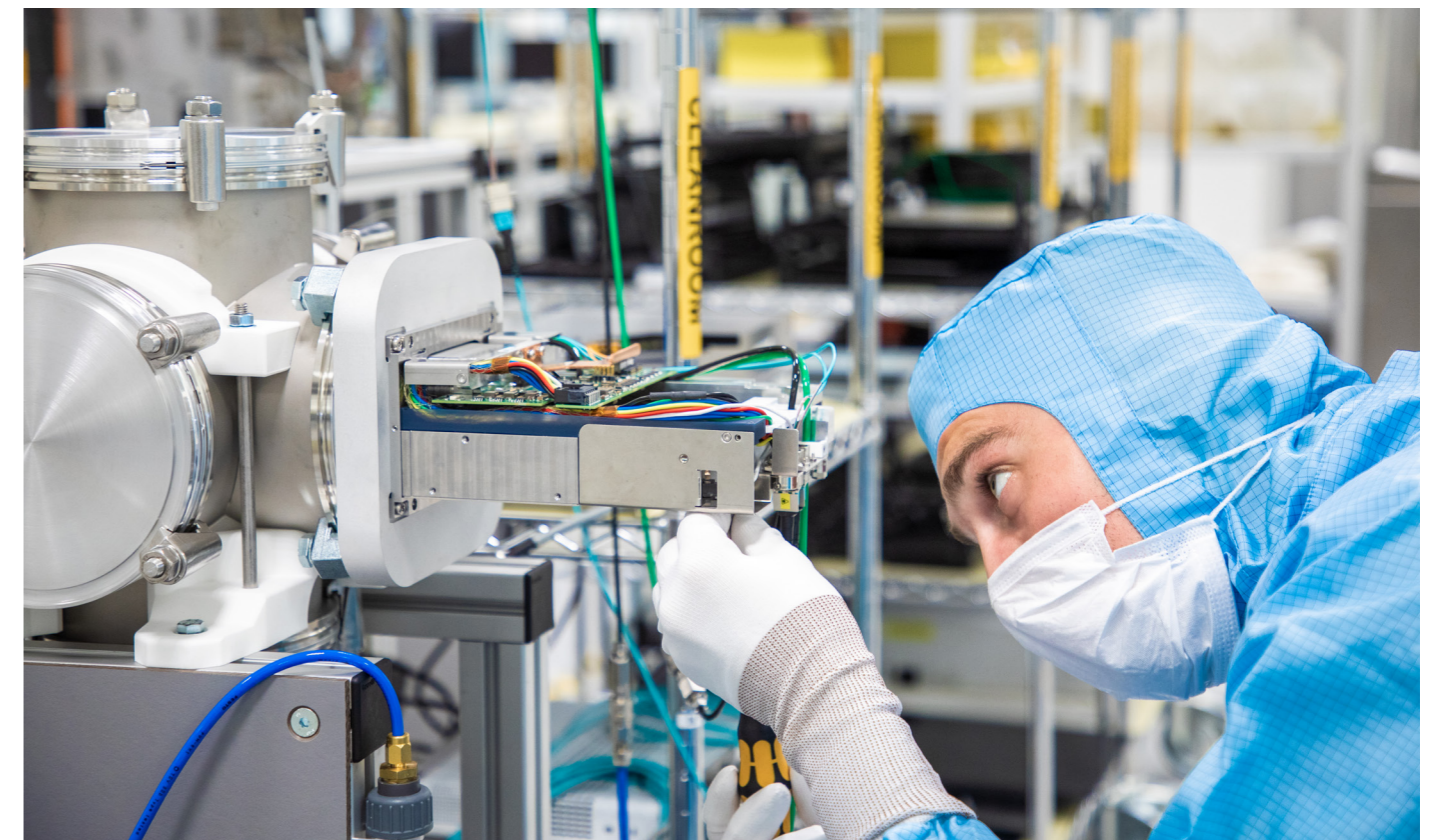


Thermo Scientific™ Falcon™ 4i
Direct Electron Detector

“We are now supplying the new camera in scaled-up, requested quantities and are delighted to support Thermo Fisher in its Mission to enable its customers to make the world healthier, cleaner, and safe.”

- Stan Geerts

Prodrive Technologies Camera Architect



From the initial product development to successful production, including a steep ramp-up, the project took only a little over 2 years, maximizing the engineering expertise from both Prodrive and Thermo Fisher. The project team at Prodrive focused on automation of the production process early in the development. This is key to Prodrive's success in achieving higher product quality and good manufacturability and yield, while reducing costs and inefficiencies.

Combining the collective expertise of Thermo Fisher and Prodrive resulted in a breakthrough innovation with improved accuracy and time-to-results, an enhanced reliability and user-experience, while accomplishing a relatively short development time and a fast production ramp-up.

Discover more about Prodrive Technologies' solutions for Imaging Applications:

[Advanced Cameras](#)

Discover more about Thermo Fisher solutions for Electron Microscopes:

[Thermo Fisher electron microscopy](#)

“The Krios G4 Cryo-TEM is a breakthrough technology in the field of electron microscopy, allowing scientists to unravel life at the molecular level easier, faster, and more reliably than ever before. The Falcon 4i Direct Electron Camera developed in conjunction with Prodrive Technologies is a crucial part of this breakthrough.”

- Bert van Gent

Thermo Fisher Scientific
Sr. Project Manager Camera's

