



Expand your vision with volume electron microscopy

thermo scientific

What is volume electron microscopy?

Volume electron microscopy or volume EM (vEM) was named one of Nature's Technologies to Watch in 2023. The emerging field of volume EM refers to a variety of imaging approaches and processing techniques that use electron microscopy to explore below the surface of cellular ultrastructure, tissue, and small model organisms in 3D, at micron to millimeter volume scales, at nanometer-level resolutions, and even at native state under cryogenic conditions.



Tissues



Intercellular



Single Cells





Serial block-face imaging

Array tomography









TEM tomography - cryo-tomography





Serial block-face imaging

Serial block-face scanning electron microscopy (SBF-SEM) collects a series of 2D images (sections) from a fixed sample in succession as thin slices are removed by a microtome from its surface. The sequential images can then be reconstructed into a 3D representation of the specimen.

Volumescope 2 SEM

Array tomography

In array tomography, samples are first cut into a series (array) of sections that are then imaged with scanning electron microscopy (SEM). Advanced software is then used to align and recombine these images into a 3D reconstruction.

Maps Software for Array Tomography

Serial FIB/PFIB imaging

A plasma focused ion beam SEM (PFIB-SEM) produces thinner slices than is possible with a microtome, resulting in efficient serial sectioning with improved Z-resolution. The combination of high current, high sputter rate, and reduced damage makes it possible to access volumes hundreds of micrometers in size while still observing nanoscale features.

Hydra Bio Plasma-FIB

Spin Mill Bio Method

The unique Thermo Scientific Spin Mill Bio Method on the Hydra Bio Plasma-FIB provides large-area planar milling up to 1 mm in diameter, with a geometry similar to microtome-based serial blockface imaging but at a slice thickness as small as 5 nm.

Hydra Bio Plasma-FIB

TEM tomography

Tomography with transmission electron microscopy (TEM) collects 2D images of electron-thin samples at a range of different angles (i.e., a tilt series). The results are recombined into a 3D reconstruction of the sample. Cryo-electron tomography (cryo-ET) is a label-free cryogenic variant that provides similar 3D data at nanometer resolution while preserving the sample's physiological context.

Talos 120C TEM Cryo-tomography Solutions



















Your volume EM workflow

Volume EM solutions from Thermo Fisher Scientific allow you to observe how tissues, cells, and organelles respond to diseases or various experimental methods. Our volume EM technology offers integrated solutions for correlative light and electron microscopy, multiple plasma ion-sources, largearea automated serial milling, as well as operation at room temperature or cryogenic conditions.



Enhance your volume EM workflow



Hydra Bio Plasma-FIB

The Thermo Scientific[™] Hydra Bio[™] Plasma-FIB is a focused ion beam scanning electron microscope (FIB-SEM) designed for volumetric imaging of frozen-hydrated and resin-embedded biological samples. The Hydra Bio Plasma-FIB also features proven automation and cryo-technologies for versatile cryoelectron tomography lamella preparation.



Volumescope 2 SEM

The Thermo Scientific[™] Volumescope[™] 2 SEM is a dedicated serial block-face imaging system with multi-energy deconvolution, enabling large-volume imaging with isotropic 3D resolution. Keep control of your experiments with easy to use technology that also protects your valuable samples.



Talos L120C TEM

The Thermo Scientific[™] Talos[™] L120C G2 TEM enables the visualization of a range of biological samples, including sections of resin-embedded cells and tissue, or isolated particles of protein complexes and viral assemblies, down to sub-nanometer resolution.







Maps Software for Array Tomography

The Array Tomography Module for Thermo Scientific Maps Software greatly reduces the time and effort needed to record nanometer-resolution datasets from resin-embedded cell and tissue sections. Fully automate the previously manual alignment of serial ultra-sections that would require hours, or even days, of input from a skilled operator.



Unstained and unfixed unicellular alga, C. reinhardtii, imaged under cryogenic conditions.

Analyze resin-embedded or cryogenic samples



The iFLM Correlative System and Maps Software combine fluorescence, reflection, and electron imaging with ion milling.

A plasma FIB enables efficient, largevolume serial sectioning thanks to a focused beam delivering currents up to 2.5 µA higher than a gallium FIB. Improved sputtering efficiency enhances performance, generating smoother cut faces and reducing curtaining artifacts, further improving throughput and providing fast access to regions of interest. The combination of higher currents, higher sputter rates, and reduced damage makes it possible to access volumes hundreds of micrometers in size while still observing nanoscale features.

View nanoscale features across large samples with PFIB-SEM serial imaging

The Thermo Scientific Hydra Bio Plasma-FIB is a versatile tool designed to explore a range of samples from tissue to proteins at both cryogenic and room temperatures. Sample preparation is critical for high quality results, which is why the PFIB source can easily switch between multiple ion species (argon, nitrogen oxygen, and xenon) for optimized sample milling. This makes the Hydra Bio Plasma-FIB compatible with all commonly used sample preparation protocols and embedding media, including high-pressure tissue freezing and critical-point drying. Acquire high-resolution 3D data through automated serial milling and imaging in Thermo Scientific[™] Cryo Auto Slice & View[™] Software, enabling new studies of frozen-hydrated specimens. The Hydra Bio Plasma-FIB is well suited for a number of volume EM methods including (large-area) serial PFIB imaging, array tomography, correlative light and electron microscopy, as well as high-throughput sample preparation for cryo-tomography.





Maps Software for Array Tomography and **Correlative Microscopy**

Auto Slice & View Software for Serial Imaging



Cross section of a tobacco leaf, stained and embedded in Quetol resin. Sample courtesy of Kirk Czymmek, Donald Danforth Plant Science Center, USA





Volumescope 2 SEM

The Thermo Scientific Volumescope 2 SEM is our stateof-the-art serial block-face imaging system. Typical SBF-SEM systems are limited in Z-resolution by the minimum slice thickness that can be achieved by the microtome. The Volumescope 2 SEM overcomes these limitations through mulit-energy deconvolution (MED), which images the sample surface at multiple accelerating voltages for each slice. This provides information on the interior of each slice, greatly enhancing the Z-resolution and providing isotropic 3D data. A range of proprietary software, including Maps Software as well as Thermo Scientific[™] Amira[™] Software, offers not only straightforward data collection and correlation, but also visualization and data analysis.

Peer within tissue samples with serial block-face imaging

During serial block-face scanning electron microscopy, the electron beam is first used to scan the surface of a resin-embedded tissue sample, capturing a 2D image of the specimen. This top surface is subsequently removed with an in-situ microtome, and an image of the fresh surface is then collected with the SEM. This process is repeated until the whole sample has been imaged; total sample height can range from tens to hundreds of micrometers or more. The serial stack of images is then processed using 3D rendering software; recent advances have enabled fully automated 3D reconstruction of even large tissue volumes.

Zebrafish embryo head imaged by Truly isotropic 3D data with SBF-SEM SBF-SEM. Sample courtesy of R. Creton, Brown University.







Amira Software for 3D visualization and analysis

Maps Software for 3D volume aquisition

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SBF-SEM imaging of a rat brain segment, collected with the Volumescope 2 SEM. Total dimensions: 85 x 85 x 123 μm^3 . Segmentation and visualization of the vasculature was performed with Amira Software. Sample courtesy of Grahame Knott, EPFL Lausanne.







Talos L120C TEM

Versatile transmission electron microscopy with cryo capability

The Talos L120C TEM offers several low-dose techniques, producing high-quality images even for beam-sensitive materials. The optional cryo-box facilitates the imaging of cryogenically preserved samples by providing maximal protection of cryo-specimens, resulting in minimal ice growth contamination over long (>8 hour) data collection sessions.



Reconstructed 3D tomogram of a 200-nm plastic section of a macrophage with density segmentation performed in Amira Software.

New insights into cellular function with serial-section TEM

Designed for multi-user and multi-discipline environments, the Talos L120C TEM automates all daily tunings, easing the learning curve for novice operators and improving time-todata for experienced users. Additionally, Thermo Scientific software packages enable automated data collection for different use cases and workflows, such as tomography and single particle analysis.





Examination of a 100-nm resin-embedded mouse liver tissue section at low magnification with a quick zoom-in to a potential region of interest.



Maps Software for **Correlative Microscopy**



Amira Software for 3D visualization and analysis

Unraveling tissue and subcellular organization with array tomography



Array tomography takes physical serial sections of a biological sample and places them in a two-dimensional array on a solid substrate. The series is then imaged with electron microscopy and recombined into a 3D representation of the sample. These high-resolution reconstructions of cellular structures enable detailed studies of tissue organization and subcellular components.

Any Thermo Scientific SEM can be turned into a volume EM microscope with the addition of automated array tomography.

Thermo Scientific Maps Software guides the acquisition of 3D volumes for array tomography. When you use an SEM-based method for 3D reconstruction, the total acquisition time can quickly become impractical if the selected volume is unnecessarily large. In that case, the ability to precisely identify an area of interest becomes particularly important. Maps Software can create large overviews at high resolution and correlate them with fluorescent images, providing 2D maps for targeted 3D acquisitions (e.g., using Auto Slice & View Software), delivering results more quickly.



Mouse brain sample recorded with Maps Software for Array Tomography on the Thermo Scientific[™] Apreo[™] 2 SEM. The reconstruction shows mitochondria, the endoplasmic reticulum, telo-lysosomes, and the nucleus in the cell body, along with an apical dendrite of a neuron. Reconstruction consists of 50 mosaics of 3x3 images, 19.97 x 13.31 x 3.5 µm in size.



Earthworm seminal vesicles. Amira Software was used to create this composite containing orthogonal views, segmented mitochondria, and volume renderings of a large field of view recorded in 46 sections. Data has 26.1 nm resolution. Sample courtesy of Karol Matola, University of Silesia, Poland.

Supporting the volume EM community

The convergence of multiple techniques, all enabling 3D visualization with electron microscopy, points to a pressing need for this kind of analysis. As our ability to image biomolecules approaches the atomic scale, it is becoming increasingly clear that the context of these observations is just as important as their resolution. Volume EM offers these critical insights, bridging the gap between large-scale 3D analysis and the *ex-situ* structural characterization of biomolecules. With volume EM, we can capture the intricacies of biological processes as they occur, within their native context. Practically, these observations can lead directly to more targeted, specific treatments for physiological disorders that manifest at these scales.

Volume EM solutions from Thermo Fisher Scientific allow you to observe how tissues, cells, and organelles respond to diseases or various experimental methods. Our volume EM technology offers integrated solutions for correlative light and electron microscopy, multiple plasma ion-sources, large-area automated serial milling, as well as operation at room temperature or cryogenic conditions.

Additional resources



Join us for exciting events and webinars that cover a wide range of volume electron microscopy (vEM) topics. These events offer the opportunity to learn from experts in the field, network with the vEM community, and gain valuable insights into the latest trends and developments. <u>Visit our volume EM resources page</u> to register or watch past webinars on demand.



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