Automated tape-collecting ultramicrotomy

Automated tape-collecting ultramicrotomy (ATUM) is an advanced technique used in electron microscopy to collect and analyze ultrathin sections of biological or material samples. This method combines the precision of ultramicrotomy with the efficiency of automation and the convenience of tape collection, making it particularly useful for large-scale projects that require high-throughput sample preparation. Here’s an overview of how ATUM works and its applications:

How ATUM Works Sample Preparation: The sample (biological tissue, materials, etc.) is embedded in a resin block to provide structural support during sectioning.

Ultramicrotomy: An ultramicrotome equipped with a diamond knife slices the resin-embedded sample into ultrathin sections, typically 30-100 nanometers thick.

Tape Collection: The ultrathin sections are automatically collected on a continuous tape loop. The tape is coated with an adhesive layer that captures the sections as they are cut. This method significantly reduces the risk of section loss or damage.

Section Staining (if necessary): Depending on the type of analysis, sections may be stained to enhance contrast for electron microscopy.

Imaging: The tape with the collected sections is fed into an electron microscope for imaging. The automated nature of ATUM allows for high-throughput imaging, making it possible to collect large datasets quickly.

Applications of ATUM Connectomics: Mapping neural connections in the brain by producing detailed 3D reconstructions of neural tissue. ATUM allows for efficient collection and imaging of large volumes of brain tissue, facilitating the study of complex neural networks.

Materials Science: Examining the microstructure of materials at high resolution. ATUM can be used to analyze the internal structure of composites, metals, polymers, and other materials, providing insights into their properties and behavior.

Cell Biology: Investigating cellular and subcellular structures. The high resolution of electron microscopy, combined with the efficient sample preparation of ATUM, makes it possible to study the intricate details of cellular organelles and their interactions.

Pathology: Diagnosing diseases by analyzing tissue samples at the ultrastructural level. ATUM can assist in identifying cellular abnormalities and understanding disease mechanisms.

Advantages of ATUM High Throughput: Automated collection and processing allow for the analysis of large volumes of samples quickly and efficiently. Consistency: Automated systems provide consistent section thickness and reduce human error. High Resolution: Combined with electron microscopy, ATUM enables imaging at nanometer resolution. Versatility: Can be applied to a wide range of biological and material samples. Summary Automated tape-collecting ultramicrotomy (ATUM) is a powerful technique that enhances the capabilities of electron microscopy by enabling high-throughput, high-resolution analysis of ultrathin sections. Its applications in various scientific fields make it a valuable tool for advancing research and diagnostics.

Like other volume electron microscopy approaches, automated tape-collecting ultramicrotomy (ATUM) enables imaging of serial sections deposited on thick plastic tapes by scanning electron microscopy (SEM). ATUM is unique in allowing hierarchical imaging and thus efficient screening for target structures, as needed for correlative light and electron microscopy. However, SEM of sections on tape can only access the section surface, thereby limiting the axial resolution to the typical size of cellular vesicles with an order of magnitude lower than the acquired xy resolution. In contrast, serial-section electron tomography (ET), a transmission electron microscopy-based approach, yields isotropic voxels at full EM resolution, but requires deposition of sections on electron-stable thin and fragile films, thus making screening of large section libraries difficult and prone to section loss. To combine the strength of both approaches, we developed 'ATUM-Tomo, a hybrid method, where sections are first reversibly attached to plastic tape via a dissolvable coating, and after screening detached and transferred to the ET-compatible thin films. As a proof-of-principle, we applied correlative ATUM-Tomo to study ultrastructural features of blood-brain barrier (BBB) leakiness around microthrombi in a mouse model of traumatic brain injury. Microthrombi and associated sites of BBB leakiness were identified by confocal imaging of injected fluorescent and electron-dense nanoparticles, then relocalized by ATUM-SEM, and finally interrogated by correlative ATUM-Tomo. Overall, our new ATUM-Tomo approach will substantially advance ultrastructural analysis of biological phenomena that require cell- and tissue-level contextualization of the finest subcellular textures [1)]

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Kislinger G, Fabig G, Wehn A, Rodriguez L, Jiang H, Niemann C, Klymchenko AS, Plesnila N, Misgeld T, Müller-Reichert T, Khalin I, Schifferer M. Combining array tomography with electron tomography provides insights into leakiness of the blood-brain barrier in mouse cortex. Elife. 2024 Aug 5;12:RP90565. doi: 10.7554/eLife.90565. PMID: 39102289.