



Biomolecular Vapor Deposition (BVD) and Grid Holder/Mounting System for In Vacuo Preparation of Cryo-Electron Microscopy Samples

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The Wisconsin Alumni Research Foundation is seeking commercial partners interested in developing a new cryo-electron microscopy (cryo-EM) sample preparation method that combines biomolecular vapor deposition (BVD) with an improved TEM grid handling system.

Overview

Single particle cryo-electron microscopy is a powerful tool for providing 3-D structural information on non-crystalline specimens. Cryo-EM approaches atomic level resolution, enabling many new biological discoveries. Unfortunately, this technique still has several limitations, primarily due to sample preparation, which requires purification and vitrification to protect the samples from radiation damage.

At present, sample preparation generally involves solubilization of protein analytes in water, followed by pipetting onto a hydrophilic EM grid. This sample preparation method imparts a preferred orientation of the particles, due largely to particle migration to the air/water interface. This destroys the required structural heterogeneity. In addition, existing preparation methods limit particle density within the grids.

The Invention

UW-Madison researchers have developed a sample preparation method for single particle cryo-EM called biomolecular vapor deposition (BVD), along with an improved TEM grid handling system. The BVD technology uses mass spectrometry to address many of the shortfalls associated with cryogenically fixing biological samples in amorphous ice for analysis by cryo-EM. The grid holder protects the TEM grid, which is thin enough to be transparent to electrons. The grid holder also provides excellent thermal and electric conductivity to the TEM grid, which is required for maintaining and analyzing the sample. In addition, the grid holder allows a user to transfer the TEM grid to an in situ cooling probe for cryo-EM while remaining submerged in liquid nitrogen.

Applications

- Single particle cryo-electron microscopy (cryo-EM). Applications for cryo-EM include structural studies of eukaryotic cells, proteins and macromolecular complexes such as liposomes, organelles and viruses.

Key Benefits

- Addresses the limitations of existing cryo-EM sample preparation methods
- Protects the TEM grid

- Provides excellent thermal and electric conductivity to the TEM grid

- Reduces exposure to liquid nitrogen, which can destroy the sample or lead to inaccurate analysis

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- Reduces sample preparation time and costs associated with handling

Stage of Development

The inventors have demonstrated portions of the system and are continuing to work on refinements that will allow for integration with their MS-based BVD system.

Additional Information

For More Information About the Inventors

- [Joshua Coon](#)

Tech Fields

- [Analytical Instrumentation, Methods & Materials : Mass spectrometry.](#)
- [Analytical Instrumentation, Methods & Materials : Microscopy.](#)

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854

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