Docket #: S22-149

Cold Gas Stream Method for CryoEM Sample Grid Vitrification

Stanford researchers have developed an innovative technology for cryo-vitrification using a temperature-controlled cold gas stream instead of traditional liquid cryogen, which prevents grid distortion, enabling gentle sample cooling and continuous imaging throughout the vitrification process.

Traditional cryo-vitrification methods which involve a plunge freezing or blot-less deposition or spraying liquid cryogen on cryoEM grids for vitrification encounter numerous challenges, from grid distortion and damage, imaging limitations, complex sample handling, equipment dependencies and constraints on time-resolved experiments. There is an urgent need for a solution that addresses these challenges for cryoEM sample preparation.

Stanford researchers have developed a technology which addresses these issues by simplifying the vitrification process. Instead of submerging samples in liquid cryogen, this innovation uses a novel approach which exposes the sample and cryoEM grid to a temperature-controlled cold-gas stream delivered via a cryo-nozzle, which eliminates grid distortion and allows continuous imaging before, during, and after vitrification. Prior to vitrification, the gas stream is blocked to prevent premature cooling. Upon activation, the cold gas rapidly cools the sample grid, ensuring efficient vitrification. Since the sample and cryoEM grid do not move during the vitrification process and not submerged in a cryogen, the grids can be continuously imaged using an optical microscope and exposed to various triggers for time-resolved measurements during and after vitrification. Additionally, the sample-grid can safely remain in the cold gas stream for other operations and removed using a specialized cryo-tong (also part of this invention) and saved for cryoEM imaging. In summary, this innovation overcomes the limitations of traditional cryo-vitrification methods, offering a comprehensive solution for advanced sample preparation in cryoEM research.

Stage of Development:

Prototype. Next steps include additional testing to optimize this invention and conduct structural biology research at Stanford and SLAC National Accelerator Laboratory with other Stanford faculty and collaborators.

Applications

- Vitrify sample grids for successful CryoEM single-particle imaging
- Preparation of sample grids for other techniques that employ rapid vitrification of samples for electron microscopy applications
- Mitigates some of the problems associated with available devices for sample-grid vitrification
- Facilitates extra sample manipulation and probing steps for time resolved CryoEM analysis

Advantages

- There is not a commercial device currently available that specializes in time-resolved cryoEM
- Grid Protection due to gentle cold-gas stream
- Continuous imaging throughout the vitrification process
- Flexible and simplified sample handling
- Streamlined sample preparation workflow, reducing complexity and costs
- Eliminates the need for specialized equipment and accessible to a wider audience

Publications

- None

Patents

- Published Application: WO2023220061
- Published Application: 20250341450

Innovators

- Aina Cohen
- Makaia Papasergi-Scott

Licensing Contact

Evan Elder

Associate Director, Licensing and Strategic Alliances, Physica

Email