Max-Planck-Innovation

Technology Offer

Ultrarapid cryo-fixation during live observation on a fluorescence microscope

Freeze native molecular patterns in milliseconds directly on the microscope

Ref.-No.: 0803-6035-IKF

This technology offer presents a standalone ultrarapid cryo-fixation module that mounts on any inverted fluorescence microscope to freeze native molecular patterns in milliseconds at −196 °C, without cryoprotectants. It enables live imaging followed by precise on-stage cryo-arrest, eliminating photobleaching and motional blur for high-resolution fluorescence and super-resolution microscopy.

Background

Fluorescence micro- and nanoscopy can in principle resolve dynamic molecular reaction patterns in living cells down to nm scales, but image quality is fundamentally limited by motional blur, photobleaching, and phototoxicity. This limit set by the photophysical properties of fluorophores cannot be surpassed by better detectors or stronger illumination. A solution to reach practically unlimited photon collection times is halting photoreactivity and bypassing motional blur by virtually instant fixation of cells at a particular instant in time by extremely rapid cooling to a temperature below -136 °C. This ultra-high cooling speed is necessary to maintain water out-of-equilibrium to prevent mechanical damage by ice crystal formation and to avoid decay of the energized microscopic biomolecular patterns.

Technology

Researchers at the Max-Planck-Institute of Molecular Physiology have developed a standalone module that perfomrs ultrarapid cryo-arrest directly on any inverted fluorescence microscope. The device cools samples on a diamond mount at rates up to ~200,000 K/s to liquid nitrogen temperature (-196°C), preventing ice crystal formation without cryoprotectants and preserving native molecular organization for prolonged cryo-imaging.

Advantages

- Cryo-arrest during live imaging enables dynamic observation followed by precise fixation at user-defined time points.
- Ultrafast cooling avoids ice damage and eliminates photobleaching and phototoxicity, allowing effectively unlimited photon collection and higher spatial resolution.
- Particularly powerful for super-resolution and slow-acquisition methods (e. g., STED. FLIM, microspectroscopy).
- Diamond-based heat exchanger maintains ultra-low temperatures under high-power irradiation, enabling high-resolution cryo-STED and multimodal correlative cryo-microscopy on the same cell.

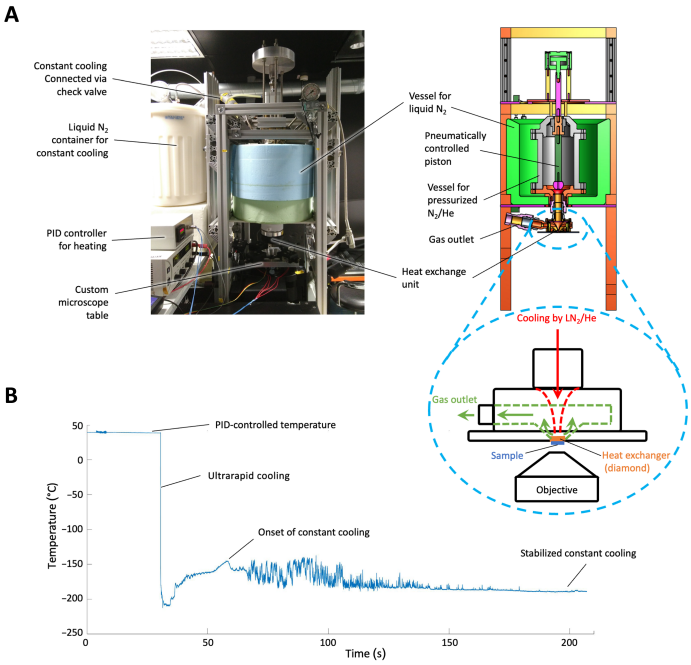

Fig. 1 Ultrarapid cryo-arrest microscopy. (A) Ultra-rapid cooling device. Cyan dashed circle: heat exchanger unit; red arrow: flow of liquid nitrogen (LN2) with gaseous He toward diamond heat exchanger; green arrows: expanded gas outflow. The cooling devide is lowered above an epifluorescence microscope objective. **(B)** Measured temperature course (50µm constantan-copper thermocouple in 100µm aqueous sample.) https://www.science.org

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We are now looking for a licensing, or collaboration partner to further develop this project.

Patent Information

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Publication

- Huebinger et al. (2021). Science Advances. DOI: 10.1126/sciadv.abk0882;
- Huebinger & Bastiaens (2025). BioRxiv. DOI: 10.1101/2025.09.26.678528

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