Max-Planck-Innovation

Technology Offer

Ultrarapid cryo-fixation during live observation on a fluorescence microscope

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A ultrarapid cryo-arrest directly on a multimodal fluorescence microscope that preserves molecular activity patterns during observation of their dynamics in living cells at any timepoint.

Technology

Our scientists have developed technology that enables ultra-rapid cryo-arrest during life observation of cells on any inverted fluorescence microscope.

Features of technology:

- Cryo-arrest to -196°C with up to 200.000K/s during live observation of cells preserves native molecular organization - without application of cryoprotectants or formation of ice crystals
- Imaging under cryo-arrest overcomes a fundamental resolution barrier imposed by motional blur and photochemical reactivity
- Allows to resolve native molecular (reaction-) patterns in the absence of phototoxicity that are not resolvable at physiological temperatures
- Enables imaging of dynamic processes before cryo-arrest in combination with precise molecular pattern determination at user-defined time point of cryo-arrest.
- Simple GUI computer control of valves activates and maintains cryo-arrest of sample during life cell observation.
- Virtually no bleaching and unlimited photon collection times enable unpreceded resolution of native molecular patterns measured by STED, FLIM or low intensity fluorescence signals
- Correlative multi-modal (e.g. FLIM and STED) cryo-microscopy enables super-resolution of complete molecular reaction patterns in the same cell
- Superior thermal conductivity of diamond mount maintains ultra-low temperature of sample enabling resolution-defining, high-radiation cryo-STED microscopy without heating the sample.
- Standalone module that can be attached to any inverted light microscope

We welcome licensing partners to commercialize this technology.

Background

Fluorescence micro- and nanoscopy has the potential to resolve dynamically established patterns of molecular reactivity inside living cells down to the nm scale. This potential is however mitigated by photon collection that is fundamentally limited by photochemical reactivity and motional blur. 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 extreme 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. Performing ultra-rapid cryo-arrest directly on a microscope enables virtually instant fixation of native molecular patterns at any timepoint during the observation of their reaction dynamics at physiological temperatures.

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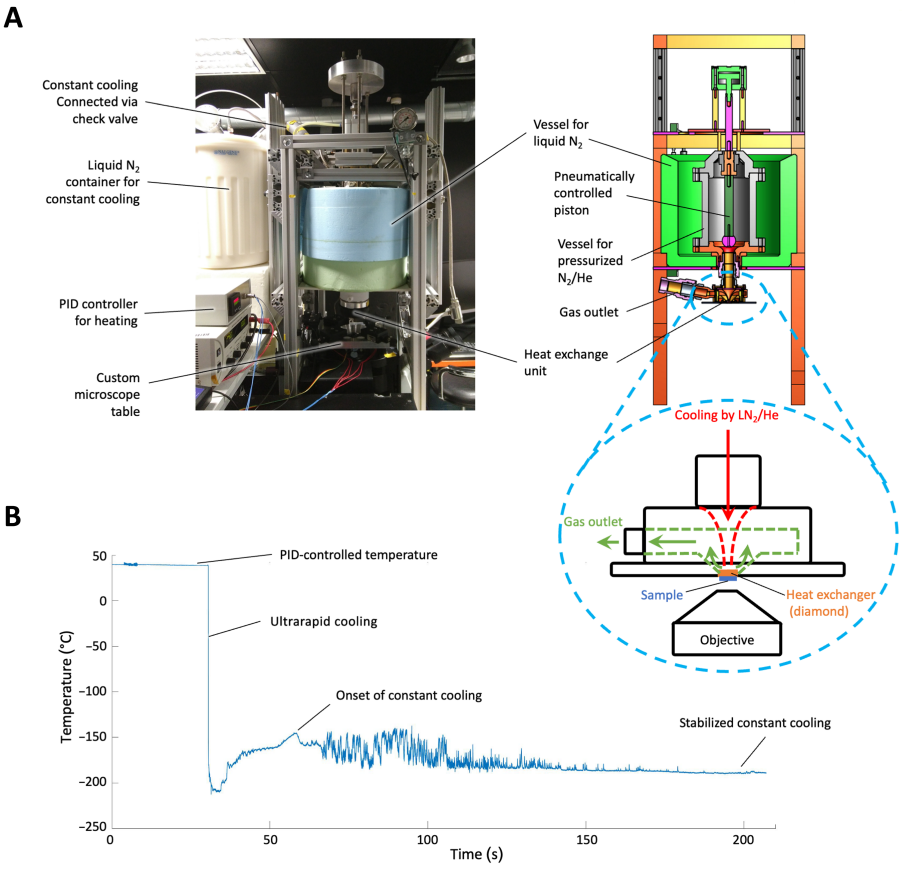

Fig. 1. Ultrarapid cryo-arrest microscopy. (A) Photograph and schematic of ultra- rapid cooling device. Cyan dashed circle: heat exchanger unit; red arrow: flow of liquid nitrogen (LN2) with gaseous He toward diamond heat exchanger; green arrows: expanded gas outflow. The whole cooling device is lowered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

Patent Information

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