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# Building of a cryo-super-resolution microscope for cryo-correlative light and electron microscopy (cryo-CLEM)

Cryo electron microscopy (cryo EM) has been at the center of many new advances and discoveries in biology. The ability to freeze biological samples in vitreous non-crystalline ice, allows us to study biological matter in its native unperturbed environment with molecular resolution. It avoids using chemicals to fix the samples which has been shown to perturb the native environment. This has allowed us to understand the structure-function relationships in the sub-cellular context and also to study interactions between sub-cellular structures and proteins which provided deep insights into the mechanisms governing different processes of life. In-spite of the progress made so far, cryo EM is limited in its ability to provide specificity of the sub-cellular structures and to identify rare-events. One approach to overcome these limitations is to combine it with light microscopy and perform correlative light and electron microscopy (CLEM). So far, there have been rapid developments for cryo-CLEM. However, when correlating light and electron microscopy images, one needs to mind the resolution gap imposed by the wave nature of light or the diffraction limit. One way to overcome the resolution gap is to develop techniques for cryo superresolution microscopy (cryo SRM) and correlate it to cryo EM. For localization-based cryo SRM techniques, there are two possible approaches based on the design of the cryostat used for cooling the vitrified samples. These are open and vacuum based cryostat designs, each with its own advantages and drawbacks. In this poster, I will present a theoretical comparison between the two types of designs and discuss the planning and progress in building a vacuum-cryostat based cryo single molecule localization microscope (cryo-SMLM) to study vitrified biological samples.

## Research type

Basic research

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