

Thermo Scientific™ Multigrid: Automation enhanced screening and data collection

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Problem Statement: Automated data collection is an integral part of modern workflows in single particle electron microscopy (1) But grid assessment and optimization steps are still time consuming and slow, requiring supervision time behind the microscope, which in some case can take a whole day sitting behind the microscope to find the right grid. Additionally, the microscope is often idle for those time that a user can't be behind the microscope.

Solution: The EPU Multi-grid option enables optimal usage of microscopes with an autoloader present. EPU multi-grid makes it possible to queue multiple automatic EPU sessions for the different grids loaded in the autoloader. EPU Multi-grid thus enables full tool utilization by making it possible to execute multiple unattended sessions. This is extra helpful for systems with high speed detectors in a 24/7 environment with limited operator availability. It also facilitates efficient scheduling of work for multi user facilities and it facilitates fast screening with queuing short runs to be executed overnight

Results: We'll show an example of the optimization of a yet undisclosed pharma relevant sample, for which multiple grids are prepared using different buffer conditions. All are loaded in one cassette. The software decides which grid squares are worth collecting from and how many are needed.

Another example will demonstrate unattended data collection from 12 grids, where each grid is prepared with the (for now undisclosed) protein, but in the presence of a different reference compounds functioning as small molecule modulators.

Workflow: Users only sit down once to define all planned acquisitions and their individual settings for overnight or weekend unattended data collection from up to 12 grids. In less than 15 minutes, users can set foil hole settings such as ice filter and define an acquisition template. EPU will select the holes and prepare the grid squares automatically. For repeat jobs users can simply re-use previous session settings.

Conclusion: Enhanced automation in cryo-EM workflow can significantly increase productivity by making use of the - otherwise - idle time of the microscope and minimize the time spent behind the microscope.

References

1. Tan YZ, Cheng A, Potter CS, Carragher B. Automated data collection in single particle electron microscopy. *Microscopy (Oxf)*. 2016;65(1):43-56. doi:10.1093/jmicro/dfv369