

# Cryofast™: Automated Cryo-Electron Microscopy Data Acquisition Using Machine Learning

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Structural Biology is a scientific field that seeks to understand the biological function of macromolecules by analyzing their three-dimensional structure and organization. Insights from structural biology can inform the development of novel therapeutics for disease research and lead to a better understanding of fundamental biological processes.

Cryogenic electron microscopy (cryo-EM) is one of the latest tools for structural biology research. Due to numerous advantages inherent to cryo-EM technology for structural biology research, the 2017 Nobel Prize in Chemistry was awarded for the development of cryo-EM for high-resolution structure determination of biomolecules in solution [1]. However, cryo-EM data collection is still a labor-intensive process that often requires lengthy and iterative sample screening for a given protein sample as experimental conditions for data collection are optimized [2]. Sample screening, wherein the user attempts to determine the best quality images for data collection, requires significant operator time; furthermore, it is usually difficult to determine which areas will yield the highest resolution reconstructions [3]. The challenge of automating sample screening by machine learning is an opportunity to improve the throughput of drug development with cryo-EM.

CryoFAST™ (Fast Acquisition for Single-particle and Tomography) is a machine-learning platform for automated Cryo-EM data acquisition. It works by analyzing images at multiple levels of magnification to optimally select targets. As targets are prioritized, CryoFAST automatically queues image acquisition and processing, providing real-time quality feedback, and updating target priorities with Bayesian optimization. CryoFAST is integrated with SerialEM and Gatan GMS/Latitude.

Last year, we presented our early development and product roadmap for CryoFAST. This year, we will report the results of our machine learning development. We present the results of simulation studies as well as early alpha testing of the performance of our algorithm and microscope control automation in collaboration with the Pacific Northwest CryoEM center and the Lyumkis lab at Salk Institute.

## References:

{1} <https://www.nobelprize.org/prizes/chemistry/2017/press-release/>

{2} Carragher, B et al. "Current outcomes when optimizing 'standard' sample preparation for single-particle cryo-EM." *Journal of*

{3} *microscopy* vol. 276,1 (2019): 39-45. doi:10.1111/jmi.12834

<https://cryoem101.org/>