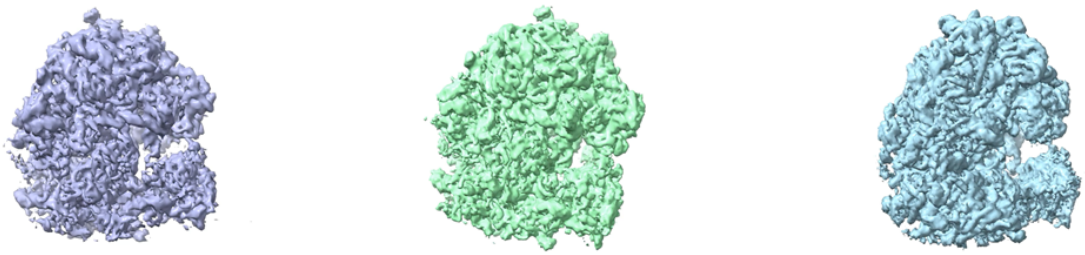
Partinet is a dynamic adaptive neural network for high-performance particle picking in cryo-EM

Mihin Perera[1,2], Andrew Leis[2], Shabih Shakeel[2,3,4], Joe Berry[1]

1. *Department of Chemical Engineering, The University of Melbourne*
2. *Structural Biology Division, Walter and Eliza Hall Institute of Medical Research (WEHI)*
3. *Department of Biochemistry and Pharmacology, The University of Melbourne*
4. *Training Centre for Cryo-Electron Microscopy of Membrane Proteins for Drug Discovery (CCeMMP)*

Cryogenic electron microscopy (cryo-EM) is a widespread methodology for visualising protein molecules. Advanced image processing techniques allow for reconstructing atomic-resolution 3D EM maps of frozen-hydrated protein molecules from noisy 2D projection images captured in a transmission electron microscope. The accuracy and resolution of cryo-EM structures is heavily dependent on the effectiveness of image analysis. Existing algorithms struggle with heterogeneous and complex datasets, leading to errors in particle identification, and ultimately leading to low resolution 3D reconstructions of proteins. We developed a new particle picking algorithm for identifying proteins in micrographs, combining new advances in cryo-EM micrograph labelling and object detection frameworks. One challenge with deep particle picking is the heterogeneity of micrographs during picking. Here we show that a dynamic neural network can achieve desired trade-offs between accuracy and efficiency when required due to changes in computational requirements of heterogeneous datasets. Our network, called "*Partinet*", utilises a novel deep-learning adaptive router to determine micrograph difficulty, changing the size of the detection algorithm accordingly. We implemented *Partinet* with two cascaded YOLOv7 detectors and the novel router. We trained our network initially on a curated, labelled representative dataset called *CryoPPP*. Next we benchmarked *Partinet* against gold-standard deep-pickers *crYOLO* and *Topaz*. We demonstrate that *Partinet* can match the performance of these networks, and in certain cases, leads to higher resolution EM maps. These findings will lead to high performance particle picking for heterogeneous datasets, significantly enhancing the overall quality and throughput of cryo-EM structure determination.



crYOLO
3,504 particles

Topaz
5,742 particles

Partinet
14,041 particles