

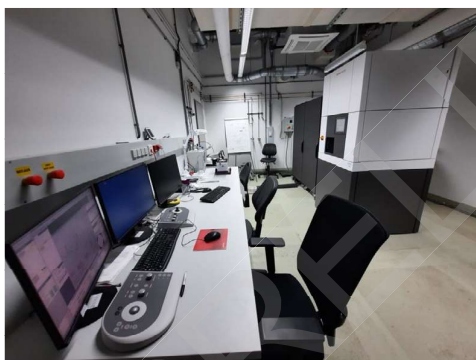
## Cryo-EM Software Packages: A Sys-admin's Point of View

*Stefano Elefante, Stephan Stadlbauer, Michael Alexander, and Alois Schlögl*

*Institute of Science and Technology Austria, Austria*

Cryo-electron microscopy (CryoEM) is a technique to determine the high-resolution structure of biomolecules in solution [1]. The method is based on the transmission electron cryomicroscopy (CryoTEM) that is also usually denoted as CryoEM. At the authors' institute (ISTA), the electron microscopy facility is equipped with two CryoEM devices: 200kV Cryo-TEM Glacios (Fig. 1) and 300kV Cryo-TEM Titan Krios G3i (Fig. 2). CryoEM samples can preserve cryogenic conditions up to 72 hours within the Krios Cryo-TEM and 24 hours within the Glacios Cryo-TEM system. These features allow researchers to collect all data that are necessary to achieve high-quality biomolecules reconstruction. However, the amount of cryoEM data required to obtain high-resolution analysis can be very large. As a consequence, the computational load can be very high requiring the use of high-performance computing (HPC) resources. Several software packages are available to process cryo-EM data: general purpose packages such as Relion [2], WarpEM [3], and CryoSPARC [4] and also software to address more specialized tasks like crYOLO, TOPAZ, etc.

**Relion** v3.0-v4.0 includes an end-to-end processing of raw cryo-EM data based on an empirical Bayesian approach. **WarpEM** v1.0.9 has been developed for the MS-Windows platform and has on-the-fly CryoEM data processing capabilities. **CryoSPARC** v3.0-v4.2.1 is a proprietary software platform for cryoEM data processing and analysis. **crYOLO** v1.9.3 is based on an algorithm for particle picking which relies on a convolution neural network. **TOPAZ** v0.2.5 is a pipeline for particle picking in cryoEM micrographs which employs neural networks.



**Fig. 1:** ISTA 200kV Cryo-TEM Glacios.



**Fig. 2:** ISTA 300kV Cryo-TEM Titan Krios G3i

### References

- [1] The development of Cryo-Electron microscopy, Scientific Background on the Nobel Prize in Chemistry 2017. <https://www.nobelprize.org/uploads/2018/06/advanced-chemistryprize2017-1.pdf>
- [2] Sjors H.W. Scheres, RELION: Implementation of a Bayesian approach to cryo-EM structure determination, *Journal of Structural Biology*, Volume 180, Issue 3, December 2012, Pages 519-530
- [3] Tegunov, D., Cramer, P. Real-time cryo-electron microscopy data preprocessing with Warp. *Nat Methods* 16, 1146–1152 (2019). <https://doi.org/10.1038>
- [4] Punjani, A., Rubinstein, J., Fleet, D. et al. cryoSPARC: algorithms for rapid unsupervised cryo-EM structure determination. *Nat Methods* 14, 290–296 (2017). <https://doi.org/10.1038/nmeth.4169>