Report of CM01 microscope use - mx2166

We were lucky to be granted 3 days of data collection during the spring of 2019. We came with pre-mounted and, for part of them, pre-screened grids. 7 of them were mounted in the microscope and 4 were screened on site. The data collection, using standard parameters (130k magnification, 8 second images with a total dose of ~40 e/Å2, 3 and then 4 images per hole) started on the first day around 4 pm. Thanks to the advice of the local contact G. Effantin, it was possible to set up an automated data treatment on our lab GPU workstation. Drift-corrected micrographs were synced to the workstation and all steps down to 2D classification were performed repetitively as images accumulated.
Thanks to this procedure it was possible to get a preliminary model by the afternoon of day 2! In parallel, more grid squares were selected for imaging, close to the ones that seemed to feature the best micrographs already taken.
When our session finished, ~4100 micrographs had been taken. Thanks to the 'online' data treatment it was also possible to know that the reconstruction from these micrographs will go to 3.1 Å or better (all steps have been performed but particle polishing, which in our system, rarely yield more than 0.1 Å resolution improvement) even if we will need a few weeks to reach the final refinement.

The density map clearly features the vortioxetine molecule bound to the serotonin receptor. This structure will provide a molecular framework to the action of the antidepressant at the 5-HT3 receptor.

We are thankful for the excellent support of the CM01 staff, and for the stability/quality of the microscope itself!

Left. Typical low density micrograph of the sample, selected 2D classes
Right panels. Preliminary map obtained 24h after data collection started. The tricyclic shape of the ligand can be seen (resolution 3.9 Å)