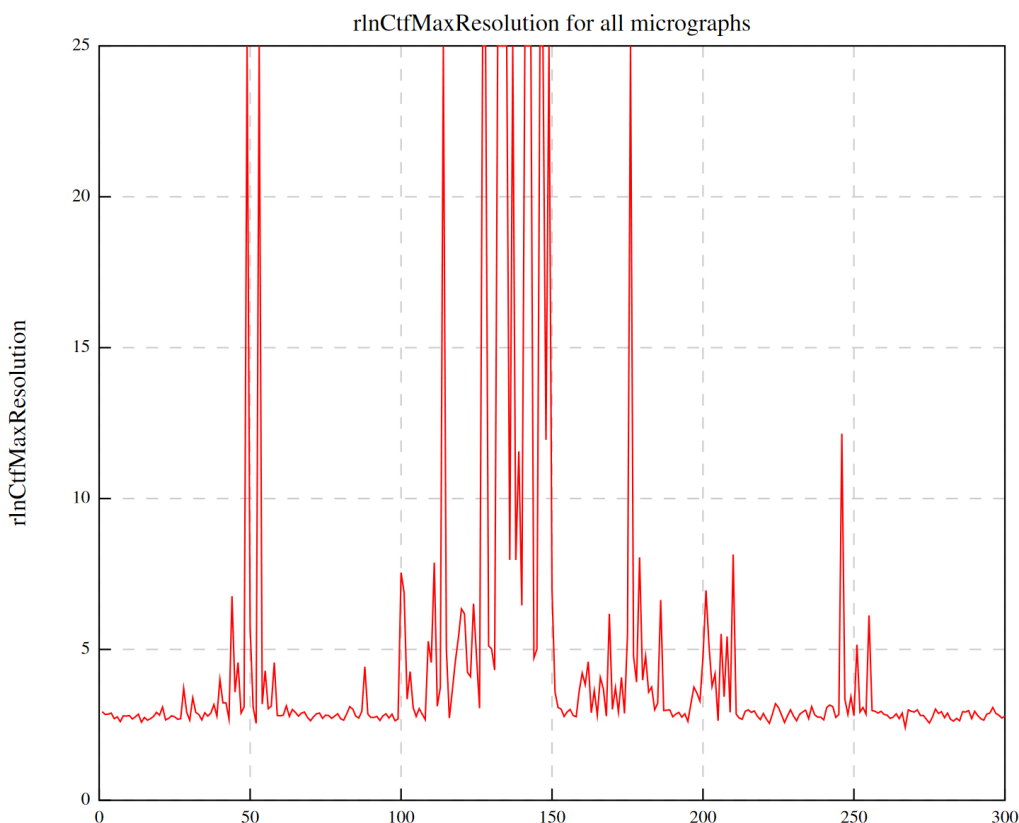


## Supplemental Data

### Methods

Motion correction was run with Relion's motioncor implementation using default parameters, except for saving sum of power spectra (grouping\_for\_ps = 4) and 5 x 3 patches. We used CtfFind for CTF determination with default parameters, except for using power spectra from motioncor job. For Particle Picking, we used Relion's LoG-picker with minimum and maximum particle diameters of 100 and 180 Å respectively, and default parameters otherwise. For 3D reference picking we used the EMDB-21992 at a pixel size of 2.2 Å, low-pass filtered to 20 Å, and a sampling of 30 degrees for 2D template generation. Particles were initially extracted with a box size of 70 pixels and a pixel size of 3.03 Å. For 3D classification we used a class number of 3, EMDB-21992 re-scaled to 3.03 Å pixel size and low-pass filtered to 20 Å as reference, a mask radius of 160 Å and default parameters elsewhere. The well-defined class average from the first round (containing ~126k particles) was selected and used with the same parameters for a second round of 3D classification, except for turning on fast subsets. The best-defined class containing 55,366 particles was selected and particles were re-extracted at a box size and pixel size of 160 pixels and 1.33 Å respectively. Particles were subjected to 3D refinement using the map from the previous Class3D job rescaled to the respective box and pixelsize, and low-pass filtered to 10 Å, and a mask incl. the micelle ( generated from the rescaled average; ini\_threshold = 0.045, extended by 5 pixels, soft edge of 10 pixels). The resulting map (4.34 Å resolution) was used to create a mask excluding the micelle (ini\_threshold = 0.018, extended by 5 pixel, soft edge of 10 pixels). Particles were subjected to a second round of 3D refinement using the shape mask excluding the micelle, the average from the previous refinement round as reference and solvent-flattened FSC's during 3D refinement - resulting in a map determined to 3.54 Å resolution (FSC 0.143 criterion). Post-processing was run with default parameters.

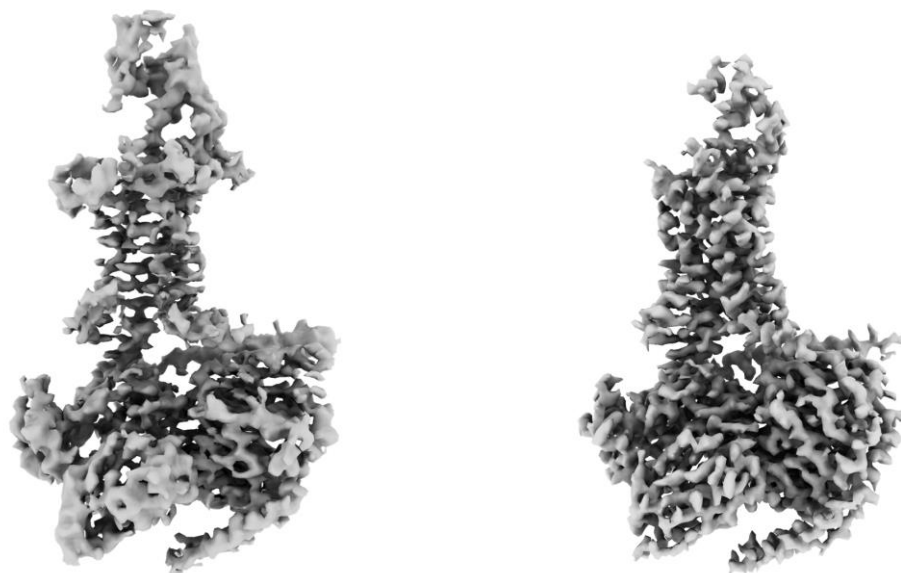
### Additional Figures



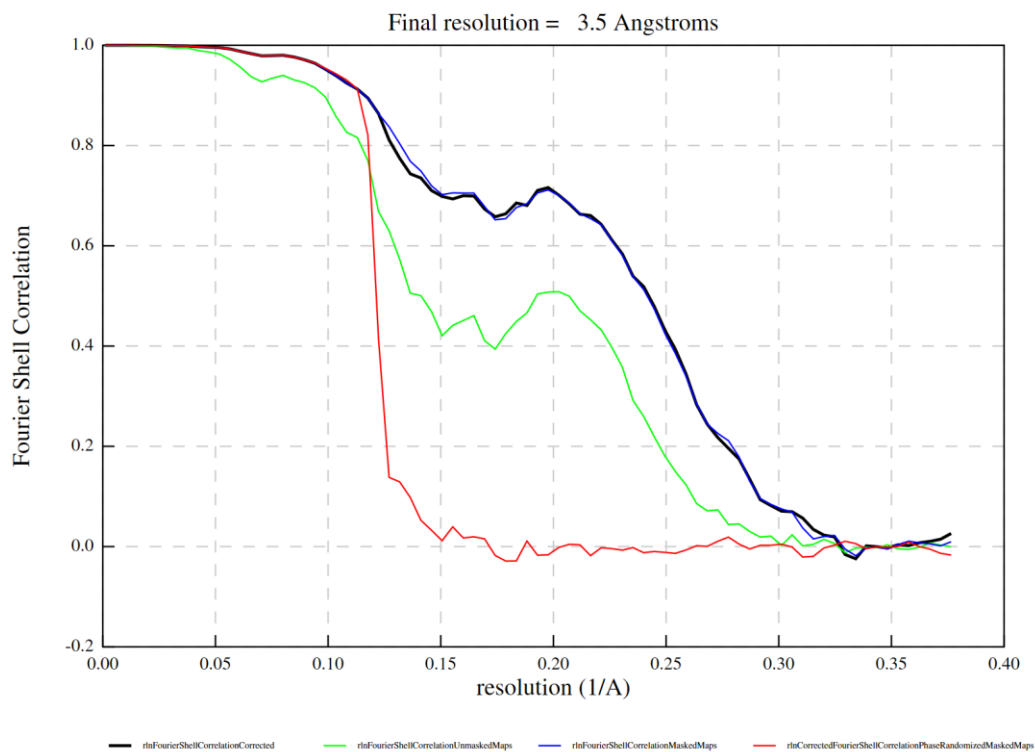
**Fig. S1: Maximum resolution of micrographs as determined by CtfFind.**

4.17 Å average from 64,868 particles  
obtained with reference-based picking and 2  
rounds of class3D & refine3D each, post-processed

3.54 Å average from 55,366 particles  
obtained with LoG-picker and 2 rounds of class3D  
& refine3D each, post-processed



**Fig. S2: Map obtained from the particle set where reference-based picking was used vs map obtained with LoG picked particles.** Using a 3D reference, 64,868 true-positive particles were obtained after two rounds of Class3D and resulted in a resolution of 4.17 Å after two rounds of 3D refinement (left) vs. 3.54 Å when the same workflow was applied to the particle set obtained with the LoG-picker (right).



**Fig. S3: FSC plot from the post-process job of the 3.54 Å reconstruction.**