

Figure supplement 1. Sphingomyelin (cyan) binding overlaps with that of agonist ML-SA1 (yellow), rapamycin analog Tem (magenta), or antagonist ML-SI3 (green).

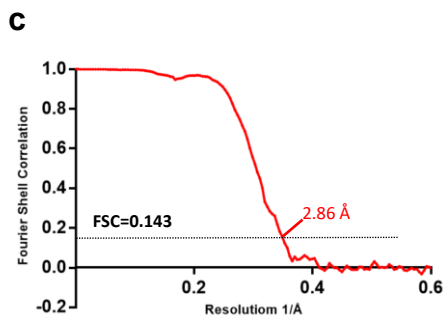
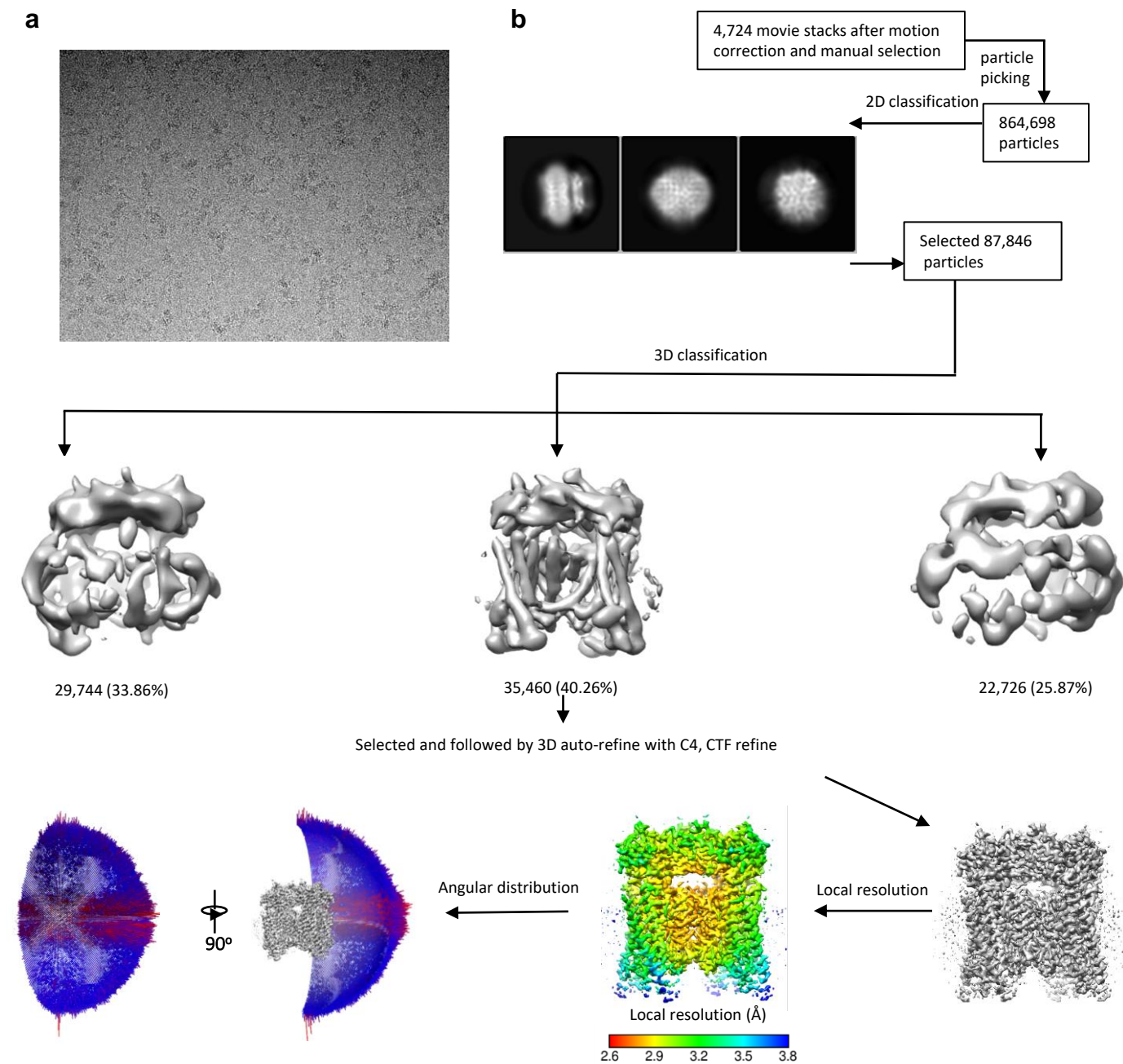


Figure supplement 2: Cryo-EM data processing scheme of the TRPML1 Y404W. (a) Representative micrograph. (b) Flow chart of the cryo-EM data processing procedure and the Euler angle distribution of particles used in the final three-dimensional reconstruction. Selected 2D class averages are shown. The final structure represent an open state. (c) Fourier Shell Correlation curves showing the overall resolution at FSC=0.143.

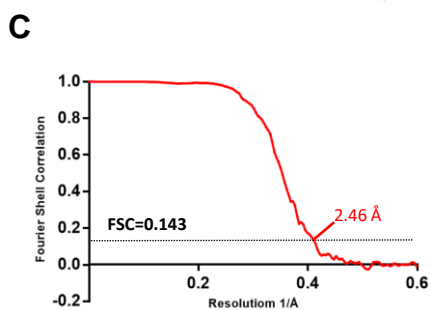
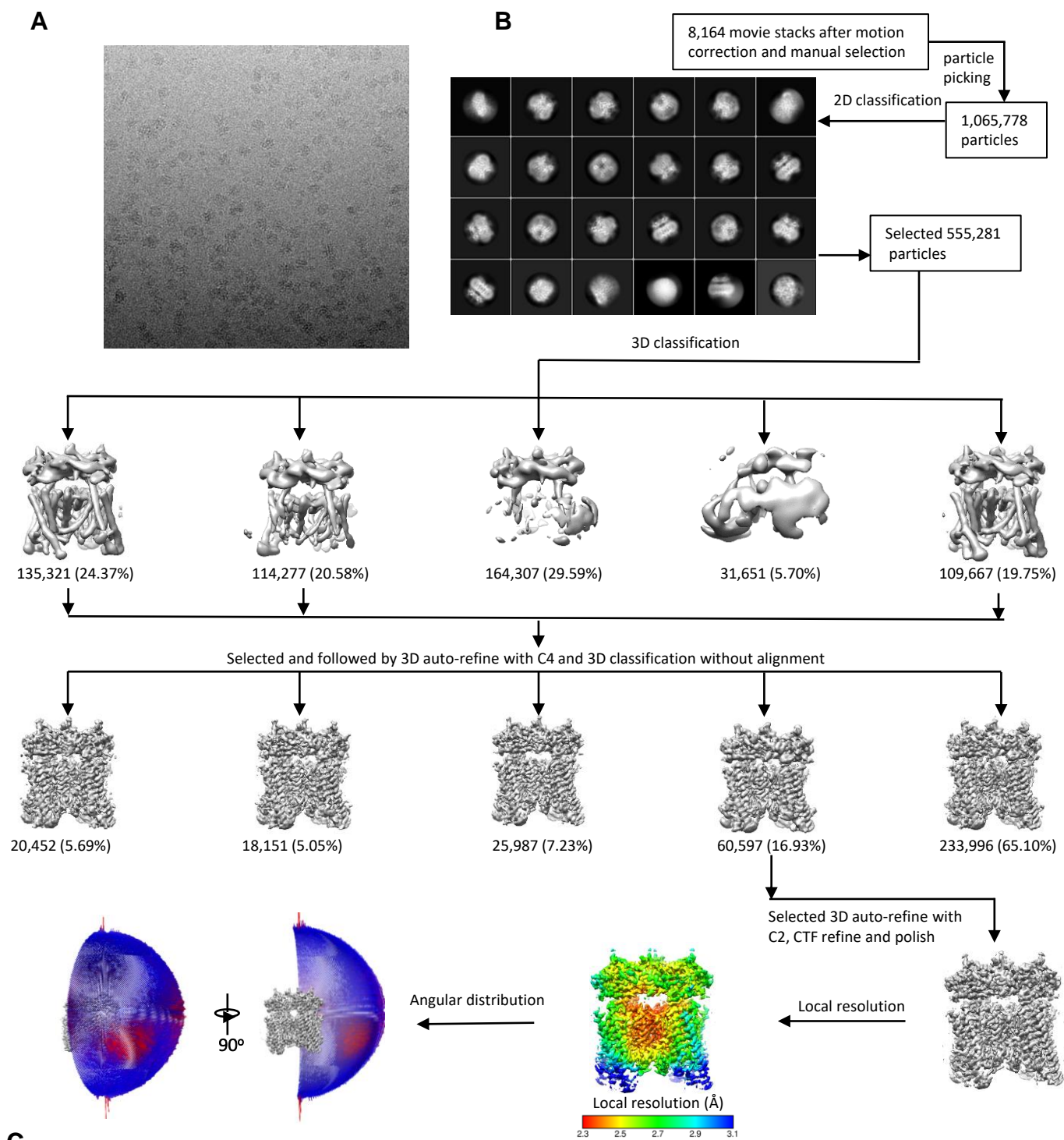


Figure supplement 3: Cryo-EM data processing scheme of the TRPML1 sample prepared in the presence of PI(4,5)P₂. (a) Representative micrograph. (b) Flow chart of the cryo-EM data processing procedure and the Euler angle distribution of particles used in the final three-dimensional reconstruction. Selected 2D class averages are shown. The final structure represent an open state. (c) Fourier Shell Correlation curves showing the overall resolution at FSC=0.143.

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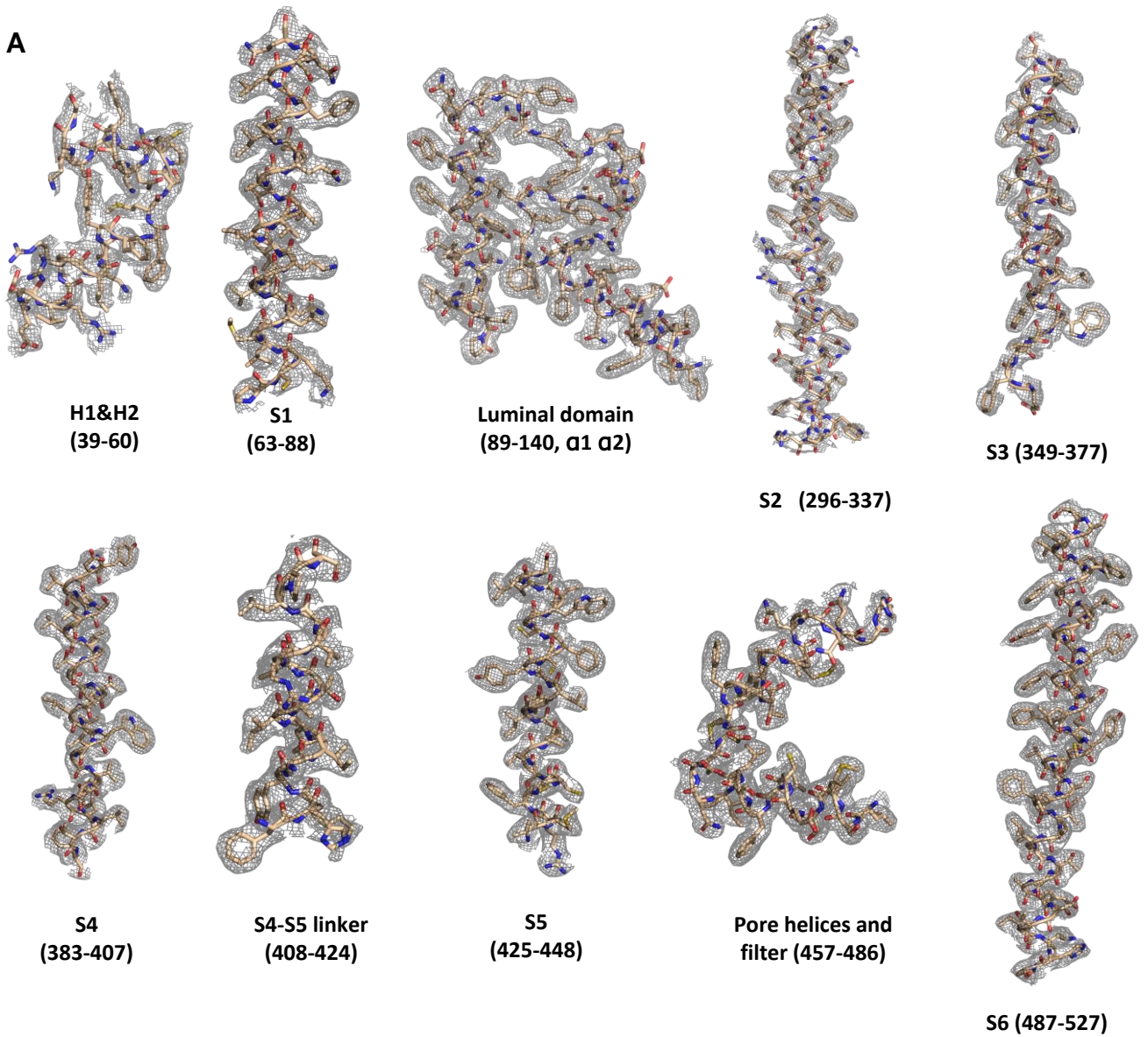
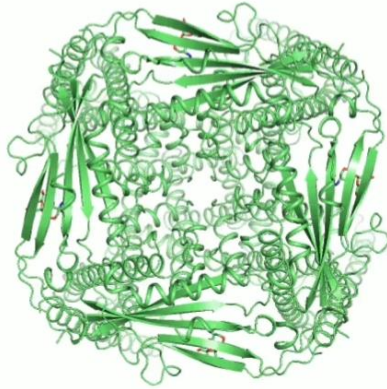


Figure supplement 4 : Sample density maps of the PI(4,5)P₂-bound closed TRPML1 structure contoured at 4 σ .

Top View



Movie supplement 1. Conformational changes between open and closed TRPML1