

Description of Additional Supplementary Files

File name: Supplementary Movie 1

Description: Atomic model of the N-terminal domain of RyR2 (PDB 7UA5), showing the residues R417 (yellow) and R420 (red) surrounded by the NTD-A (blue), NTD-B (light blue), and NSol (grey) domains

File name: Supplementary Movie 2

Description: Atomic model of primed RyR2-R420W + Ca²⁺ + CaM (PDB 8UXL) overlapped with its respective cryo-EM map, showing the residues in the interface between RyR2-R420W (cyan) and CaM (orange).

File name: Supplementary Movie 3

Description: Cryo-EM volumes of the 3D Variability Analysis RyR2-S2808D showing the movement of the cytoplasmic shell from the most upward-inward conformation (cyan) to the most downward-outward conformation (red) from the side view.

File name: Supplementary Movie 4

Description: Cryo-EM volumes of the 3D Variability Analysis RyR2-S2808D showing the movement of the cytoplasmic shell from the most upward-inward conformation (cyan) to the most downward-outward conformation (red) from the top view.