

Supporting Information

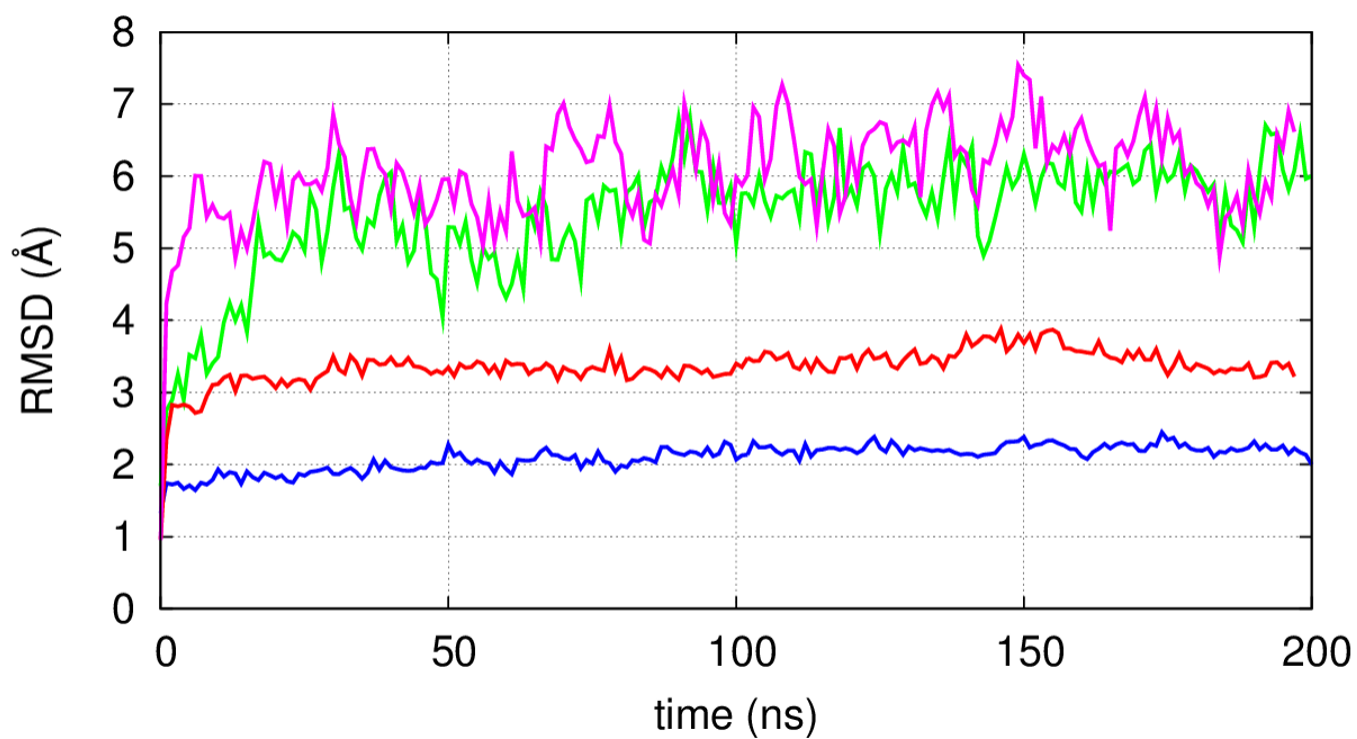


Figure S1. RMSD as a function of time for two representative MD trajectories in the C state at 30°C and the O state at 60°C using the following color scheme: expanded TMD in the C state (blue) and the O state (red), entire TRPV1 in the C state (green) and the O state (purple).

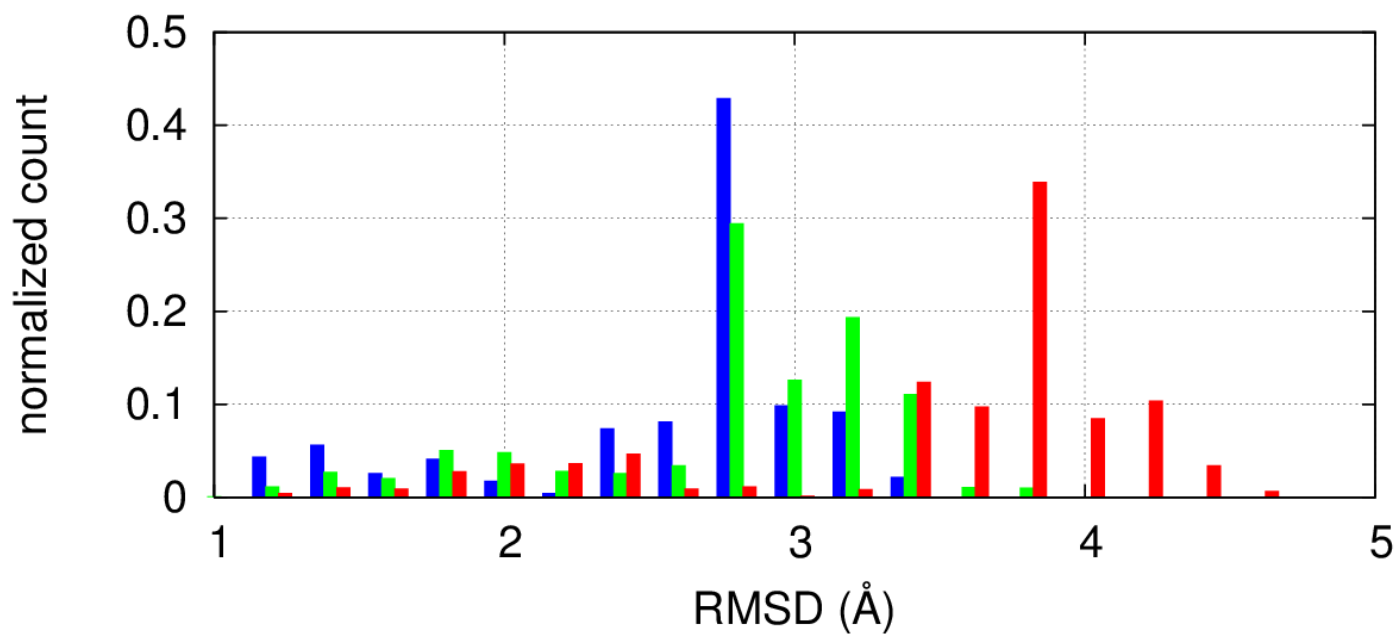
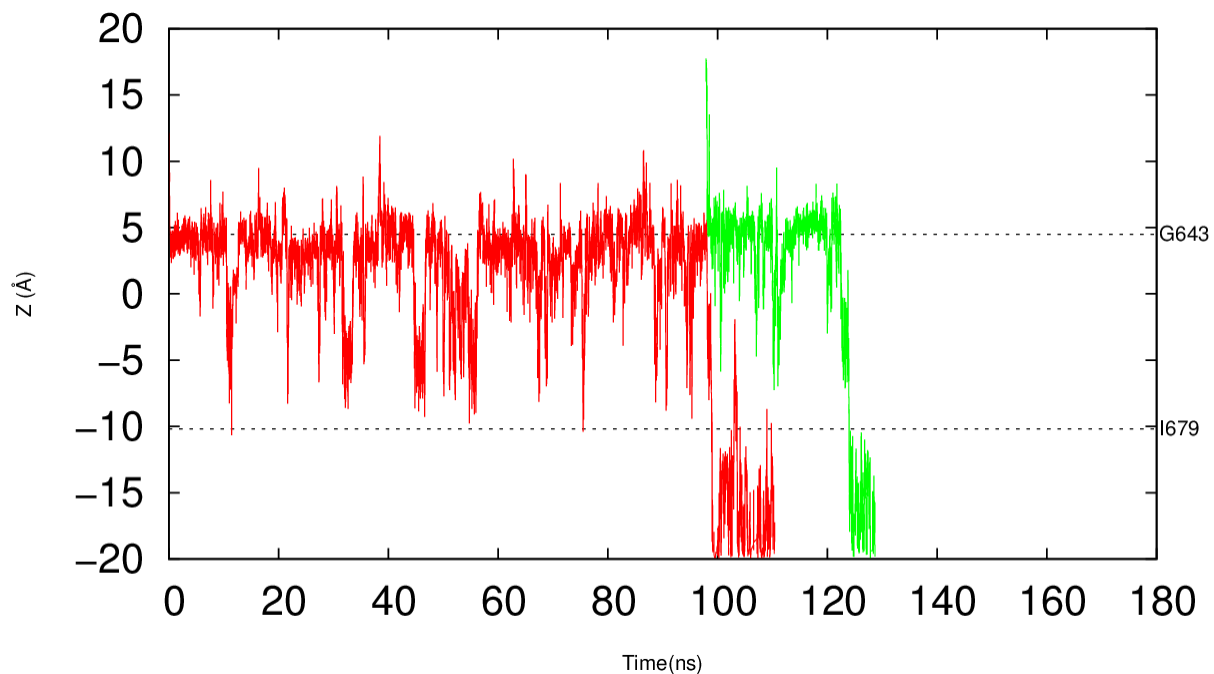
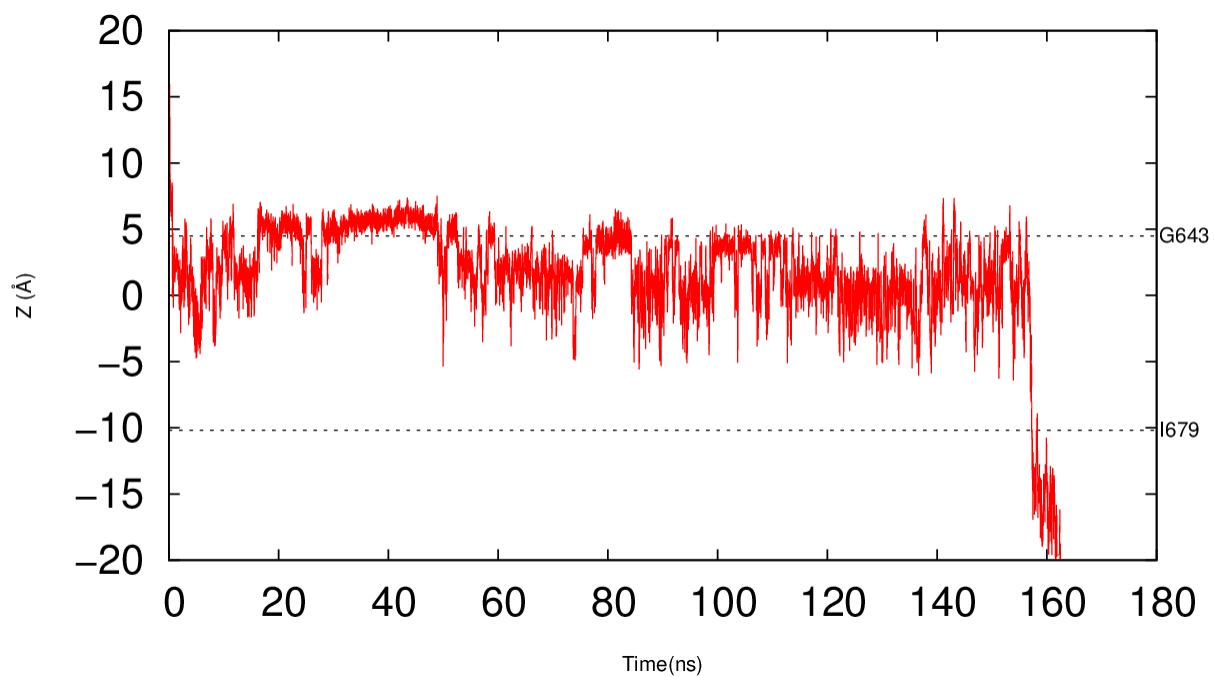


Figure S2. Distribution of all-to-all RMSD in the expanded TMD (blue: the C state at 30°C, green: the heated C state at 60°C, red: the O state at 60°C). The O-state distribution is shifted toward higher RMSD relative to the C-state distribution, suggesting a higher conformational diversity.



a



b

Figure S3. Three ion conduction events observed in two trajectories in the O state at 60°C: The Z coordinate gives the position of a conducting K^+ ion along the channel pore axis. The horizontal dashed lines mark the Z coordinates of the upper gate (at G643) and the lower gate (at I679). Two and one conduction events were shown in (a) and (b), respectively.

Movie S1. Bottom view of the conformational changes predicted by the first PCA mode (same color coding as Fig 1a). For clarify, only part of the ARDs, the MPD linkers, the S2-S3 linkers, the lower S6 helices, and the TRP helices are shown. Residues R409, E692, and I679 are shown as spheres.

Movie S2. Side view of the conformational changes predicted by the first PCA mode (same color coding as Fig 1a). Only the MPD linkers, the S2-S3 linkers, the pore domain, and the TRP helices are shown in two diagonally opposing subunits. Residues R409, E692, G643, and I679 are shown as spheres.