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Supplemental Information

Gating Charge Calculations by Computational Electrophysiology Simulations

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Gating Charge Calculations by Computational Electrophysiology simulations

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SUPPORTING MATERIAL

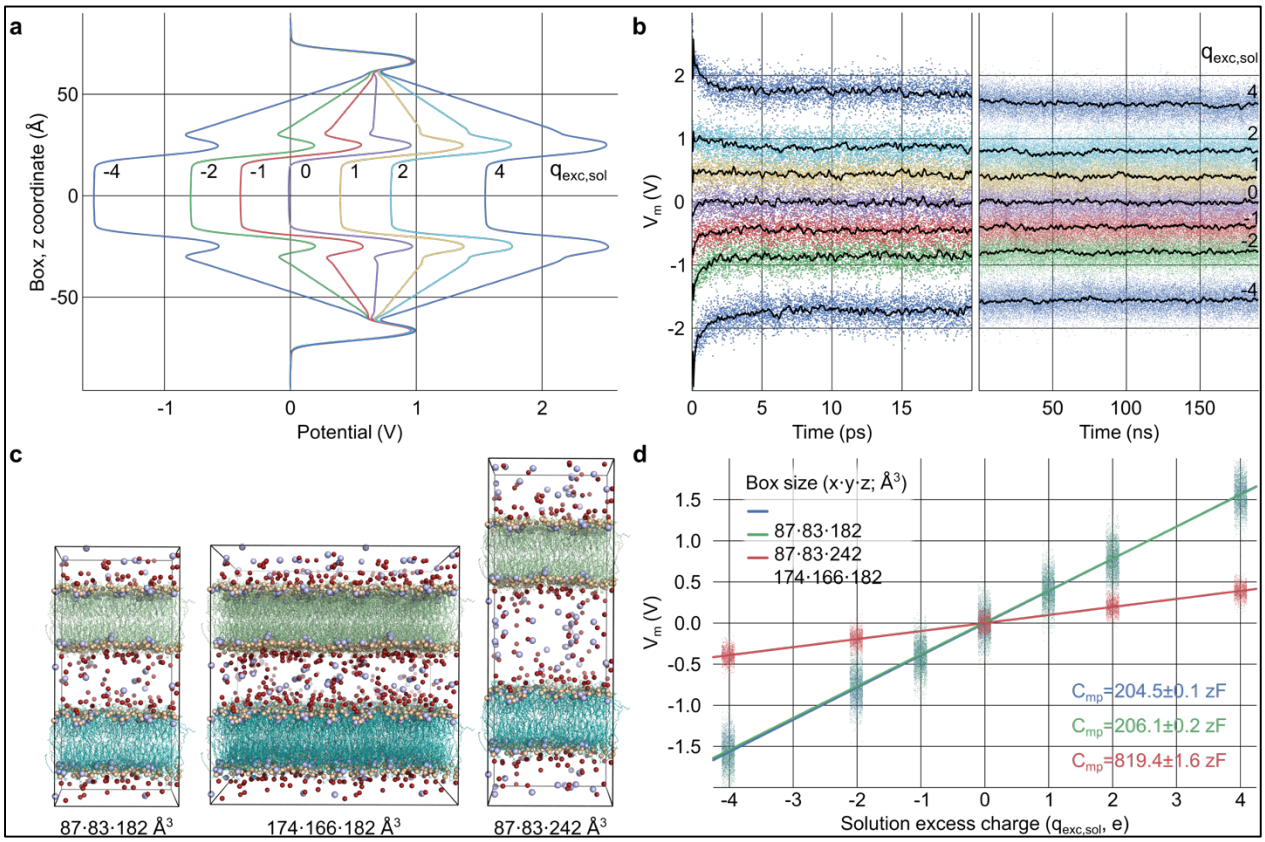

FIGURE S1 Capacitor properties of a double-bilayer system. **(a)** Averaged electrostatic potential profiles from 150 ns simulations along the membrane normal of the two-bilayer simulation system (87·83·182 Å^3) illustrated in (c). Numbers indicate the ionic excess charges in the aqueous compartments established by CompEL. $z = 0$ is defined as the center between the two lipid bilayers. **(b)** Time course of V_m upon charging of the lipid bilayer by CompEL. **(c, d)** Charge titration plots demonstrate that the dependence of V_m on charge imbalance and bilayer area conforms to an electrical plate capacitor (dots, calculated electrostatic potential for each frame of the trajectory; solid lines, linear fits according to the capacitor Eq. 3).

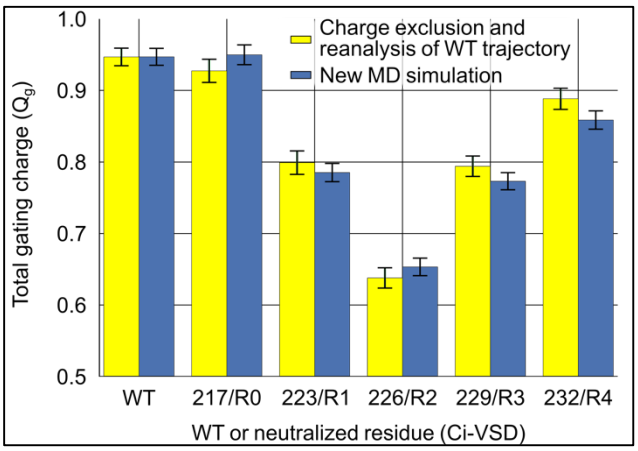

FIGURE S2 Evaluation of gating charge contributions via "charge exclusion" from the charge density. Gating charges are calculated for WT Ci-VSD and with neutralized arginines (R0–R4) in the S4 segment to determine the fractional gating charge contribution of the respective residues (Figs. 2a and 3a,b). Gating charges are either calculated by reanalyzing the original WT trajectory and excluding all partial charges of the residue of interest from the electrostatic potential calculation (Eq. 2; yellow), or by MD simulations to generate new trajectories of the respective charge neutralization "mutants" (blue). The fractional gating charge contribution is given by the difference between the WT and the mutant gating charge.

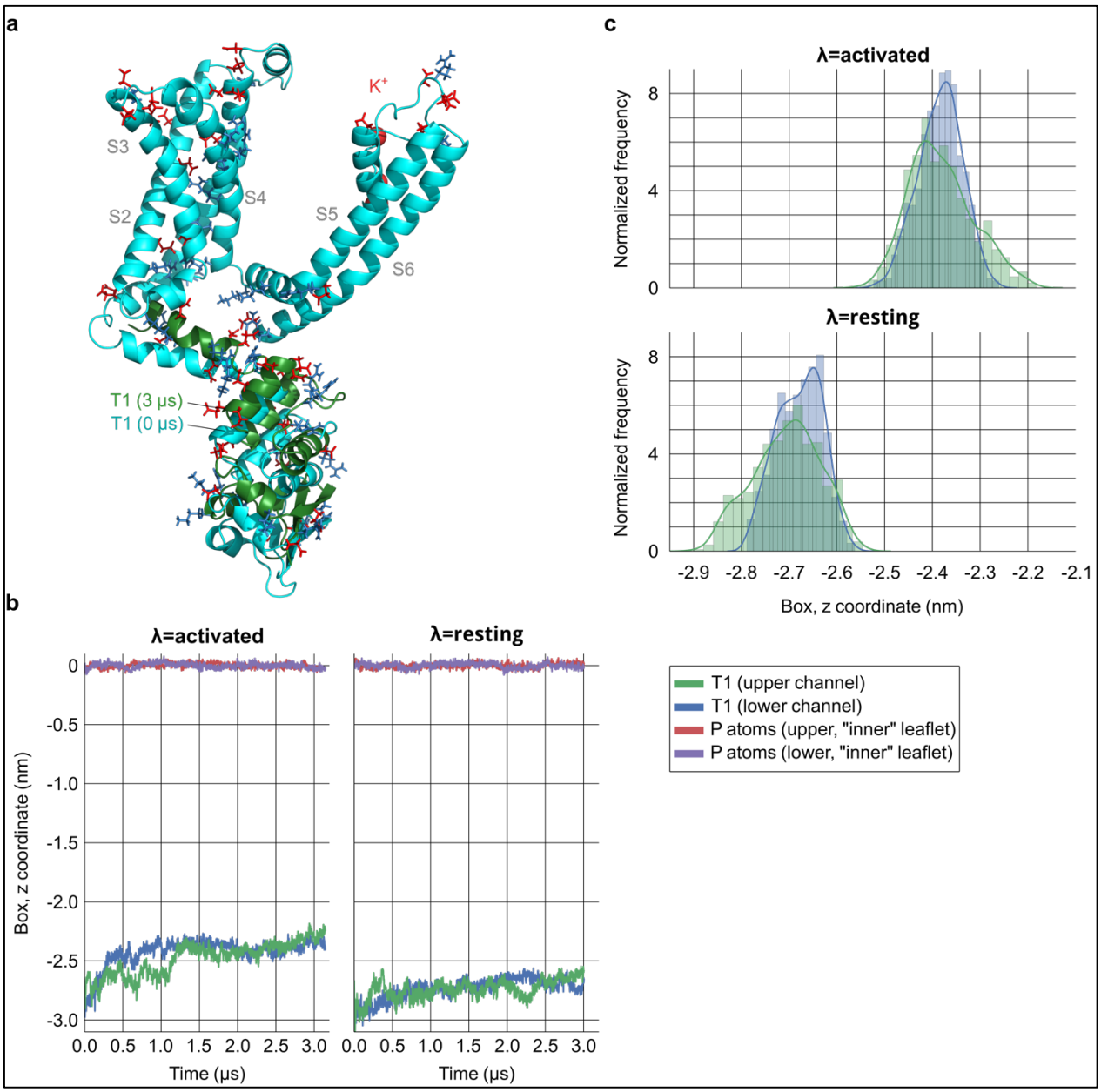

FIGURE S3 T1/linker movements during Kv1.2 activation. **(a)** Representative conformation of the T1/linker domain in the activated state of Kv1.2 obtained through 3 µs MD equilibration at +100 mV (green cartoon, T1/linker structure of the equilibrated channel shown with its backbone atoms of the S1–S6 helices superimposed on the initial structure (5); cyan cartoon, initial structure, activated Kv1.2 monomer from Pathak *et al.*(5)). Charged residues are shown as sticks (red, negative; blue, positive charge). **(b)** Time course of the T1/linker domain position along the membrane normal (z) during microsecond-long equilibration, calculated as the center-of-geometry of the charged residues in the sequence range from 32–149. z=0 was defined as the average position of the plane defined by the P atoms of the "inner" leaflet of the bilayer. Analyses on the two channels in the double-bilayer CompEL systems are shown for the activated and resting states, which were subjected to +100 mV or -100 mV, respectively. **(c)** Histogram visualization of the positional change of the T1/linker domain upon channel activation using the data from the second half of the equilibration phase (1.5 µs to end) in (b).

File S1 Spreadsheet containing the gating charge contributions for all residues in Ci-VSD, including all fit parameters.

File S2 Spreadsheet containing the gating charge contributions for all residues in Kv1.2, including all fit parameters. Gating charges are given per tetramer.