Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supplementary Material for

In silico investigation of the interaction between the voltage-gated potassium channel Kv4.3 and its auxiliary protein KChIP1

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Content

Figure S1

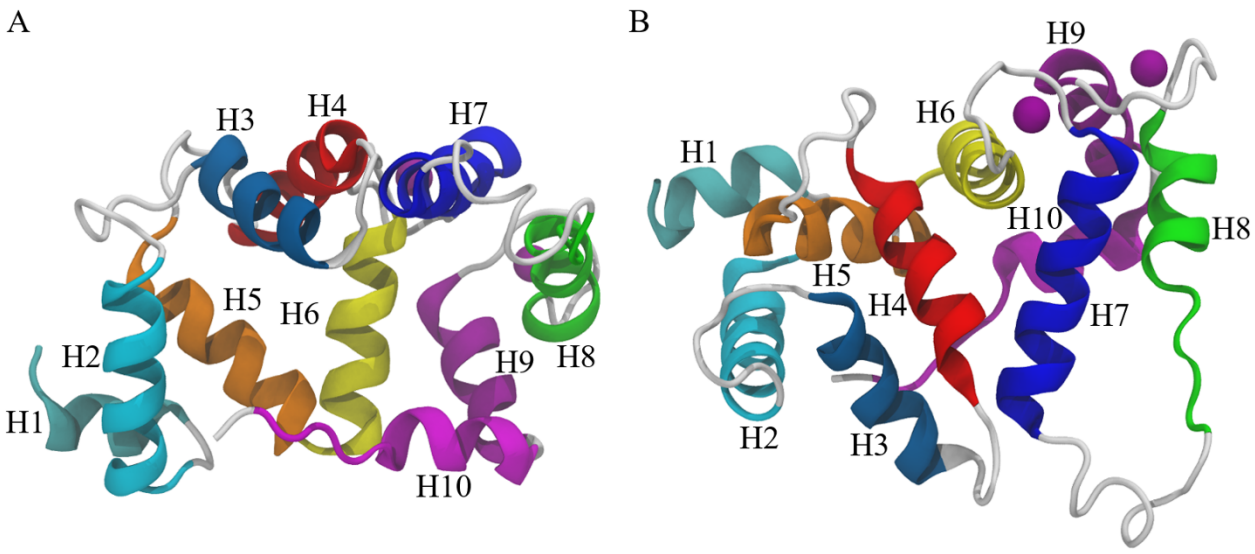

Figure S1 (A) Side and (B) top views of a KChIP1 auxiliary subunit showing all its α-helical domains in different colors and in ribbon representation. H1 (residues 39-45) and H2 helices (residues 50-63) mainly mediate the second interface interaction between Kv4.3 (residues 70-78) and KChIP1. The remaining loops are in white. Calcium ions are shown in purple spacefilling representation.

Figure S2

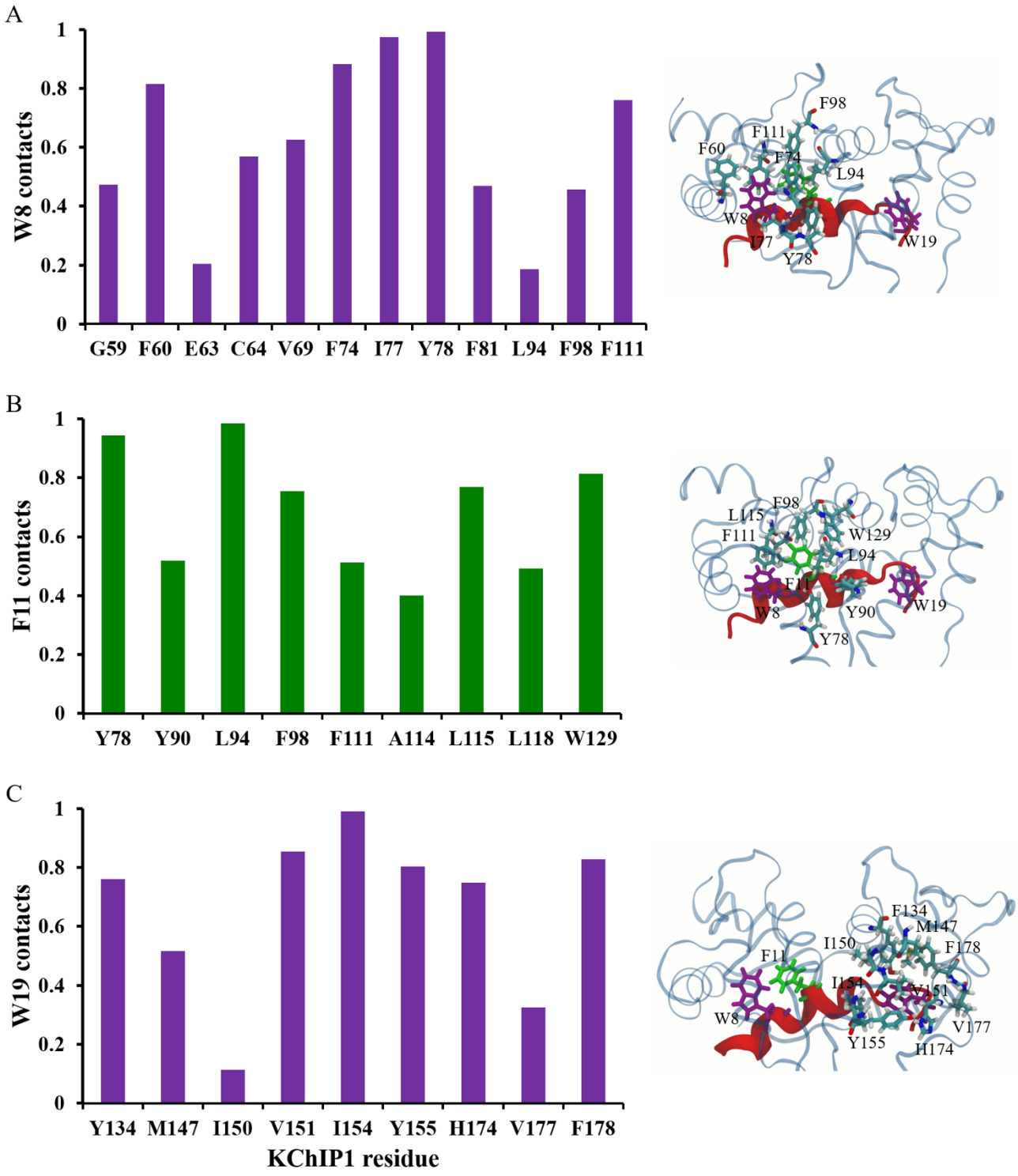

Figure S2 Average number of contacts of (A) W8 (purple), (B) F11 (green) and (C) W19 (purple) residues of the WT Kv4.3 T1-KChIP1 complex. The cutoff used to define a contact was 3 Å. The Kv4.3 N-terminus (residues 1-20) and the KChIP1 subunit of the starting model are shown in red and transparent skyblue ribbon representations, respectively. W8, W19 and F11 amino acids are shown in purple and green licorice representations, respectively. Residues displaying the largest average number of contacts are also shown for W8 (top right, panel A), F11 (middle right, panel B) and W19 (bottom right, panel C).

Figure S3

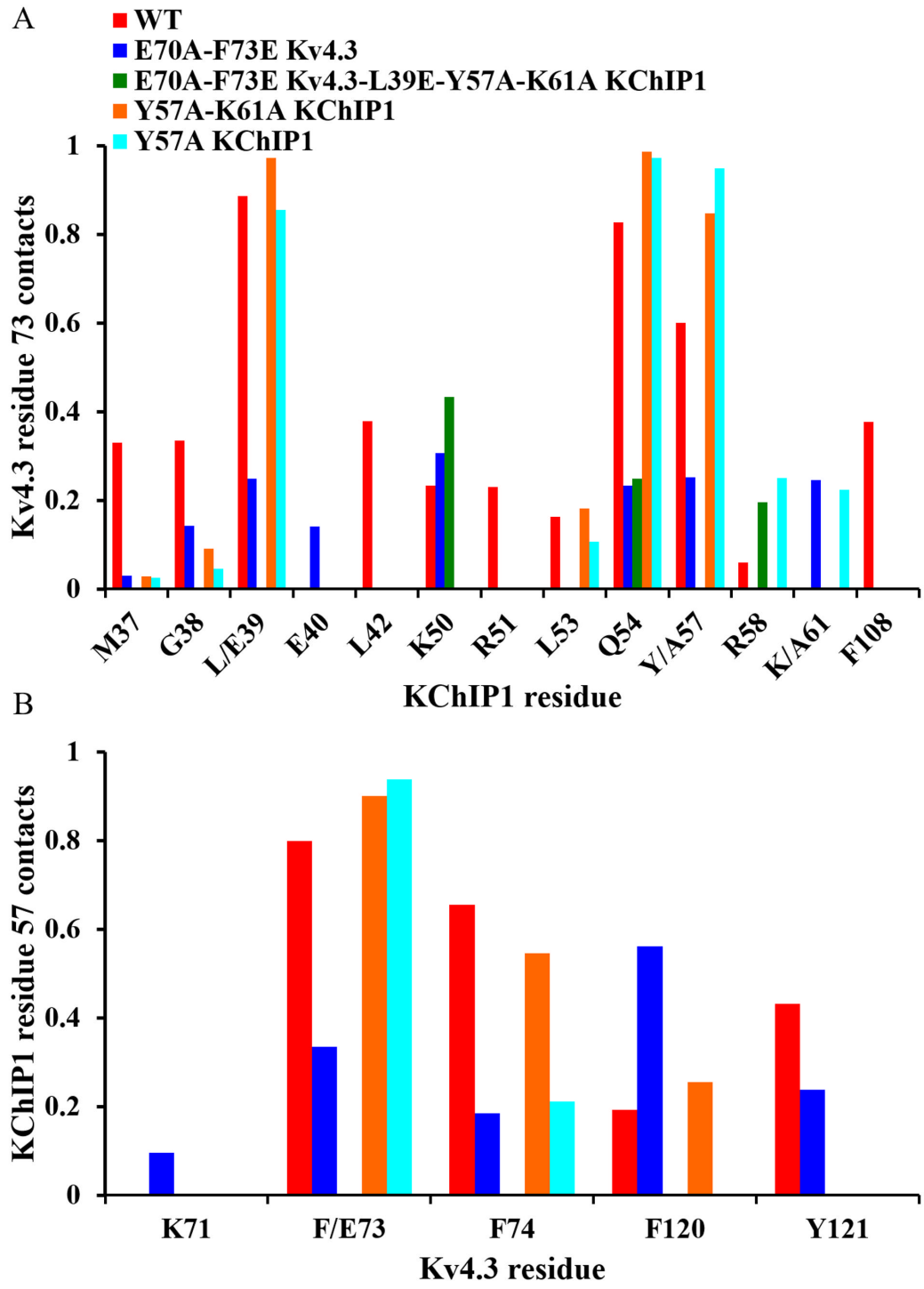

Figure S3 (A) Average number of contacts of Kv4.3 residue 73 with KChIP1 residues from MD simulations of WT (red), E70A-F73E Kv4.3 (blue), E70A-F73E Kv4.3 + L39E-Y57A-K61A KChIP1 (green), Y57A-K61A KChIP1 (orange) and Y57A KChIP1 (cyan) Kv4.3 T1-KChIP1 complexes. (B) Average number of contacts of KChIP1 residue 57 with Kv4.3 residues from MD simulations of WT and mutated Kv4.3 T1-KChIP1 complex models. The cutoff used to define a contact was 3 Å.

Figure S4

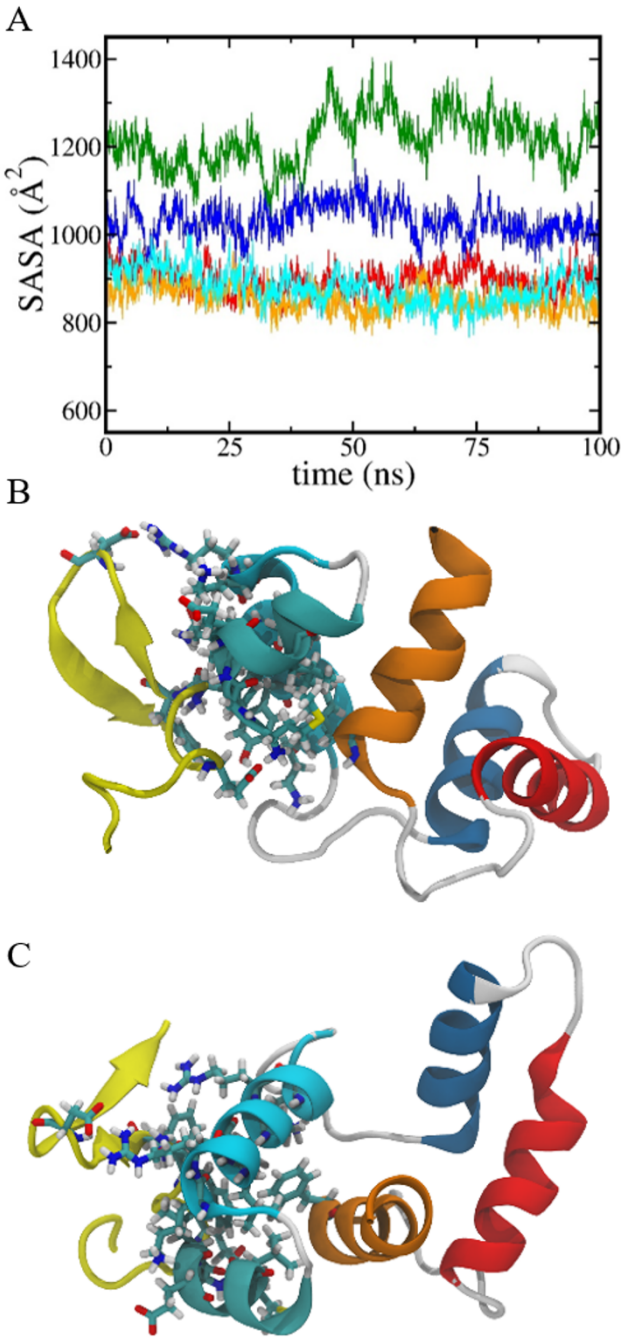

Figure S4 (A) Solvent accessible surface areas (SASAs) of residues interacting in the second interface, namely Kv4.3 residues E70, F73, F74 and D78 and KChIP1 residues M37-E40, L42, K50, R51, L53, Q54, Y57, R58, K61 and F108, from 100 ns AA MD simulations of WT (red, 892 ± 33 Å^2), Y57A-K61A KChIP1 (orange, 853 ± 30 Å^2), Y57A KChIP1 (cyan, 880 ± 40 Å^2), E70A-F73E Kv4.3 (blue, 1018 ± 31 Å^2) and E70A-F73E Kv4.3 + L39E-Y57A-K61A KChIP1 (green, 1235 ± 45 Å^2), Kv4.3 T1-KChIP1 complexes. Mutations in the second interface side of Kv4.3 induce an increase in the SASA as compared to WT, KChIP1 mutants and Kv4.3 triple mutant systems. All SASAs were computed over the last 40% of each trajectory, saved every 50 ps. The errors are reported as standard deviations. (B) Side and (C) top views of residues interacting in the second interface. The same color code of Fig. S1 is used for helices of the KChIP1 subunit. The region of the Kv4.3 T1 domain interacting with H2 helix of KChIP1 is shown in yellow.

Table S1 Salt bridges of the second interface from MD simulations of WT and mutated Kv4.3 T1-KChIP1 complexes.

Kv4.3[a]	KChIP1[a]	WT[b]	Kv4.3 DM[b]	Kv4.3 DM + KChIP1 TM[b]	KChIP1 DM[b]	KChIP1 M[b]
E70	K61	16.4	0	0	0	0
K71	E40	0	25.6	11.3	0	0
K71	E39	0	0	23.4	0	0
K71	E109	0	0	0	32.3	30.5
K71	E43	0	6.7	19.0	0	0
E72	K50	0	14.4	0	0	5.4
E72	R51	0	0	43.1	0	0.4
E72	R58	0	0	84.5	0	0
E73	K50	0	26.4	42.9	0	0
E73	R58	0	0	21.4	0	0
E73	K61	0	21.9	0	0	0
E77	K50	35.6	17.7	0	14.4	4.5
E77	R51	59.9	14.4	22.5	44.1	63.8
D78	R51	73.0	43.4	0	1.6	20.5
D85	R58	0	0	0	23.6	0
D85	K61	0	0	0	0	24.9

[a] All charged residues (Arg, Lys, Glu, Asp) whose side-chain distance (i.e., N--O) was found below 5 Å were considered in the analysis. The more persistent salt bridges, those with an average percentage of >10% over the total simulation time, are reported. Percentages are also averaged over the four monomers.

[b] Legend of simulated Kv4.3 T1-KChIP1 complexes. WT: wild type, Kv4.3 DM: E70A-F73E Kv4.3, Kv4.3 DM + KChIP1 TM: E70A-F73E Kv4.3 + L39E-Y57A-K61A KChIP1, Kv4.3 TM: W8E-P10E-A15E Kv4.3, KChIP1 DM: Y57A-K61A KChIP1 and KChIP1 M: Y57A KChIP1.

Table S2 Salt bridges of the third interface from MD simulations of WT and mutated Kv4.3 T1-KChIP1 complexes.

Kv4.3[a]	KChIP1[a]	WT[b]	Kv4.3 DM[b]	Kv4.3 DM + KChIP1 TM[b]	KChIP1 DM[b]	KChIP1 M[b]
D39	R51	21.4	69.9	49.8	47.5	24.8
D39	R58	80.5	93.7	72.0	49.8	64.3
R60	E63	43.7	66.9	53.3	65.5	86.5

[a] All charged residues (Arg, Lys, Glu, Asp) whose side-chain distance (i.e., N--O) was found below 5 Å were considered in the analysis. The more persistent salt bridges, those with an average percentage of >10% over the total simulation time, are reported. Percentages are also averaged over the four monomers.
[b] Legend of simulated Kv4.3 T1-KChIP1 complexes. WT: wild type, Kv4.3 DM: E70A-F73E Kv4.3, Kv4.3 DM + KChIP1 TM: E70A-F73E Kv4.3 + L39E-Y57A-K61A KChIP1, Kv4.3 TM: W8E-P10E-A15E Kv4.3, KChIP1 DM: Y57A-K61A KChIP1 and KChIP1 M: Y57A KChIP1.