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Supporting Material

INTERACTION OF DIVERSE VOLTAGE SENSOR HOMOLOGUES WITH LIPID BILAYERS REVEALED BY SELF-ASSEMBLY SIMULATIONS

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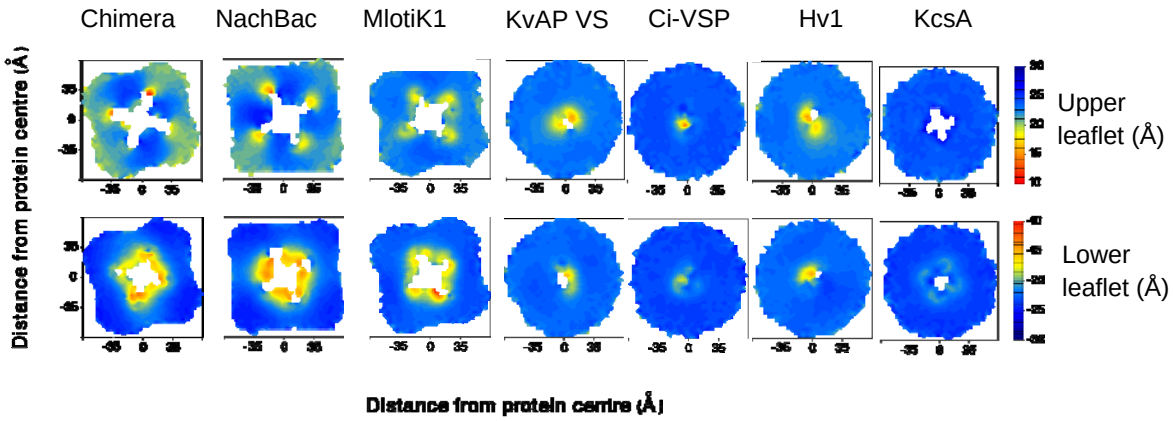

Figure S1. VS domains cause a major distortion to the DOPC during simulations (related to Figure 3). Contour plots show the average position relative to the membrane centre of lipid phosphate groups of the upper or the lower leaflet averaged over the last 220 ns of the simulations.

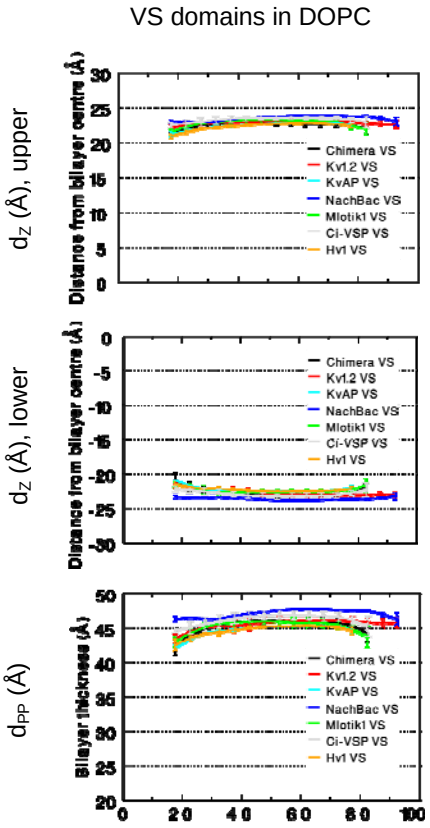

Figure S2. Impact of isolated VS domains on DOPC lipid bilayer structure (related to Figure 4). The average positions of phosphate groups in the upper leaflet (top), the lower leaflet (middle), and bilayer thickness (bottom) plotted against the radial distance from the protein centre of mass. Error bars represent 95% confidence intervals.

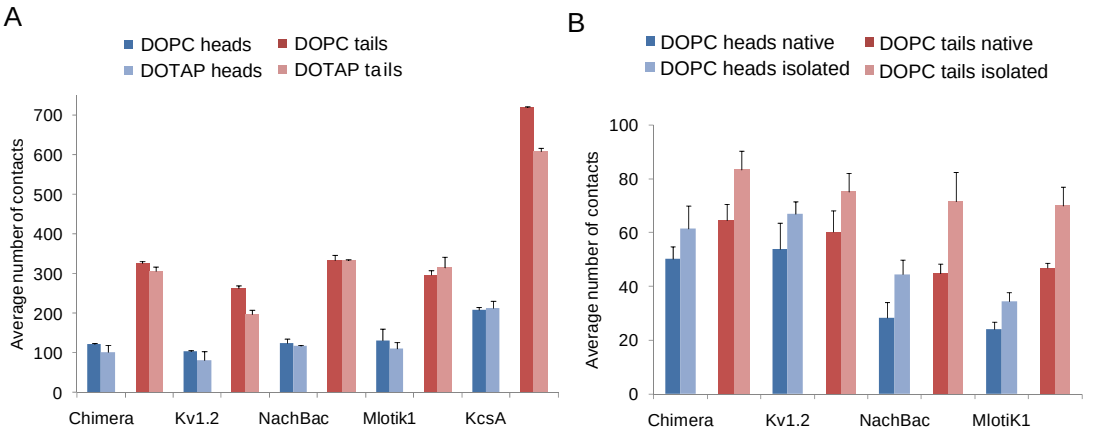

Figure S3. (A) Pore domains of VS homologues interaction with lipids is unaffected by the absence of phosphate head groups (related to Figure 6). Plotted is the average number of contacts between the pore domains and lipid heads or tails in simulations of the native channel tetramers in either in DOPC or DOTAP. KcsA is shown for comparison. **(B)** Increased interaction of paddle motifs with DOPC lipids in isolated VS domains relative to those in VS domains that are part of the native channel tetramers (related to Figure 5). Error bars represent 95% confidence intervals.

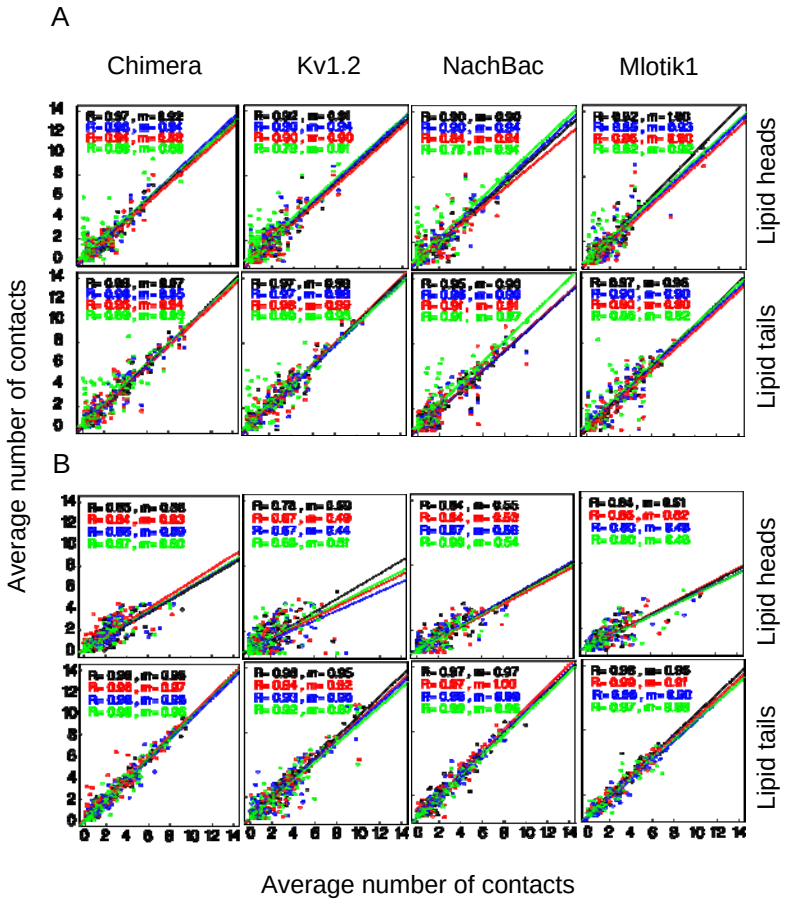

Figure S4. (A) VS domains in tetrameric channels show symmetrical lipid interactions during the simulations. Plotted is the correlation between the average protein side chain-lipid contacts made by one VS domain and those made by each of the other three VS domains in the same tetramer (black, blue and red), and by the VS domain simulated in isolation (green). **(B)** All four VS in the various channels are affected similarly by the absence of lipid phosphate groups. Plotted is the correlation between DOPC and DOTAP contacts for each VS domain in each tetrameric channel. Correlation coefficients (R) and slopes (m) are indicated.

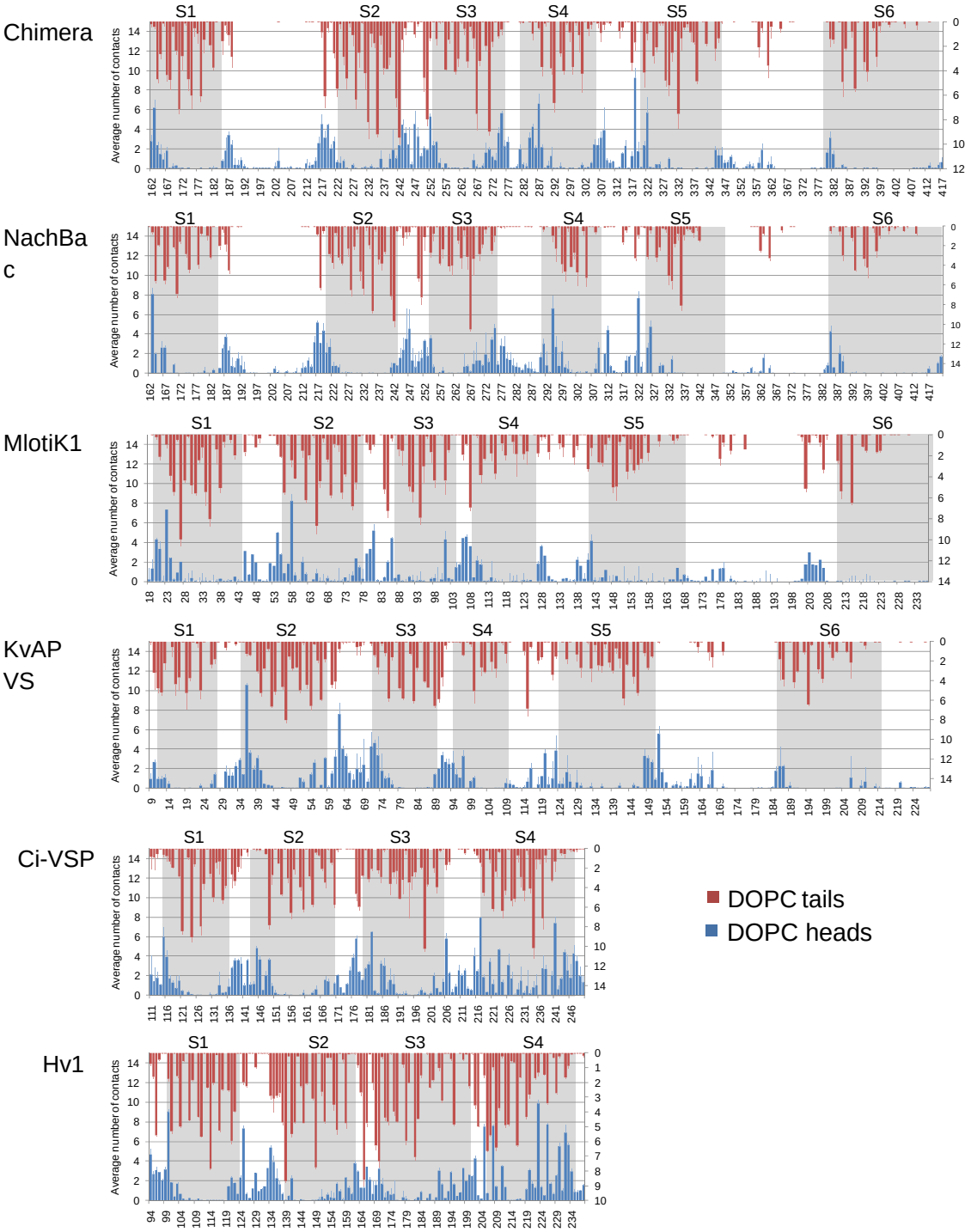

Figure S5. Lipid interaction profiles for various VS homologues. The average (over each MD simulation) of the number of contacts with lipid (DOPC) head groups (blue) and tail groups (red) are shown as a function of residue number for the various VS homologues. The grey blocks indicate the positions of the TM helices. Error bars represent 95% confidence intervals.

Table S1. Details of Molecular Dynamics simulations performed (Related to Methods).

VS homologue	Time (ns)	Bilayer	Repeats	lipids	Water	Counter$^-$ charge ions	Box size (Å)
Chimera	320	DOPC	x3	356	9960	0	15x15x13
	320	DOTAP	x3	389	9979	Cl^- (778)	15x15x13
Kv1.2	320	DOPC	x3	361	9877	Na^+ (40)	15x15x13
	320	DOTAP	x3	389	9995	Cl^- (738)	15x15x13
NachBac	320	DOPC	x3	379	10372	Cl^- (64)	15x15x13
	320	DOTAP	x3	387	9952	Cl^- (838)	15x15x13
MlotiK1	320	DOPC	x3	373	10773	Cl^- (46)	15x15x13
	320	DOTAP	x3	392	9988	Cl^- (830)	15x15x13
KvAP VS	320	DOPC	x3	273	7475	Cl^- (2)	15x15x13
	320	DOTAP	x3	322	8247	Cl^- (646)	15x15x13
Ci$^-$vsp	320	DOPC	x3	286	7832	0	13x13x13
	320	DOTAP	x3	318	8262	Cl^- (636)	13x13x13
Hv1	320	DOPC	x3	285	7833	Cl^- (6)	13x13x13
	320	DOTAP	x3	322	8224	Cl^- 650	13x13x13
Chimera VS	320	DOPC	x3	285	7728	Cl^- (8)	13x13x13
Kv1.2 VS	320	DOPC	x3	286	7728	0	13x13x13
NachBac VS	320	DOPC	x3	290	7818	Cl^- (22)	13x13x13
Mlotik1 VS	320	DOPC	x3	284	7843	Cl^- (10)	13x13x13
KcsA	320	DOPC	x3	275	7525	Cl^- (16)	13x13x13
	320	DOTAP	x3	309	7904	Cl^- (634)	13x13x13
MScl	320	DOPC	x3	405	10942	0	15x15x13
	320	DOTAP	x3	488	12477	Cl^- (976)	15x15x15