Electronic Supplementary Material (ESI) for Molecular BioSystems.
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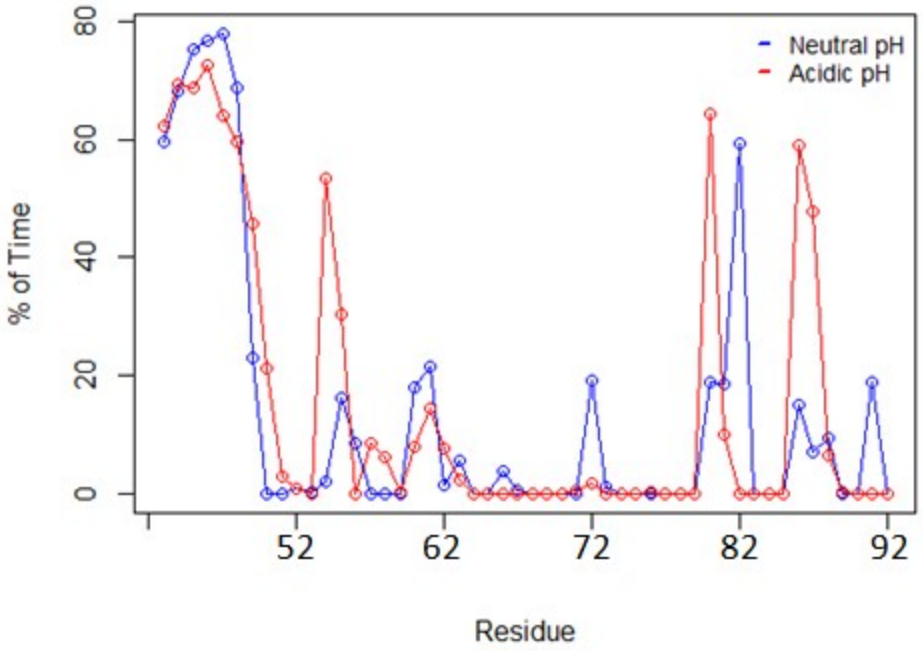
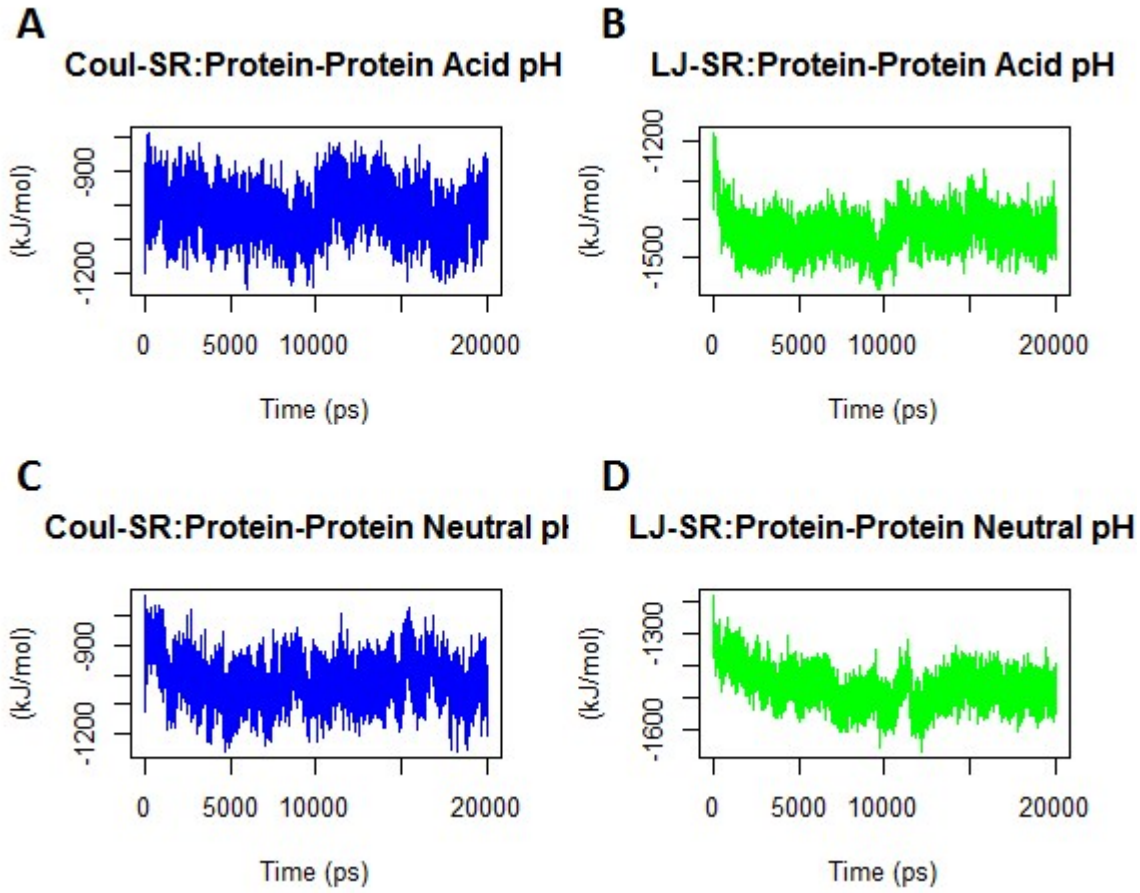
Property	43------51--------61--------71--------81--------91--
seq.	QQDVKKRRSYGNSSDSRYDDGRGPPGNPPRRMGRINHLRGPSPPPMAGGCGR
Aggrescan	----------X----
Aggrescan 3D	----------X------
Metamyl	----------
AMYPdb ->Pafig	----------XX----------
AMYPdb ->Tango	---XXXXXXXXXX----------

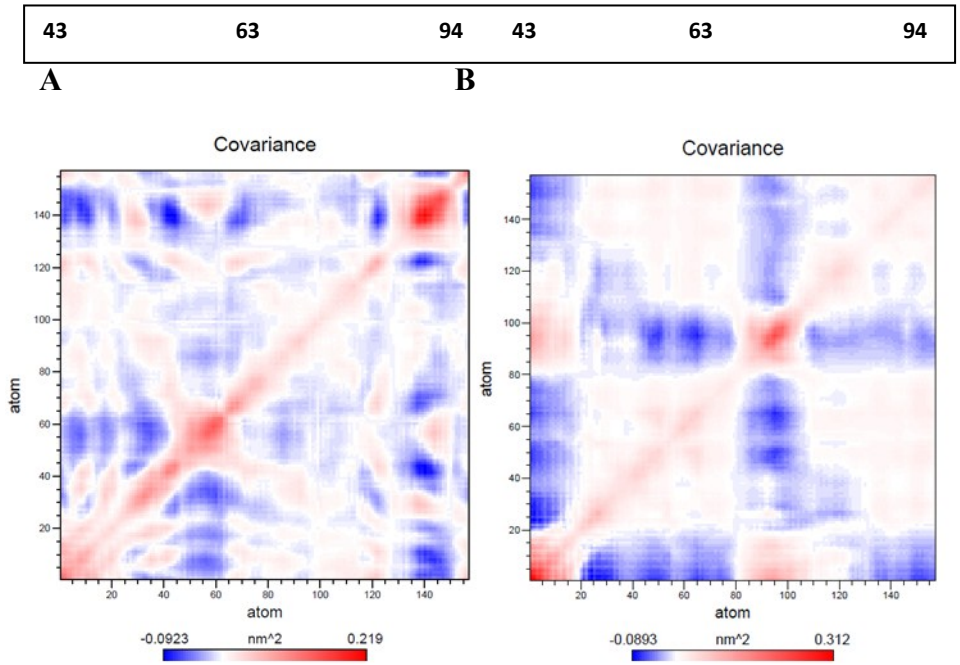
S1 Fig. Prediction of the possible propensity to aggregate of the C-terminal domain of SELK by different tools: Aggrescan[36]; Aggrescan 3D[37]; Metamyl[38]; AMYPdb[39]; Pafig[40]; Tango[41,42,43]



S2 Fig. Helicity evaluation. The figure reports the percentage of time in which each residue remains in helix during MD simulations at neutral (in blu) and acidic (in red) pH.



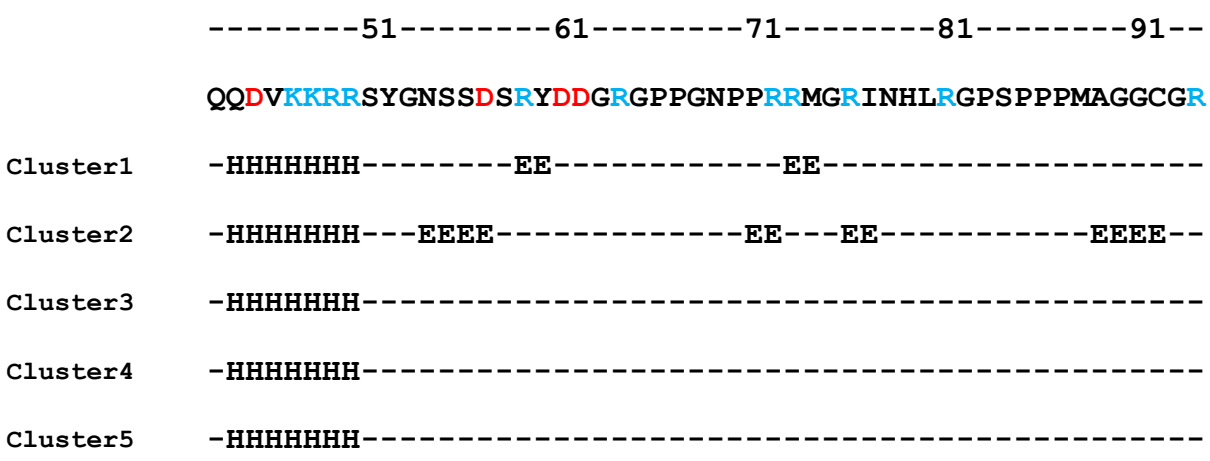
S3 Fig. Evaluation of Lennard Jones (LJ) and Coulomb potential during the MD simulation at neutral (A and B) and acidic pH (C and D).



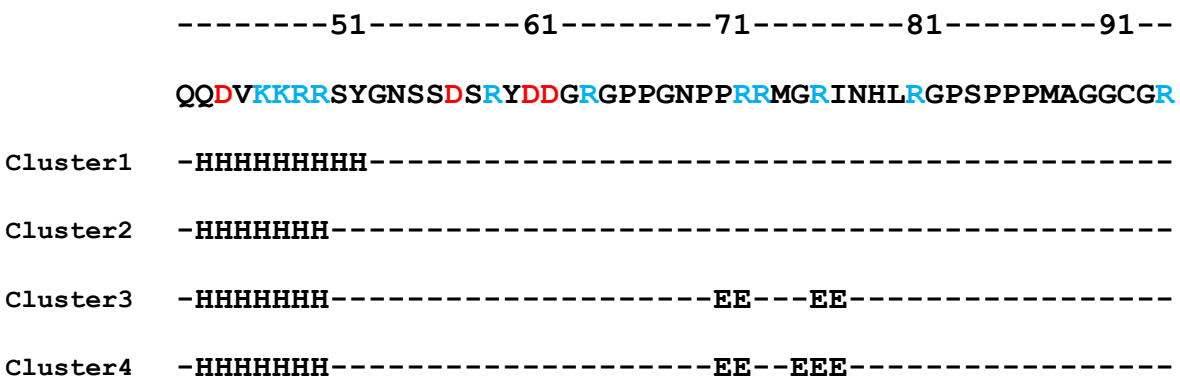
S4 Fig. Covariance matrix for the C-terminal domain of SELK during MD simulation at neutral (A) and acidic (B) pH

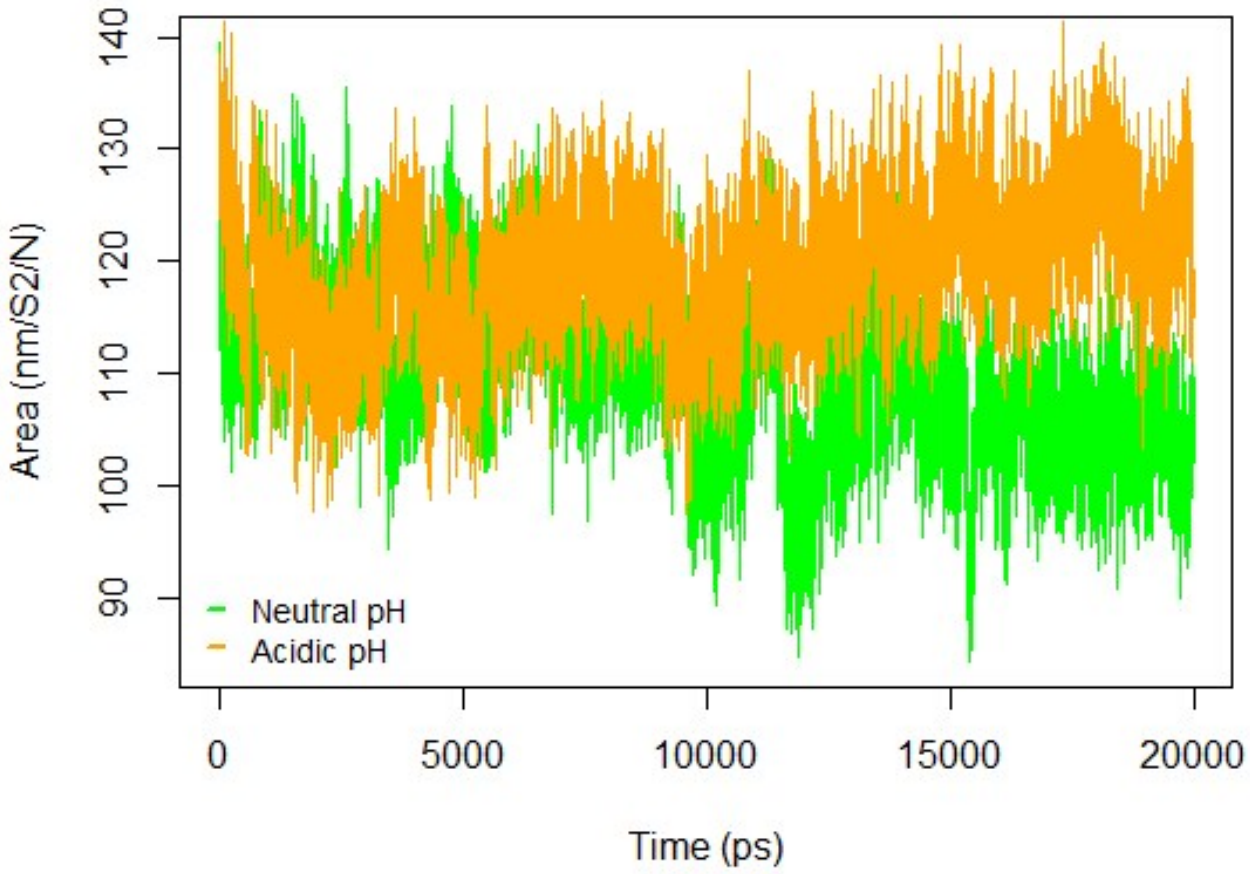
S5 Fig. Secondary structures for the C-terminal region of SELK during MD simulation at neutral (A) and acidic (B) pH where we indicate the residues in α-helix, 3_{10} helix and β-strand with H, G and E, and those in coil with "-".

A



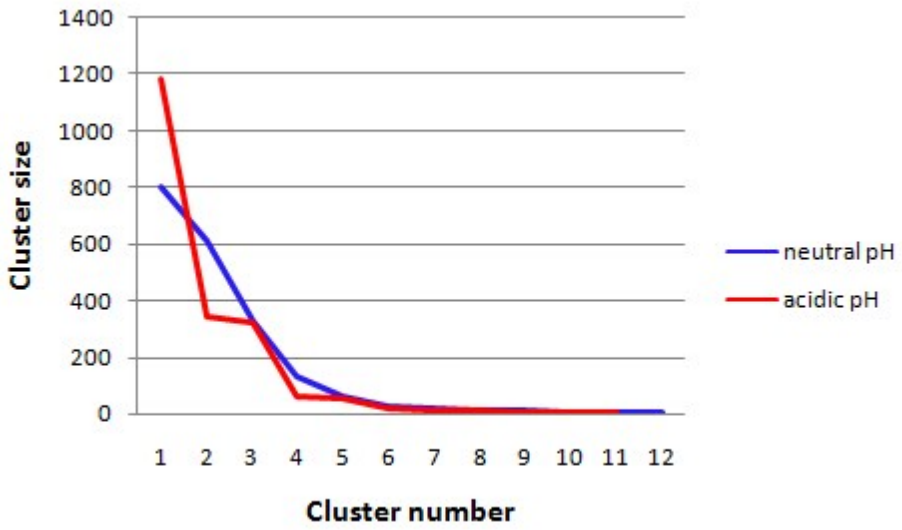
B



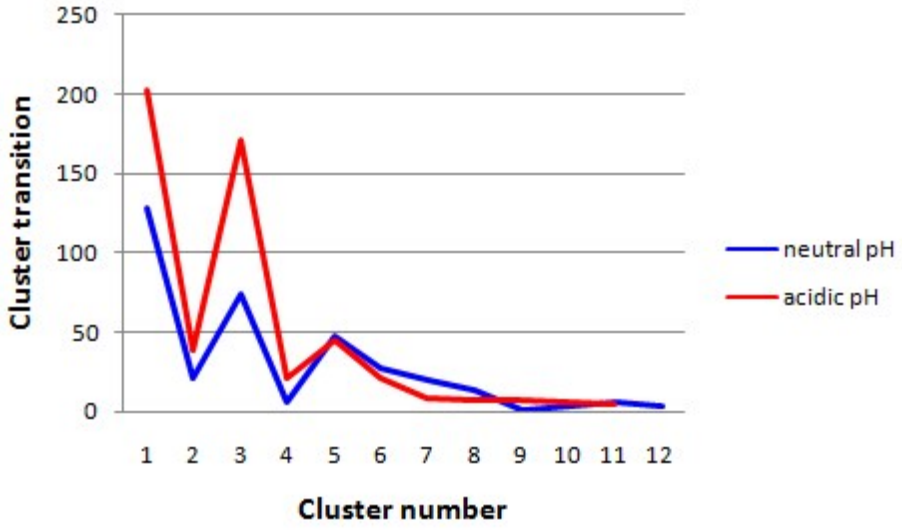


S6 Fig. Evaluation of the Solvent Accessible Area evaluated for the C-terminal domain of SELK during MD simulations at neutral and acidic pH.

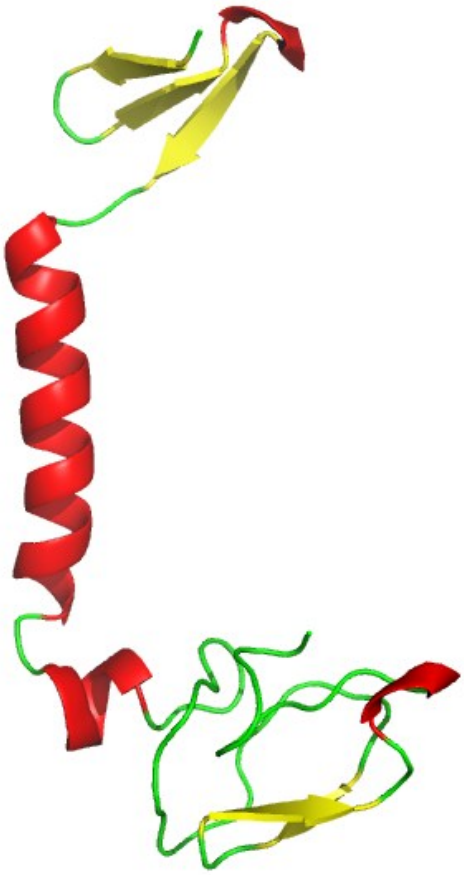
A



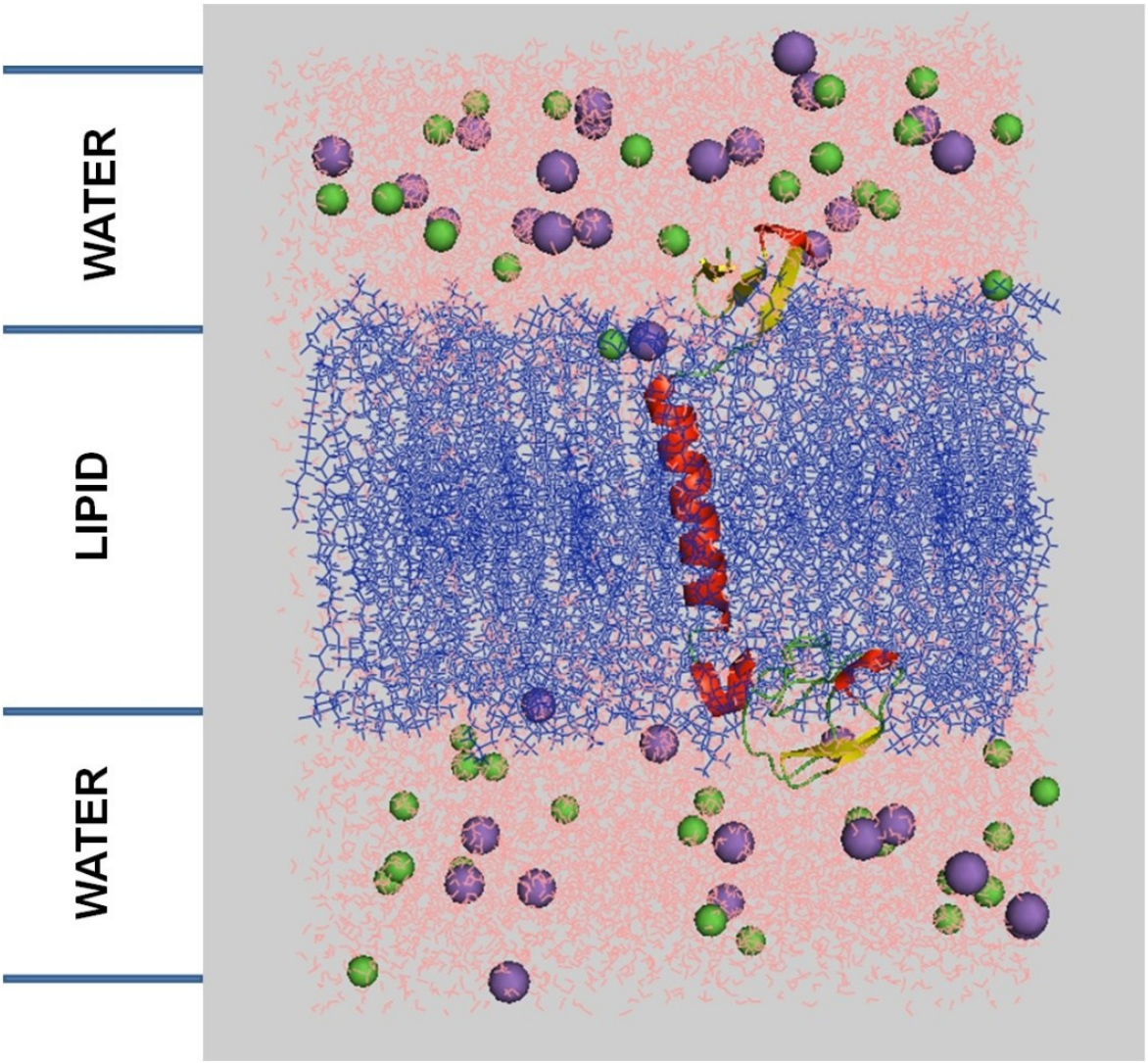
B



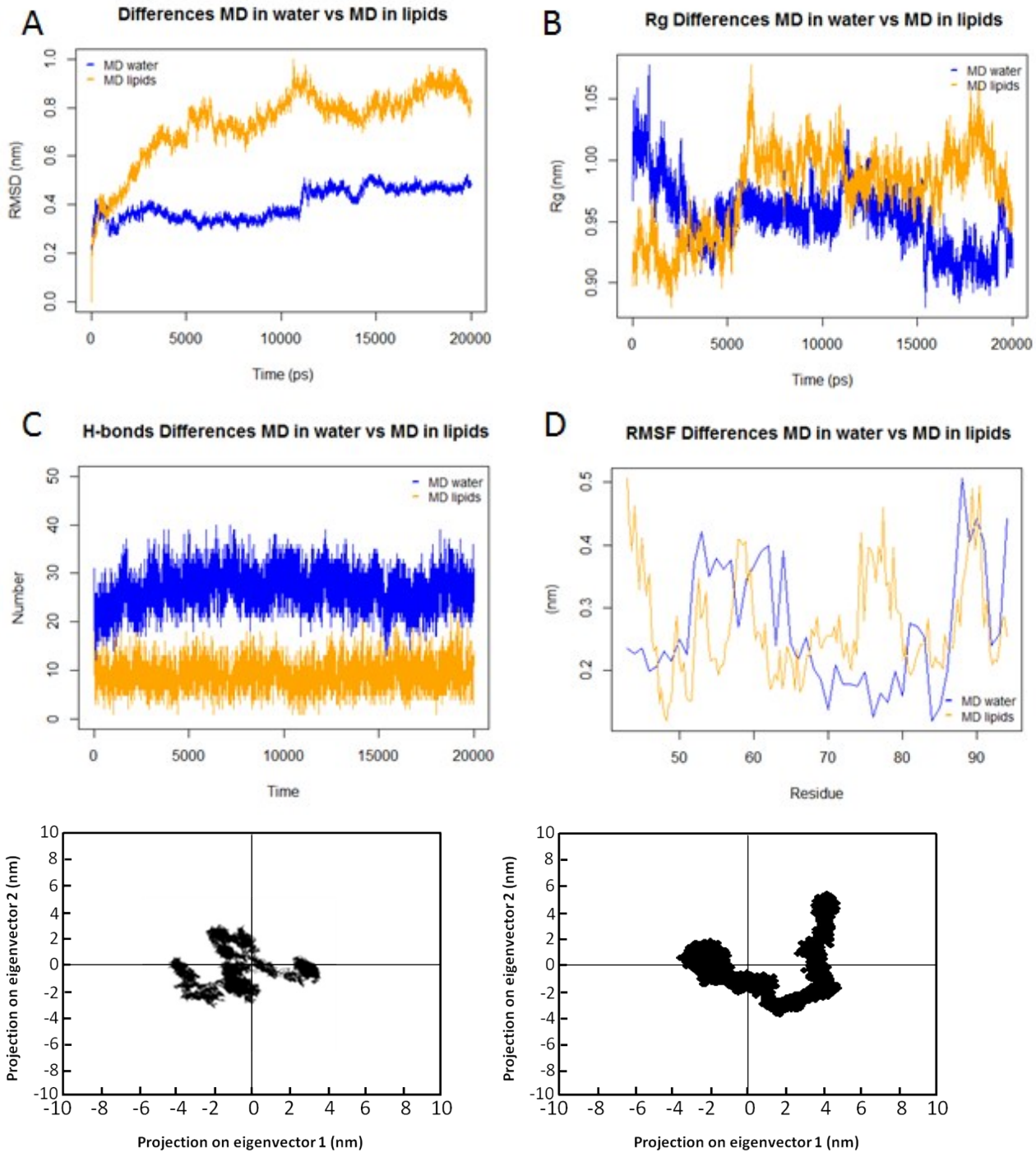
S7 Fig. Evaluation of cluster sizes in terms of conformation number (A) and frequency of transitions (1/ns) (B) for the C-terminal domain of SELK during MD simulation at neutral (in blu) and acidic (in red) pH.



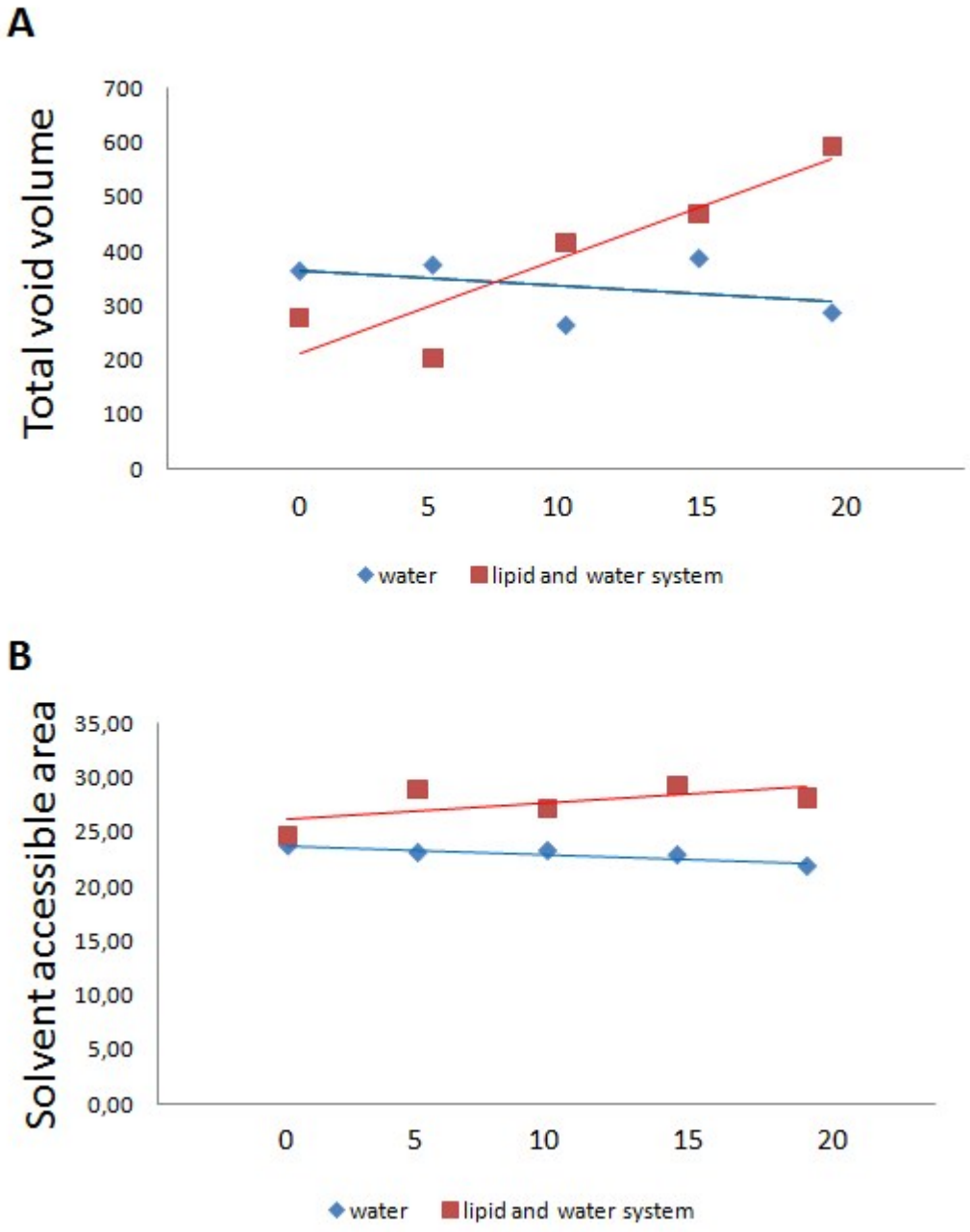
S8 Fig. The complete model obtained for SELK where we show structural details as helices and the β-strands in red and yellow, respectively



9S Fig. The complete model of SELK in membrane. POPC are shown as lines and colored in blue; the protein labeled as cartoon and colored by secondary structure elements with helices,β-strands and coils in red, yellow and green, respectively. The water molecules are depicted as lines and colored in salmon whereas two ions, Na^{+} and Cl^{-}, are shown by violet and green spheres.

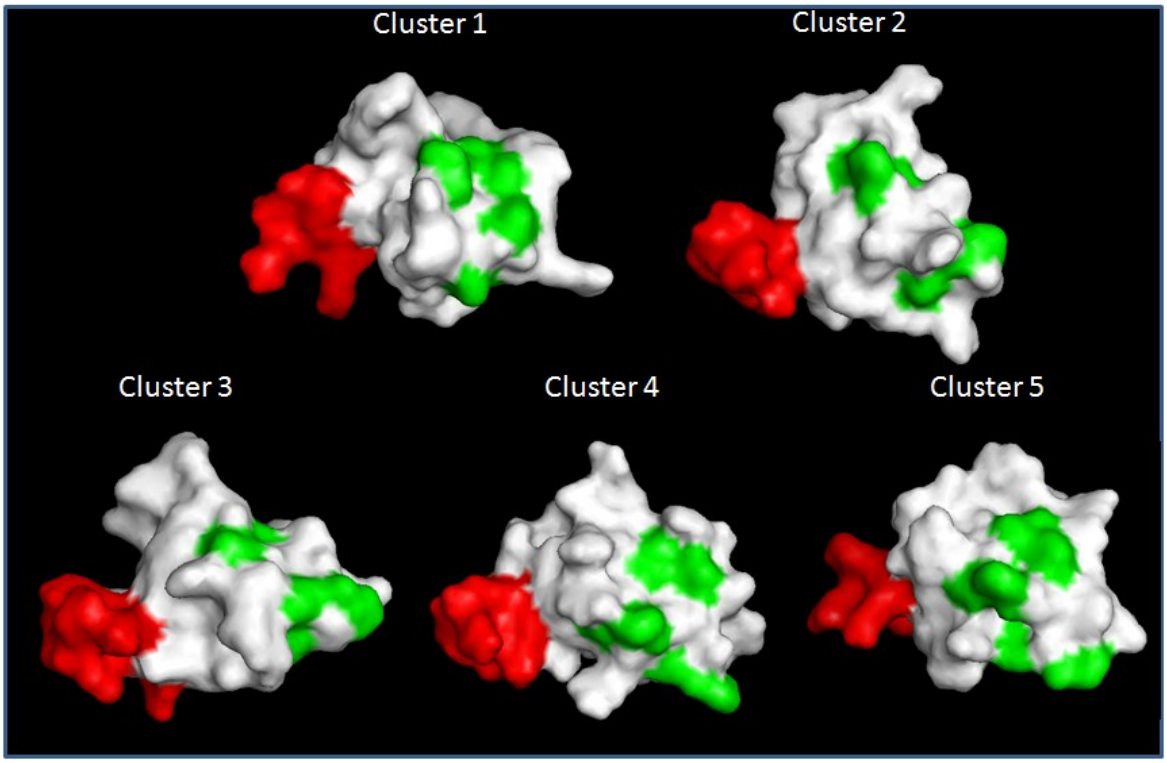


S10 Fig. A) RMSD plot, B Gyration Radius plot, C) H-bond plot, and D) RMSF plot for the C-terminal domain of SELK during MD simulations in water (in blue) and in lipids (in orange). Moreover, the projection plots for the C-terminal domain of SELK during MD simulations in water (E) and in lipids (F).

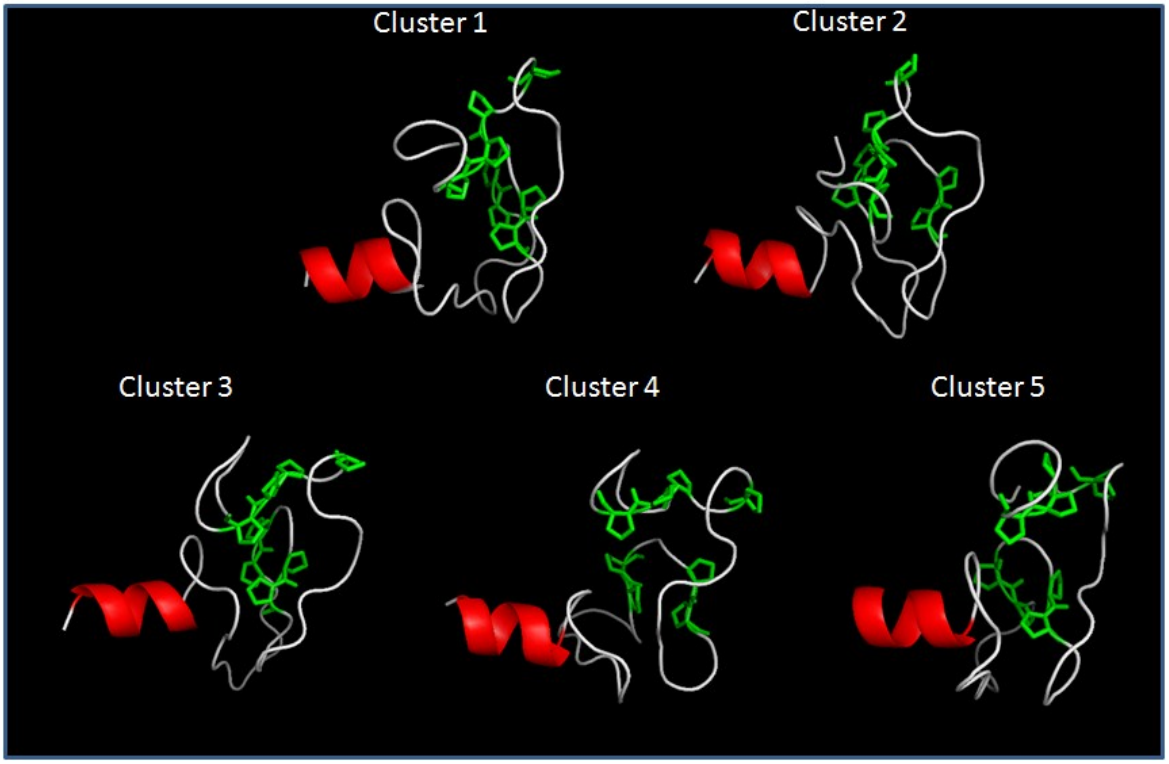


S11 Fig. Total void volume (A) and solvent accessible area (B) evaluated on the structure of the C-terminal domain of SELK free in water and in lipid and water system after 0, 5, 10, 15 and 20 ns of MD simulation.

A



B



S12 Fig. Representations of five clusters by surface (A) and ribbon (B) representations where we report the helix region and the prolines in red and green, respectively.

S1 Table. Total number of H-bonds involving the charged residues between them (R_charged) and with water molecules (SOLV.) at neutral (A) and acidic (B) pH.

A

	Specific H-Bonds Charged Residues Neutral pH									
	0ns		5ns		10ns		15ns		20ns	
	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged
45_ASP	8	2	5	1	7	1	7	1	6	1
47_LYS	2	1	3	0	2	1	2	0	2	0
48_LYS	7	0	3	0	3	0	4	0	3	0
49_ARG	5	2	3	1	2	1	4	1	5	1
50_ARG	4	1	3	1	4	1	7	0	5	1
57_ASP	4	3	7	0	9	0	7	0	8	0
59_ARG	5	3	7	1	5	1	9	0	8	1
61_ASP	2	2	10	0	9	0	9	0	6	2
62_ASP	5	1	7	1	6	0	7	1	6	2
64_ARG	6	1	8	0	8	0	6	1	4	2
72_ARG	3	0	1	2	4	1	4	2	3	2
73_ARG	6	1	3	1	5	0	8	0	3	1
76_ARG	4	0	4	1	6	1	4	1	2	0
81_ARG	5	0	5	0	8	0	8	0	9	0
94_ARG	7	0	4	0	5	0	2	0	6	0

B

	Specific H-Bonds Charged Residues Acidic pH									
	0ns		5ns		10ns		15ns		20ns	
	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged	SOLV.	R. Charged
45_ASP	6	1	4	0	4	0	7	2	6	1
47_LYS	3	1	3	0	4	0	2	0	2	0
48_LYS	6	0	4	0	6	0	5	1	5	0
49_ARG	4	1	3	1	1	3	8	1	7	1
50_ARG	3	1	6	0	1	1	4	2	6	1
57_ASP	6	2	6	1	7	2	5	1	4	1
59_ARG	4	1	4	2	5	2	2	2	6	1
61_ASP	2	2	9	1	7	1	5	0	8	1
62_ASP	11	1	9	1	13	0	10	1	6	0
64_ARG	7	0	7	0	6	0	9	0	8	0
72_ARG	5	0	5	1	7	1	3	1	7	1
73_ARG	8	1	6	1	3	1	6	0	6	0
76_ARG	2	0	4	2	4	2	3	1	6	1
81_ARG	5	0	7	0	7	0	7	0	8	0
94_ARG	2	0	5	0	5	0	6	0	6	0

S2 Table. Total number of H-bonds between HUB residues and the rest of the C-terminal region during MD simulation at neutral (A) and acidic (B) pH.

A)

HUB	0 ns	5 ns	10 ns	15 ns	20 ns
69_ASN	1	3	2	3	3
87_PRO	0	0	0	1	1
60_TYR	2	2	2	1	2
71_PRO	0	0	0	0	0
55_SER	1	1	2	0	1

B)

HUB	0 ns	5 ns	10 ns	15 ns	20 ns
60_TYR	2	2	3	1	4
52_TYR	1	1	2	1	3
79_HIS	0	2	1	2	1
94_ARG	0	1	2	0	1
87_PRO	0	1	2	1	2

S3 Table. ASA evaluation for HUB Residues during MD simulation at neutral (A) and acidic (B) pH.

A)

HUB	0 ns	5 ns	10 ns	15 ns	20 ns
69_ASN	0.000000	0.000000	0.000000	0.006830	0.006830
87_PRO	0.063423	0.056376	0.133893	0.000000	0.000000
60_TYR	0.065506	0.196518	0.065506	0.042111	0.135691
71_PRO	0.253692	0.014094	0.042282	0.211410	0.422820
55_SER	0.827604	0.034128	0.051192	0.017064	0.000000

B)

HUB	0 ns	5 ns	10 ns	15 ns	20 ns
60_TYR	0.084222	0.004679	0.056148	0.088901	0.018716
52_TYR	0.196518	0.510011	0.664418	0.435147	0.154407
79_HIS	0.703616	0.126431	0.120934	0.159413	0.142922
94_ARG	0.829540	0.515188	0.414770	0.611240	0.519554
87_PRO	0.035235	0.077517	0.105705	0.140940	0.112752

S4 Table. Comparison between the MD simulations conducted at neutral pH on the C-terminal domain of SELK and various globular proteins of similar length. We report the protein name, PDB codes, protein class, number of clusters using a cut-off = 0.25 and 0.15 nm, the final RMSD value (nm), the mean number of H-bonds, and the final Rg values (nm).

Protein	**PDB code**	**Protein class**	**number of clusters using a cut-off of 0.25 nm**	**number of clusters using a cut-off of 0.15 nm**	**Final RMSD value (nm)**	**Mean number of H-bonds**	**Final Rg value (nm)**
C-terminal domain of SELK		IDP	12	47	0.5	28	0.95
Kappa-scoloptoxin-Ssm1a	2M35	alpha	3	8	0.19	37	0.93
Pheromone en-1	2NSV	alpha	0	2	0.3	41	0.97
Antifungal protein from aspergillus giganteus	1AFP	beta	0	9	0.3	35	0.88
Antifungal protein paf from penicillium chrysogenum	2KCN	beta	5	26	0.42	35	1
Brazzein	2LY5	alpha-beta	3	15	0.18	34	0.99
Defensin-like protein 1	2N2Q	alpha-beta	2	11	0.29	38	1