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

Electronic Supplementary Information

The Ebola virus protein VP40 hexamer enhances the clustering of $PI(4,5)P_2$ lipids in the plasma membrane

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Table S1: Lipid composition used in the simulations. Lipid abbreviations are -POPC: 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine, POPE: 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine, PSM: sphingomyelin(SM), POPS: 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-Serine, PIP_2: phosphatidylinositol-4, 5-biphosphate, CHOL: Cholesterol.

a) The lipid composition for the membrane-protein system.

Lipid type	Outer (Upper)	%	Inner (Lower)	%
CHOL	140	20	160	21
POPC	290	41	85	11
POPE	60	8	275	37
POPS	25	4	125	16
PIP_2	30	4	75	10
PSM	167	23	40	5

b) The lipid composition for the membrane only system, in the absence of the protein.

Lipid type	Outer (Upper)	%	Inner (Lower)	%
CHOL	140	20	160	21
POPC	290	41	85	11
POPE	60	8	275	37
POPS	25	4	125	16
PIP_2	30	4	75	10
PSM	155	22	40	5

Table S2: Summary of simulations used in the present work.

Run	Simulation	Length of Simulation
	Membrane-VP40 hexamer simulation	
0	CGMD	30 μs
1	CGMD (Elastic network removed for top CTDs)	10 μs
2	CGMD (starting conformation obtained from Run 4)	10 μs
3	CGMD (repeat of Run 0)	10 μs
4	All-atom MD (for Run 2)	10 ns
	Membrane-only simulation	
5	CGMD simulation of membrane only system	30 μs

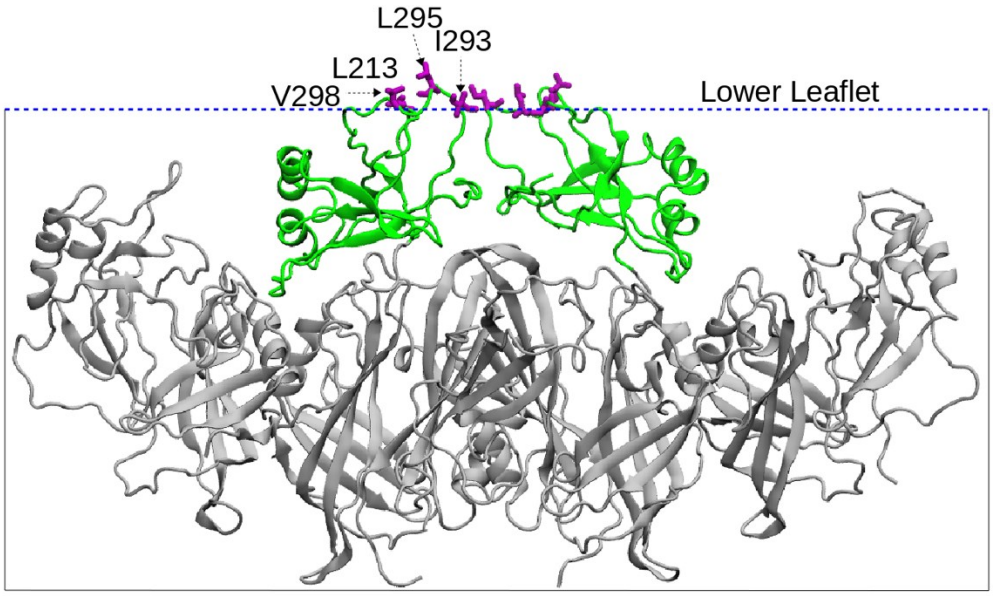

Figure S1: VP40 hexamer-membrane setup showing the hydrophobic residues in the CTDs that penetrate the plasma membrane.

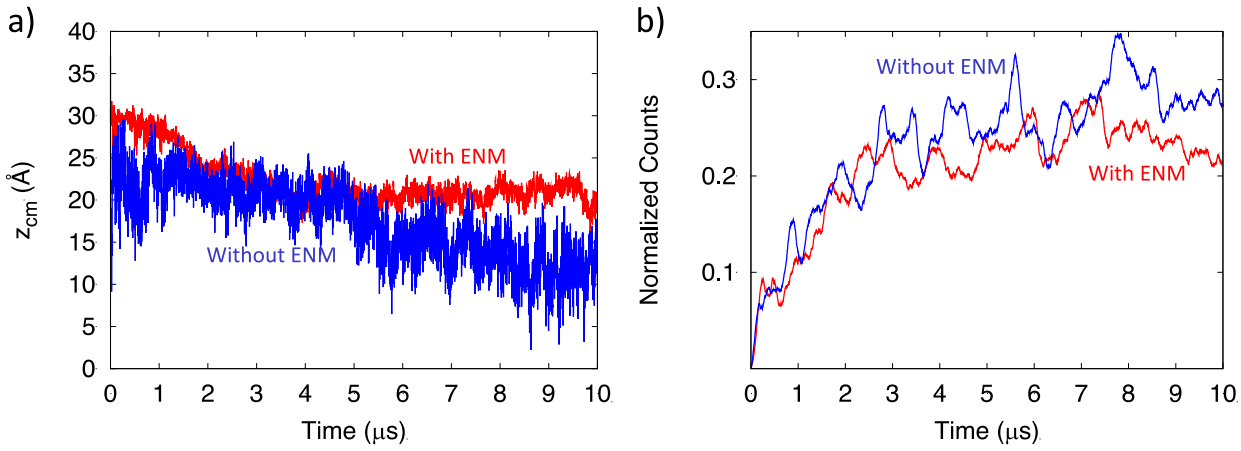

Figure S2: a) Center of mass distance between the phosphate beads of the lower leaflet of the plasma membrane and the backbone beads for the protein with and without ENM constraints in the interacting CTDs. b) Normalized counts of PIP_2 around the protein for the membrane-protein system with and without ENM constraints in the CTDs.

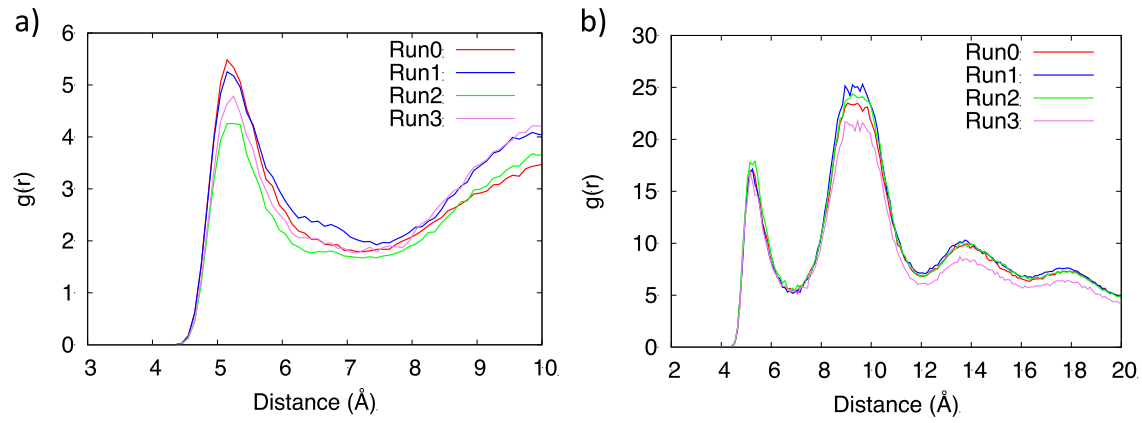

Figure S3. a) Radial pair distribution between hexamer and PIP_2 lipids during 10 μs b) self-clustering of PIP2 lipids. (Run0: first 10 μs from the 30 μs simulation, Run1: without elastic network constraints in the middle CTDs, Run2: different initial conformation obtained after 10-ns of all-atom simulation, Run3: Rerun of Run0).

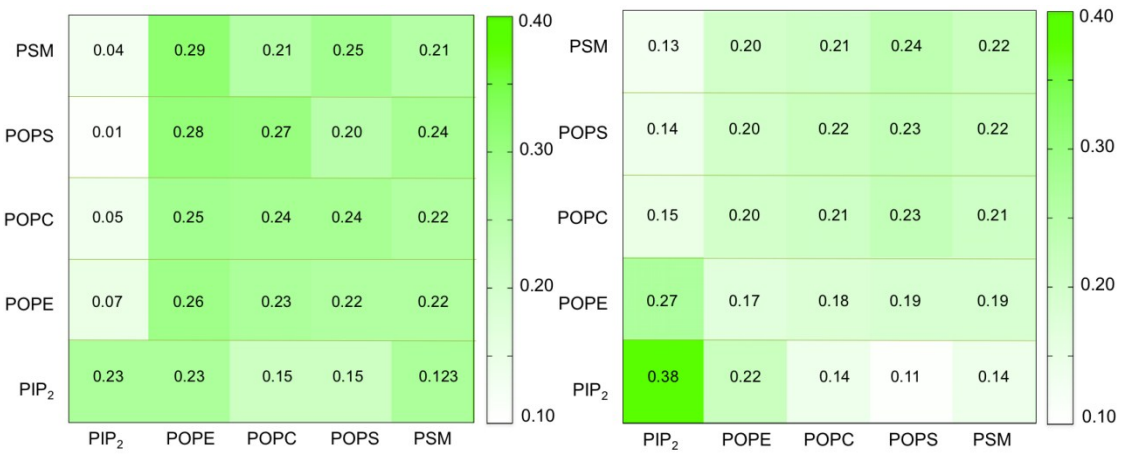

Figure S4. Fractional interaction matrix of lipids in the lower leaflet of the plasma membrane in the presence of the VP40 hexamer, a) for the first solvation layer (within 7Å) and b) for the second solvation layer (between 7-12Å).

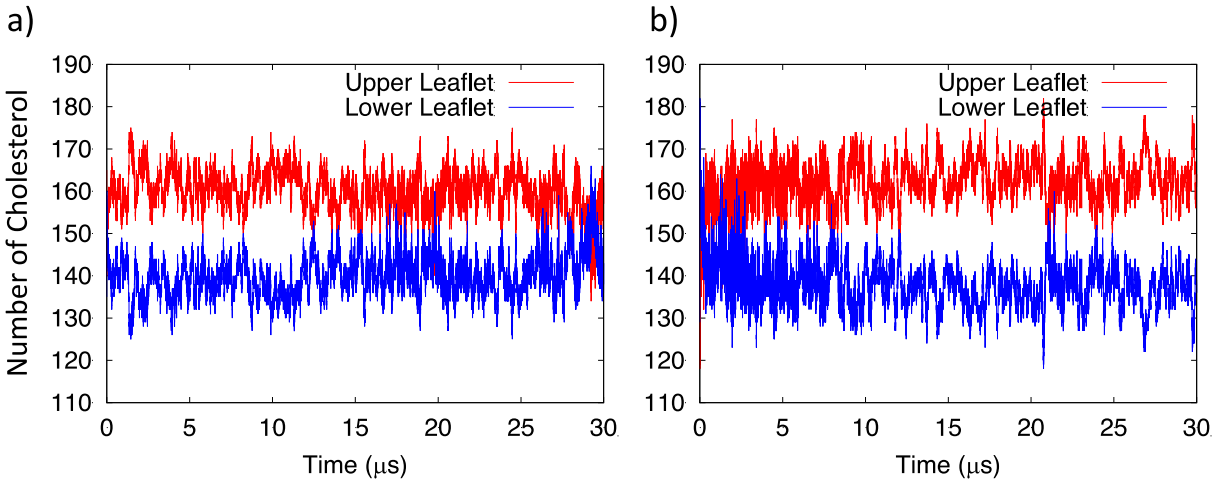

Figure S5. Number of cholesterol molecules in the upper and lower leaflet of the PM as a function of time. a) protein-membrane system and b) membrane-only, no protein system.

Movie S1:

Movie showing the VP40-hexamer interacting with the plasma membrane lower leaflet. To show cholesterol flip-flops, cholesterols head group (ROH) beads at the lower leaflet are colored blue and at the upper leaflet are colored red at time $t = 0$.