Electronic Supplementary Information

Effect of polymer coating on nanoparticles interaction with lipid membranes by coarse-grained molecular dynamics simulations

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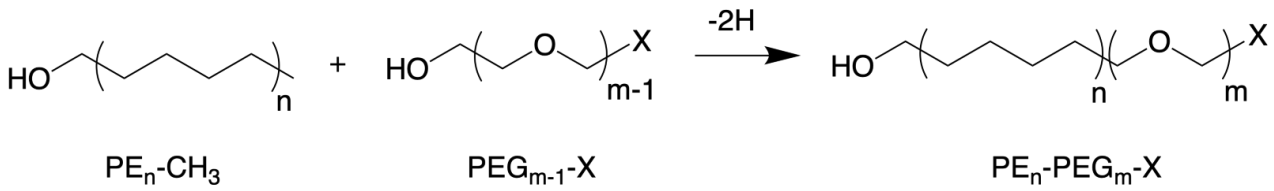

Scheme S1. Formation of mixed PE_n-PEG_m-X chains.

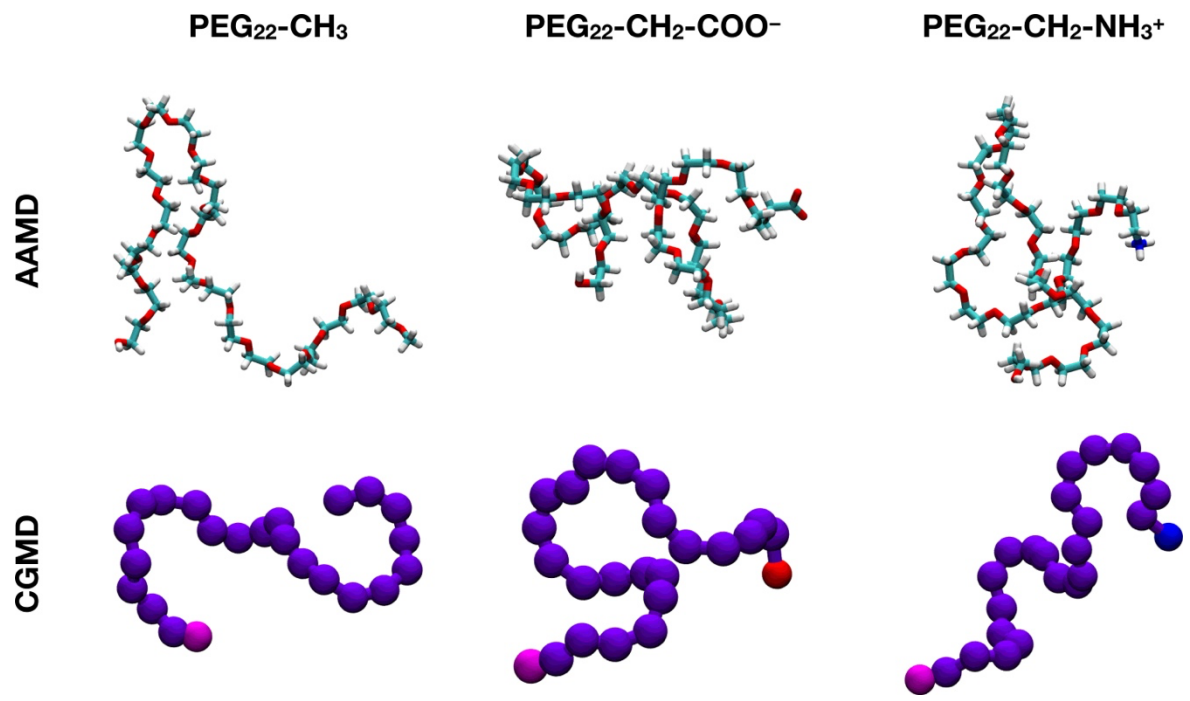

Fig. S1. Last-frame snapshots of a single PEG_{22}-X chain in a 0.15 M NaCl water solution from 100 ns AAMD and 30 μs CGMD simulations. In AAMD, carbon is shown in cyan, oxygen in red and hydrogen in white. In CGMD, the SP2 bead is shown in magenta, the EO one in violet, the Qa one in red and the Qd one in blue. Water and ions are not shown for clarity.

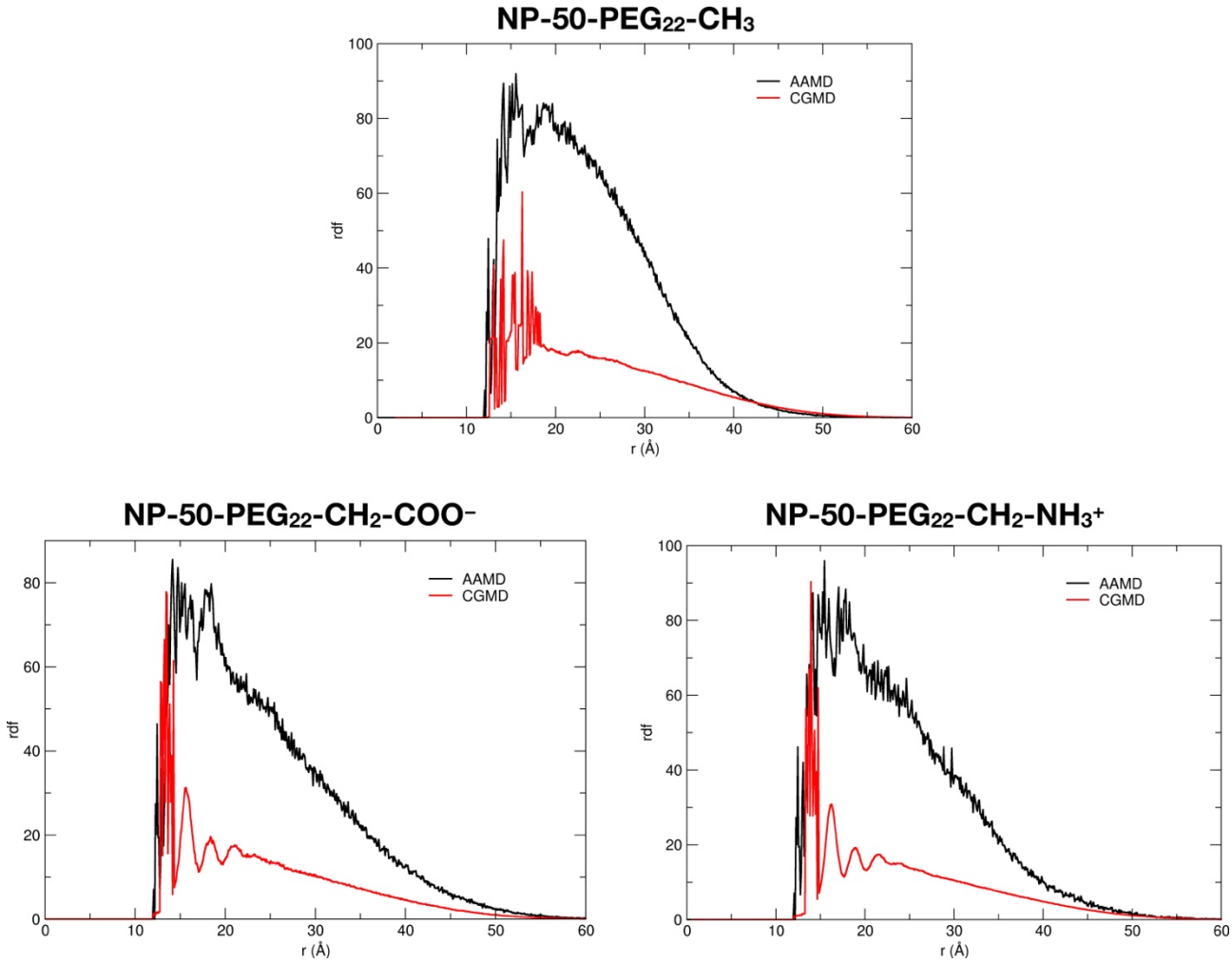

Fig. S2. Average radial distribution functions of the PEG chains with respect to the center of the NP, on the last 1 μs of 10 μs CGMD simulations of NP-50-PEG$_{22}$-X systems in water at 303 K and 1 atm (in red) and from the last 10 ns of 30 ns AAMD simulations of the corresponding systems (in black).

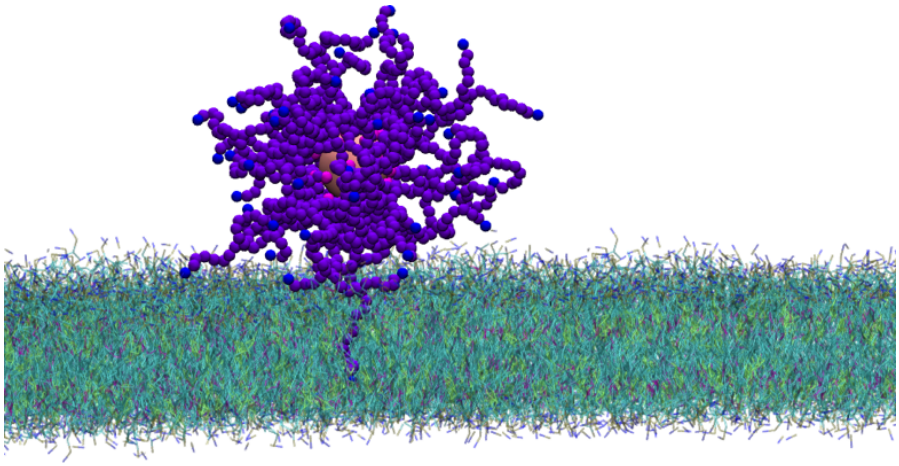

Fig. S3. Final snapshot of the 1 μs CGMD simulation of the MEMB/NP-50-PEG_{22}-CH_2-NH_3^+ system, starting from the structure at 5 μs of the original simulation and assigning different initial velocities. For the polymer chains, the SP2 bead is shown in magenta, the EO one in violet and the Q_d one in blue. The NP is shown in pink. For the membrane, POPC is shown in cyan and cholesterol in green. POPC choline is represented in blue, phosphate in tan and C=C bead in magenta. Water and ions are not shown for clarity.

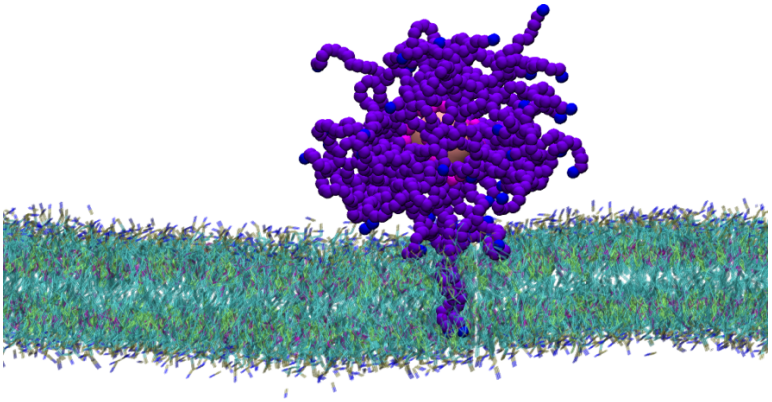

Fig. S4. Final snapshot of the 5 μs CGMD simulation of the MEMB/NP-50-PEG_{22}-CH_2-NH_3^+ system, starting from the equilibrated structure of the original simulation and assigning different initial velocities. For the polymer chains, the SP2 bead is shown in magenta, the EO one in violet and the Q_d one in blue. The NP is shown in pink. For the membrane, POPC is shown in cyan and cholesterol in green. POPC choline is represented in blue, phosphate in tan and C=C bead in magenta. Water and ions are not shown for clarity.

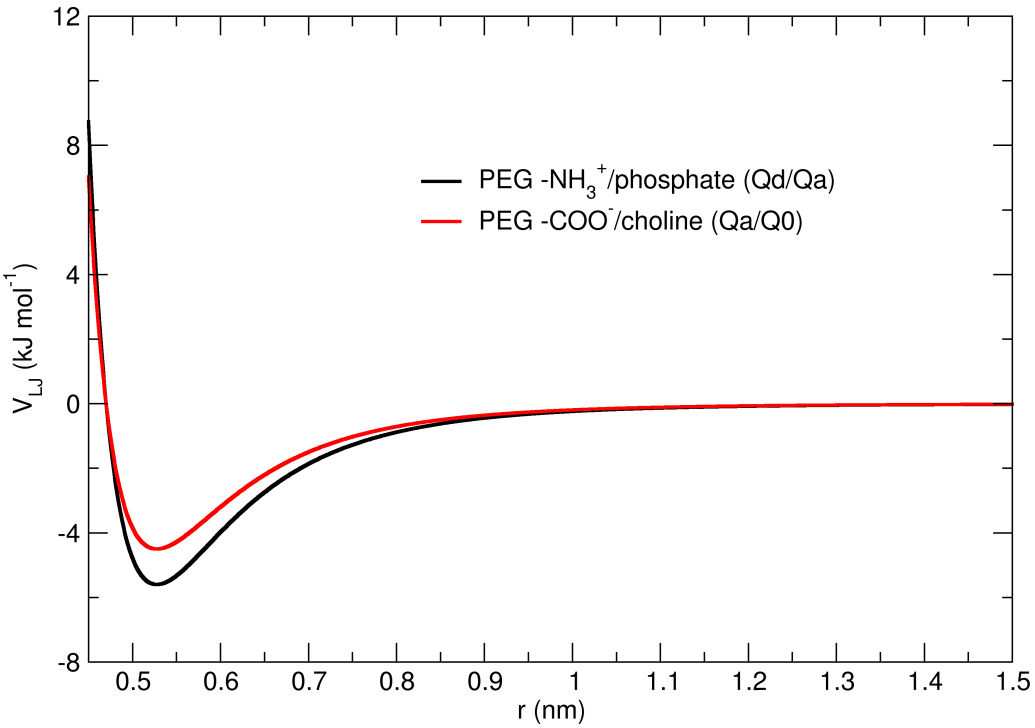

Fig. S5. Lennard-Jones interaction profiles of the Qd/Qa and Qa/Q0 bead pairs.

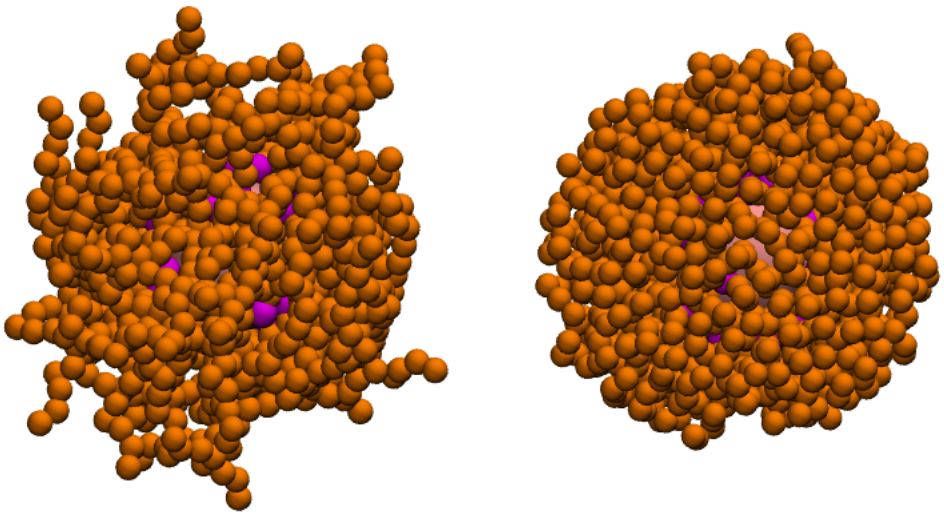

Fig. S6. Initial (left) and final (right) configuration from the 5 μs CGMD simulation of the NP coated with 50 PE_{22}-CH_3 chains in water at 303 K and 1 atm. The PE monomer beads are shown in orange, the anchoring -OH group bead in magenta and the NP in pink. Water is hidden for clarity.

Table S1.PE-PE and PE-water non-bonded interaction energies computed on the last 1 μs of the 5 μs CGMD simulation of the NP-50-PE_{22}-CH_3 system in water at 303 K and 1 atm.

System	**Non-bonded interaction energy (kcal mol^{-1})**	
	PE-PE	**PE-water**
NP-50-PE_{22}-CH_3	-4270 (±29)	-663 (±29)

Table S2. Average root-mean-square deviation (RMSD) and relative standard deviation of the chains' SP2 beads position on the last 1 μs of 5 μs CGMD simulations of MEMB/NP-50-PEG_{22}-X, MEMB/NP-50-PE_{22}-CH_3 and MEMB/NP-50-PE_{11}-PEG_{11}-X systems.

System	RMSD (±st. dev.) [nm]
NP-50-PEG_{22}-CH_3	0.835 (±0.093)
NP-50-PEG_{22}-CH_2-COO^-	0.853 (±0.066)
NP-50-PEG_{22}- CH_2-NH_3^+	0.852 (±0.070)
NP-50-PE_{22}-CH_3	0.710 (±0.095)
NP-50-PE_{11}-PEG_{11}-CH_3	0.777 (±0.145)
NP-50-PE_{11}-PEG_{11}- CH_2-COO^-	0.836 (±0.126)
NP-50-PE_{11}-PEG_{11}- CH_2-NH_3^+	0.782 (±0.116)

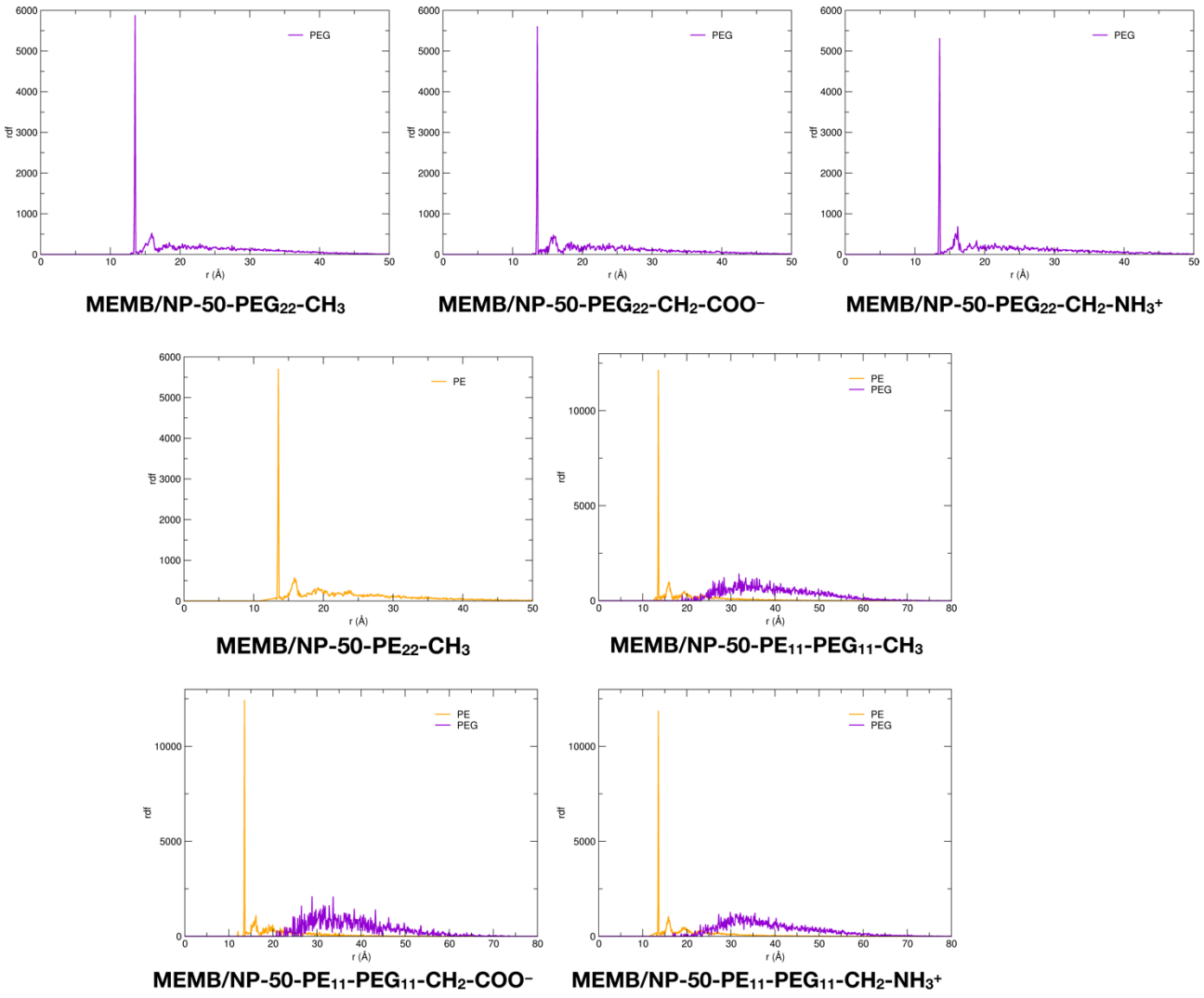

Fig. S7. Polymer chains average radial distribution functions with respect to the center of the NP, on the last 1 μs of 5 μs CGMD simulations of MEMB/NP-50-PEG_{22}-X, MEMB/NP-50-PE_{22}-CH_3 and MEMB/NP-50-PE_{11}-PEG_{11}-X systems at 300 K and 1 atm.

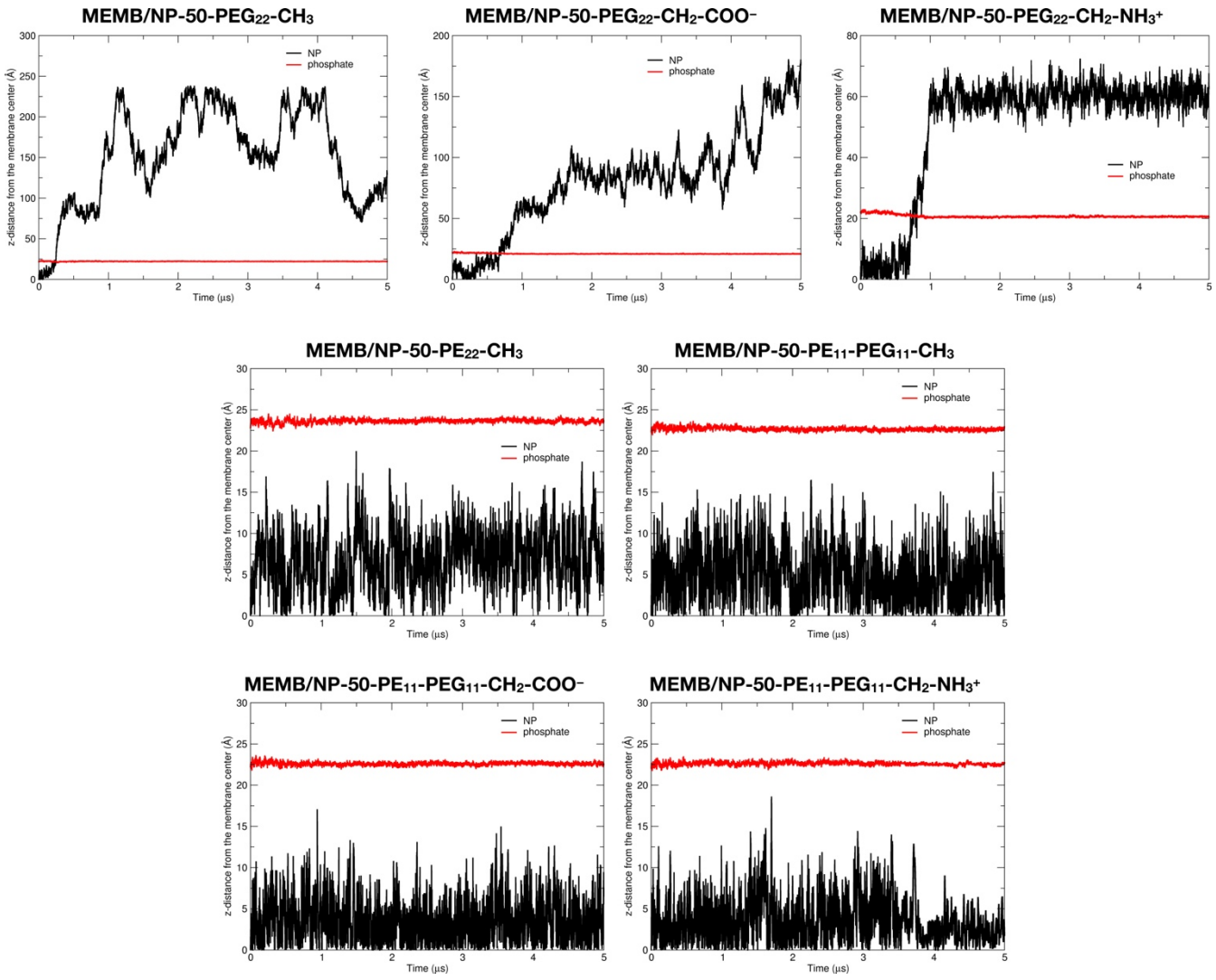

Fig. S8. Time evolution of the *z*-position of the NP center (black) and that of the POPC phosphate groups (red) along the 5 μs MD simulation of the MEMB/NP-50-PE_{22}-CH_3, MEMB/NP-50-PEG_{22}-X and MEMB/NP-50-PE_{11}-PEG_{11}-X systems.

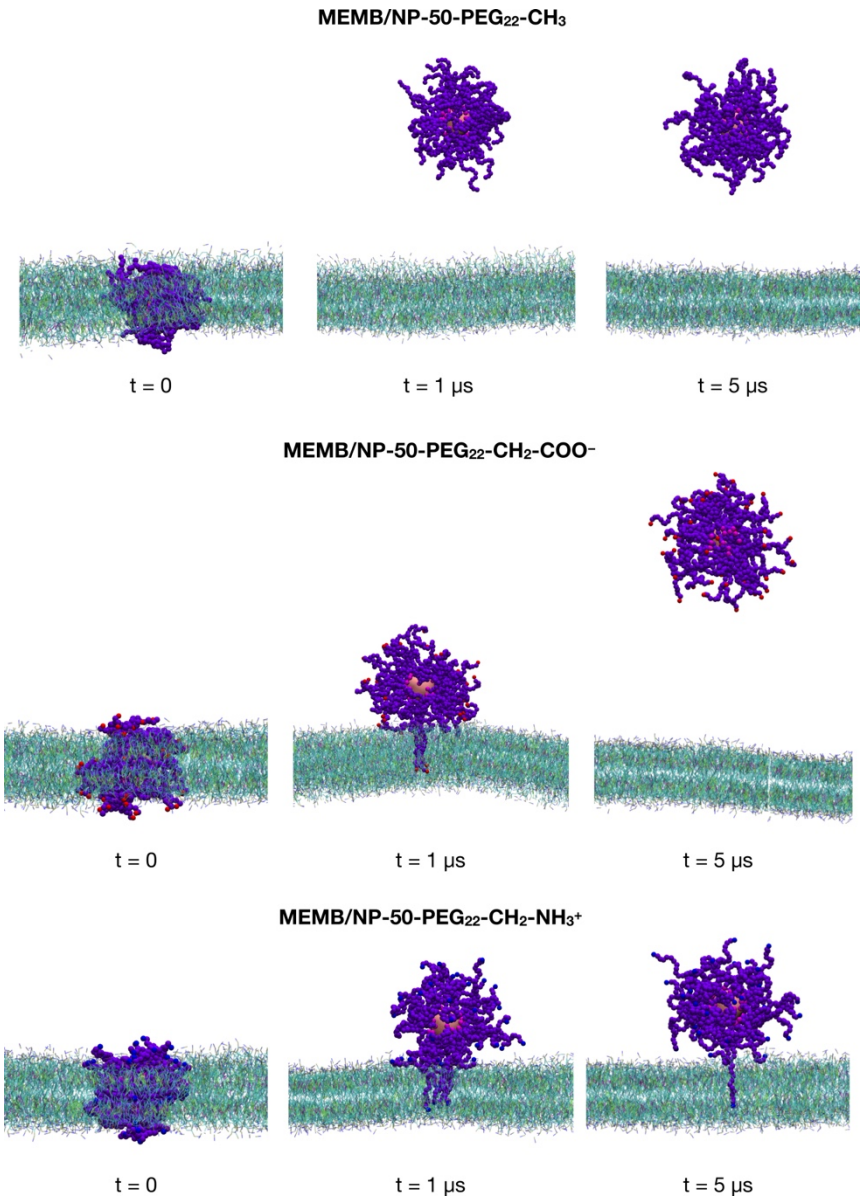

Fig. S9. Dynamic evolution of PEGylated NPs' position relative to the membrane along the 5 μs MD simulations. For the polymer chains, the SP2 bead is shown in magenta, the EO one in violet, the C1 in orange, the Qa one in red and the Qd one in blue. The NP is shown in pink. For the membrane, POPC is shown in cyan and cholesterol in green. POPC choline is represented in blue, phosphate in tan and C=C bead in magenta. Water and ions are not shown for clarity.

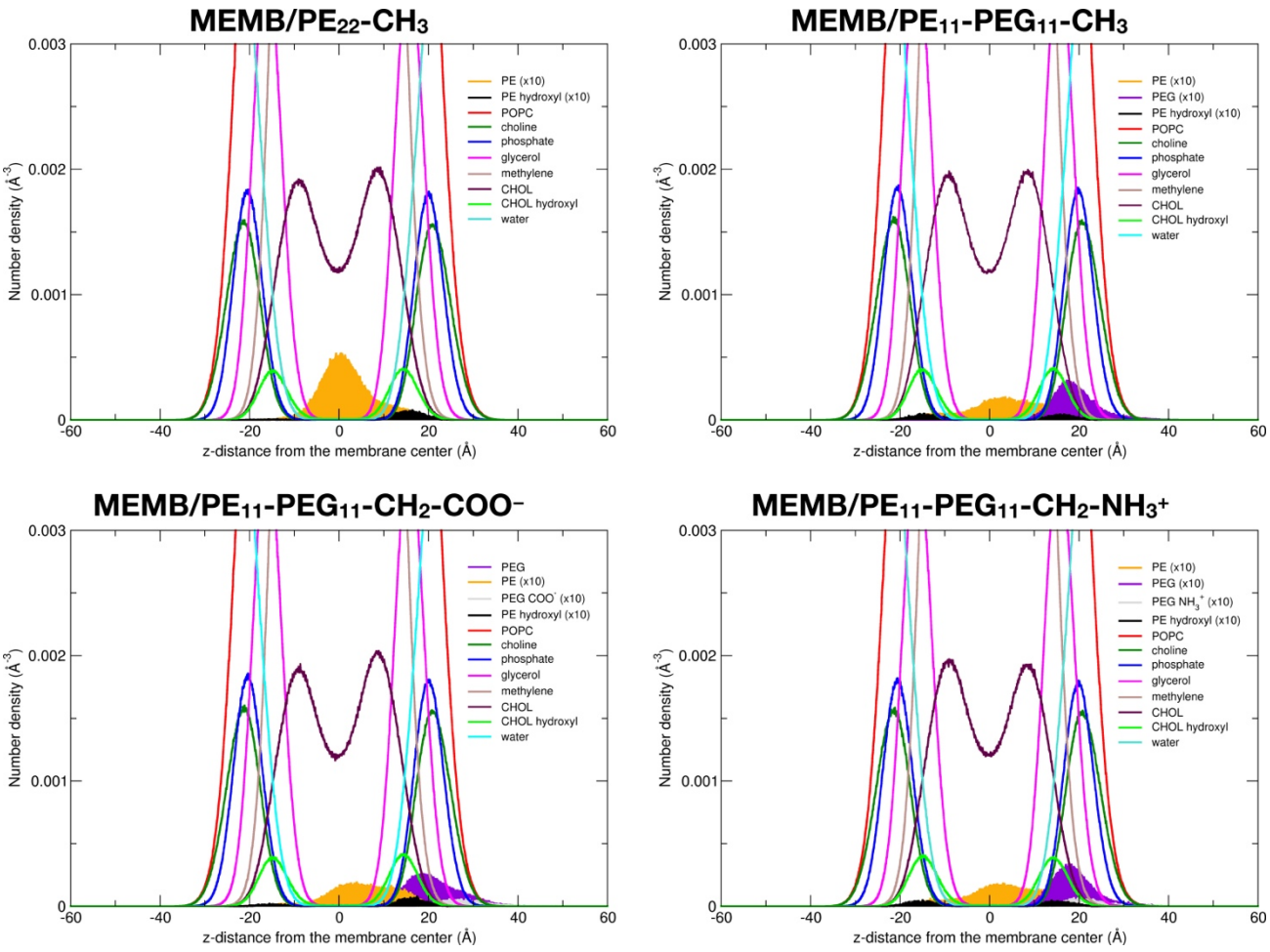

Fig. S10. Number density profiles as functions of the *z*-distance from the membrane center and averaged over the last 1 μs of the 5 μs MD simulations of a single PE_{22}-CH_3, PE_{11}-PEG_{11}-CH_3, PE_{11}-PEG_{11}-CH_2-COO^- or PE_{11}-PEG_{11}-CH_2-NH_3^+ polymer chain inserted into the center of the POPC/CHOL membrane.

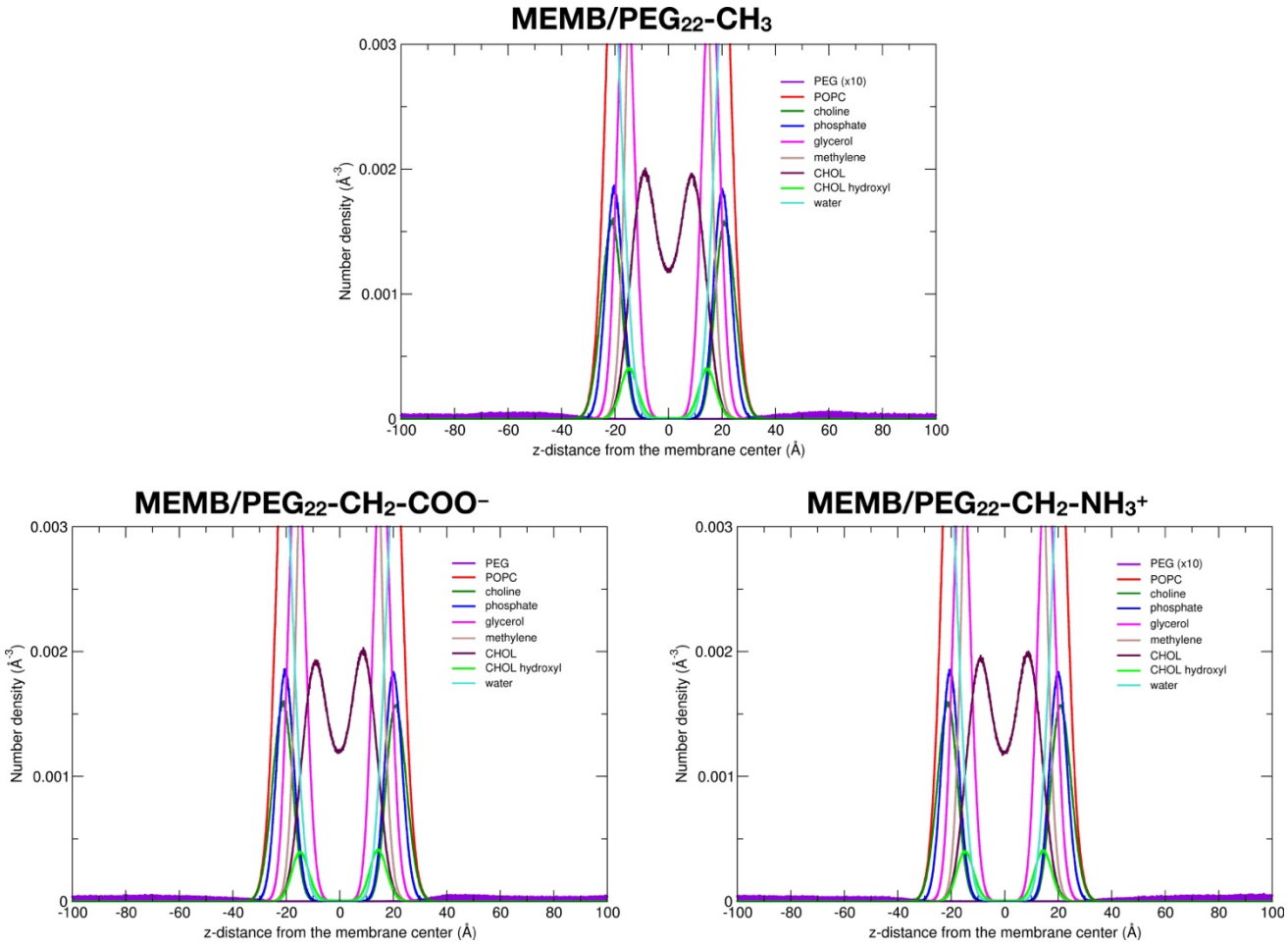

Fig. S11. Number density profiles as functions of the *z*-distance from the membrane center and averaged over the last 1 μs of the 5 μs MD simulations of a single PEG_{22}-CH_3, PEG_{22}-CH_2-COO^- or PEG_{22}-CH_2-NH_3^+ polymer chain inserted into the center of the POPC/CHOL membrane.

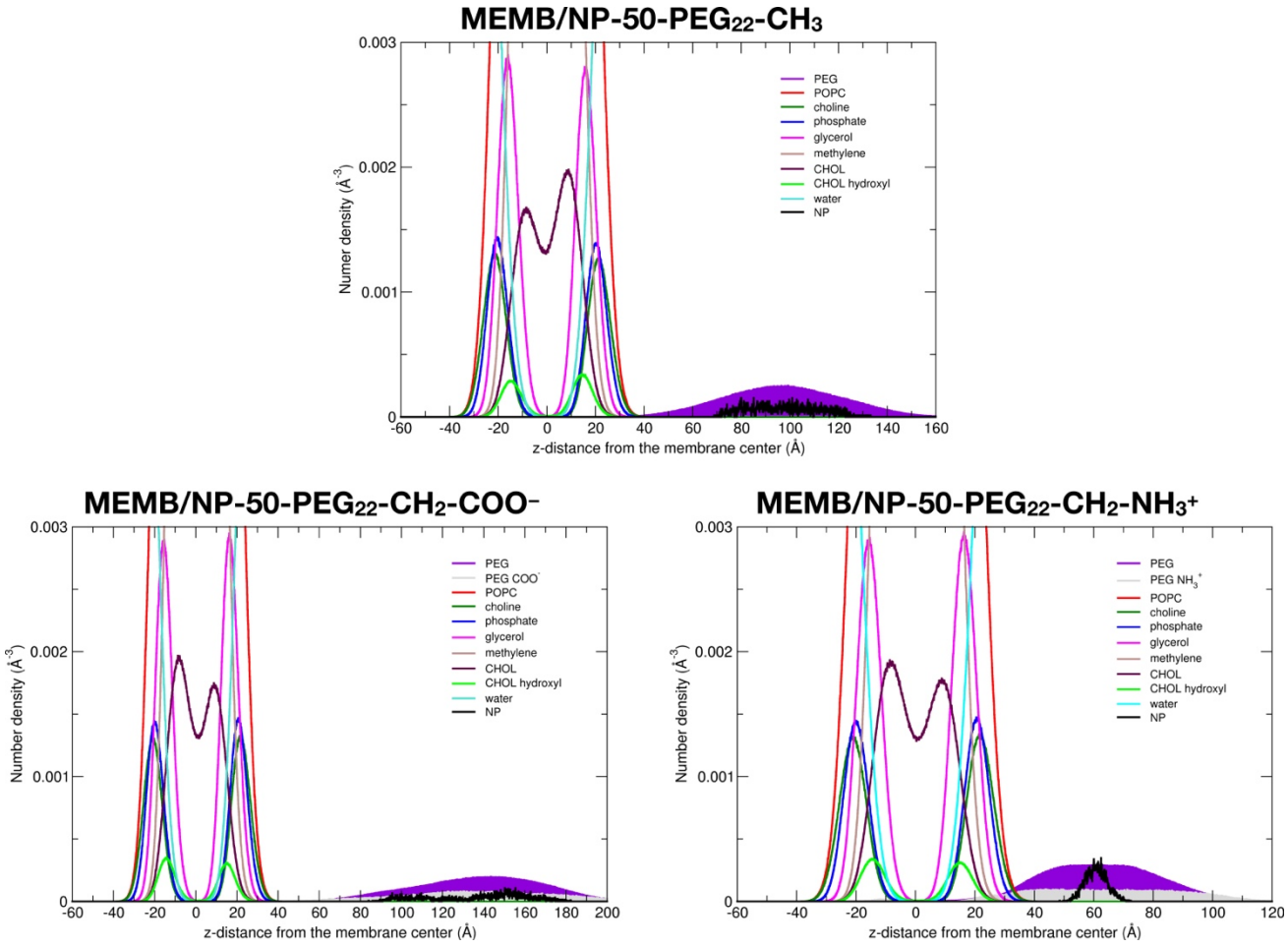

Fig. S12. Number density profiles as functions of the *z*-distance from the membrane center and averaged over the last 1 μs of the 5 μs MD simulations of the NP-50-PEG_{22}-CH_3, NP-50-PEG_{22}-CH_2-COO^- and NP-50-PEG_{22}-CH_2-NH_3^+ NP systems inserted into the center of the POPC/CHOL membrane.

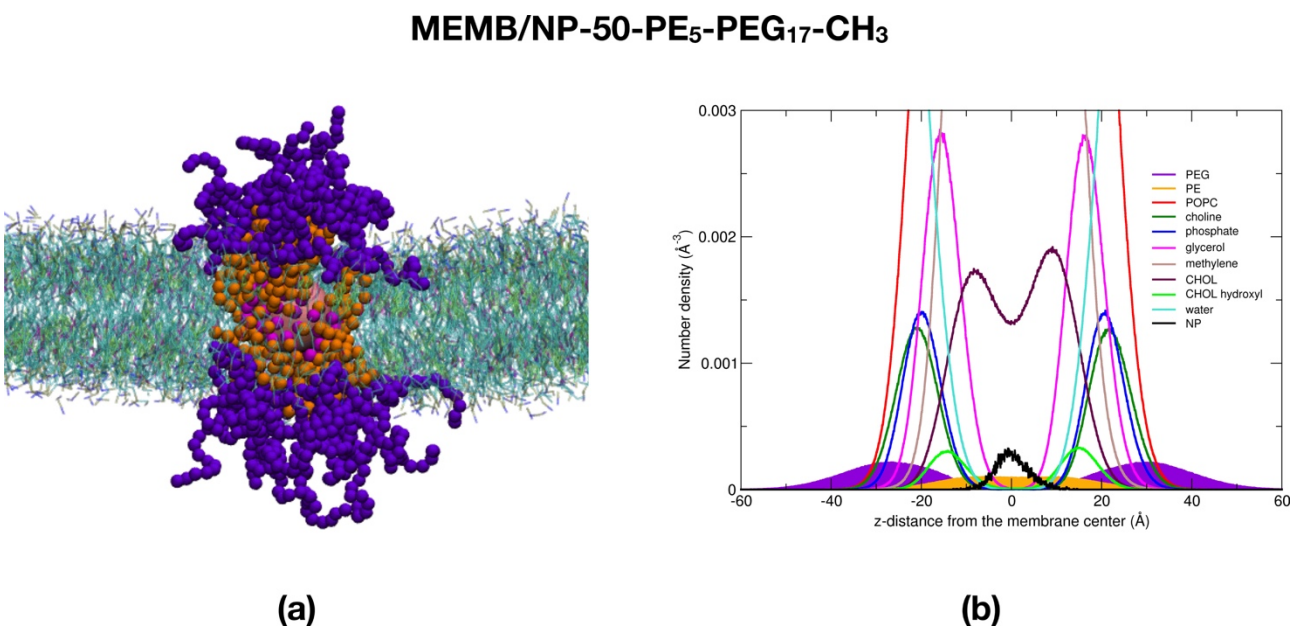

Fig. S13. (a) Last-frame snapshot from the 5 μs MD simulation of MEMB/NP-50-PE_5-PEG_{17}-CH_3 system. For the polymer chains, the SP2 bead is shown in magenta, the EO one in violet, the C1 in orange, the Qa one in red and the Qd one in blue. The NP is shown in pink. For the membrane, POPC is shown in cyan and cholesterol in green. POPC choline is represented in blue, phosphate in tan and C=C bead in magenta. Water and ions are not shown for clarity. (b) Number density profile as a function of the *z*-distance from the membrane center and averaged over the last 1 μs of the 5 μs MD simulation of the MEMB/NP-50-PE_5-PEG_{17}-CH_3 system.

Table S3. Polymer chain/membrane non-bonded interaction energy, averaged over the last 1 μs of the 5 μs MD simulations of the MEMB/NP-PE_{22}-CH_3, MEMB/NP-PEG_{22}-X and MEMB/NP-PE_{11}-PEG_{11}-X systems.

System	Non-bonded interaction energy (kcal mol^{-1})	
	Polymer chains/POPC	**Polymer chains/CHOL**
MEMB/PEG_{22}-CH_3	0	0
MEMB/PEG_{22}-CH_2-COO^-	0	0
MEMB/PEG_{22}-CH_2-NH_3^+	0	0
MEMB/PE_{22}-CH_3	PE: -145 (±1) CH_3: -7 (±1) TOT: -152 (±1)	PE: -19 (±1) CH_3: -1 (±1) TOT: -20 (±1)
MEMB/PE_{11}-PEG_{11}-CH_3	PE: -84 (±1) PEG: -40 (±1) CH_3: -4 (±1) TOT: -128 (±1)	PE: -11 (±1) PEG: -0.8 (±0.2) CH_3: -0.1 (±0.2) TOT: -12 (±1)
MEMB/PE_{11}-PEG_{11}-CH_2-COO^-	PE: -84.2 (±0.3) PEG: -39 (±1) CH_2-COO^-: -2 (±1) TOT: -125 (±1)	PE: -9.0 (±0.4) PEG: -0.6 (±0.1) CH_2-COO^-: -0.007 (± 0.005) TOT: -9.6 (±0.4)
MEMB/PE_{11}-PEG_{11}-CH_2-NH_3^+	PE: -83.1 (±0.4) PEG: -45 (±1) CH_2-NH_3^+: -8 (±1) TOT: -136 (±1)	PE: -11 (±1) PEG: -1.1 (±0.2) CH_2-NH_3^+: -0.08 (±0.03) TOT: -12 (±1)

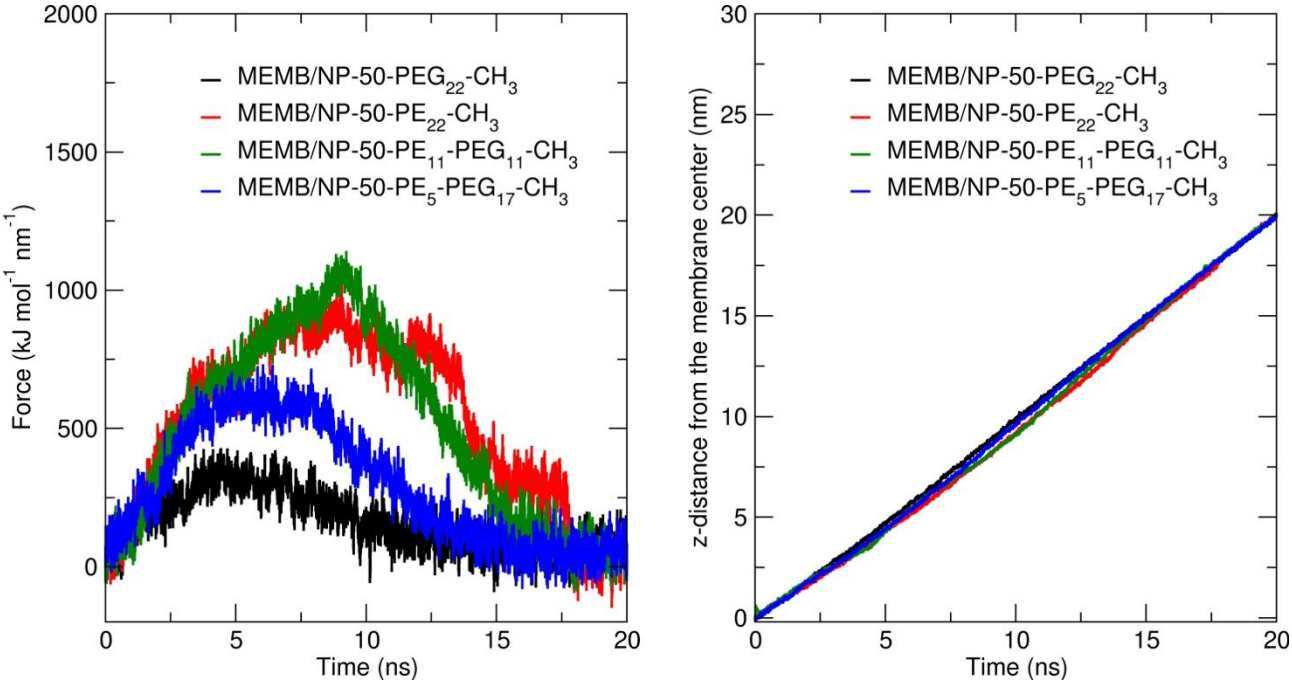

Fig. S14. Intensity of the pulling force (a) and the NP *z*-position along the 20 ns SMD trajectory for the MEMB/NP-50-PEG_{22}-CH_3, MEMB/NP-50-PE_{22}-CH_3, MEMB/NP-50-PE_{11}-PEG_{11}-CH_3 and MEMB/NP-50-PE_5-PEG_{17}-CH_3 systems.

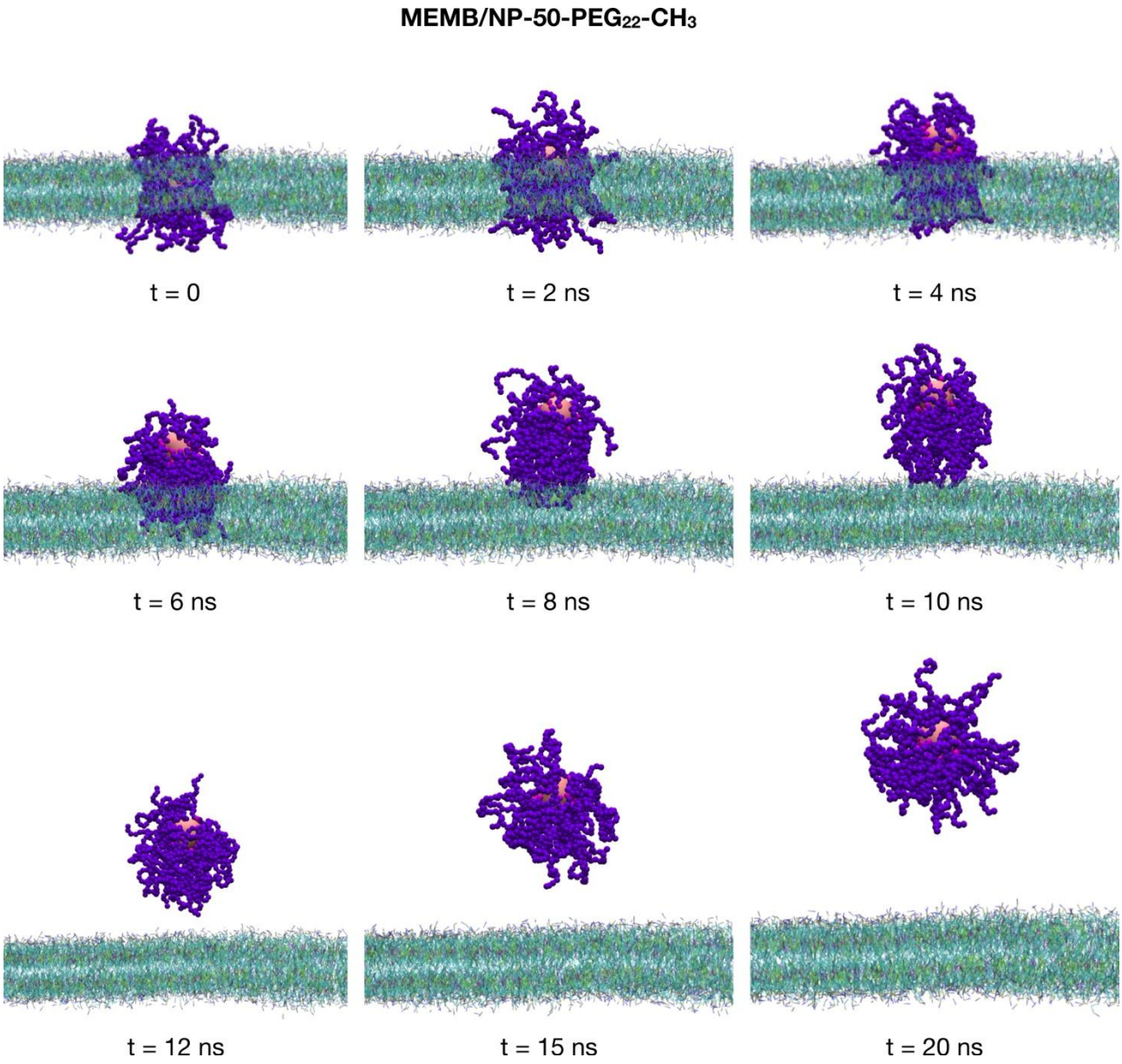

Fig. S15. Selected snapshots from the SMD trajectory of the MEMB/NP-50-PEG_{22}-CH_3 system. For the polymer chains, the SP2 bead is shown in magenta, the EO one in violet, the C1 in orange, the Qa one in red and the Qd one in blue. The NP is shown in pink. For the membrane, POPC is shown in cyan and cholesterol in green. POPC choline is represented in blue, phosphate in tan and C=C bead in magenta. Water and ions are not shown for clarity.

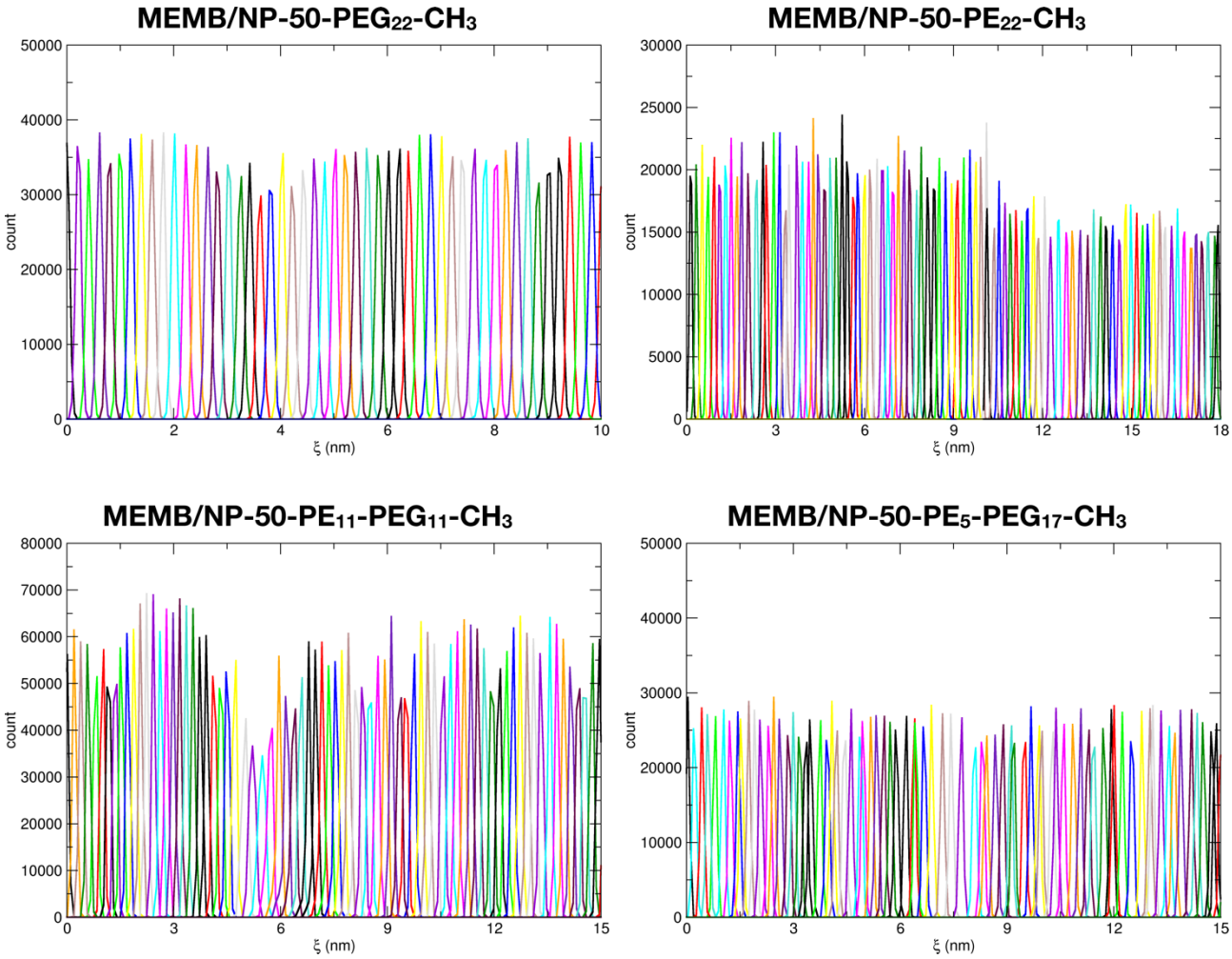

Fig. S16. Umbrella histograms for the US calculations of the MEMB/NP-50-PEG_{22}-CH_3, MEMB/NP-50-PE_{22}-CH_3, MEMB/NP-50-PE_{11}-PEG_{11}-CH_3 and MEMB/NP-50-PE_5-PEG_{17}-CH_3 systems.