Dynamic Interactions Between Lipid Tethered DNA and Phospholipid Membranes

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Supplementary Information:

Table S1: Maximum surface density and K_d values obtained from the gel shift assay. The table lists the averages and standard deviations from binding assays, with a minimum of three repeats for each data set.

Buffer	Lipid type	DNA length [nt]	DNA	K_d [μM]	DNA load [mol. p. ves.]	Surface density [DNA molec. per nm^2]	Diameter of vesicle [nm]
0.3 M KCl	PCPE	20	ss	45.9 ± 18.4	1140 ± 120	0.033 ± 0.004	106
0.3 M KCl	PCPE	20	ds	8.5 ± 4.9	1030 ± 40	0.029 ± 0.001	106
0.3 M KCl	PCPE	40	ss	51.6 ± 13.0	1220 ± 65	0.035 ± 0.002	106
0.3 M KCl	PCPE	40	ds	11 ± 1.2	1070 ± 10	0.031 ± 0.000	106
PBS	PCPE	20	ss	29.9 ± 13	1050 ± 30	0.030 ± 0.001	106
PBS	PCPE	20	ds	165 ± 55.1	1650 ± 190	0.047 ± 0.005	106
PBS	PCPE	40	ss	40.6 ± 16.9	1160 ± 60	0.033 ± 0.002	106
PBS	PCPE	40	ds	39.9 ± 12.3	1180 ± 60	0.034 ± 0.002	106
0.3 M KCl	PGPE	20	ss	466 ± 134	487 ± 159	0.033 ± 0.011	68.6
0.3 M KCl	PGPE	20	ds	109 ± 43.9	520 ± 141	0.035 ± 0.010	68.6
0.3 M KCl	PGPE	40	ss	164 ± 36.1	322 ± 96	0.022 ± 0.007	68.6
0.3 M KCl	PGPE	40	ds	104 ± 36.3	546 ± 27	0.037 ± 0.002	68.6
PBS	PGPE	20	ss	17.9 ± 2.2	565 ± 57	0.038 ± 0.004	68.6
PBS	PGPE	20	ds	68.6 ± 18.8	639 ± 28	0.043 ± 0.002	68.6
PBS	PGPE	40	ss	22.4 ± 2.0	607 ± 14	0.041 ± 0.001	68.6
PBS	PGPE	40	ds	20.7 ± 9.5	320 ± 55	0.022 ± 0.004	68.6

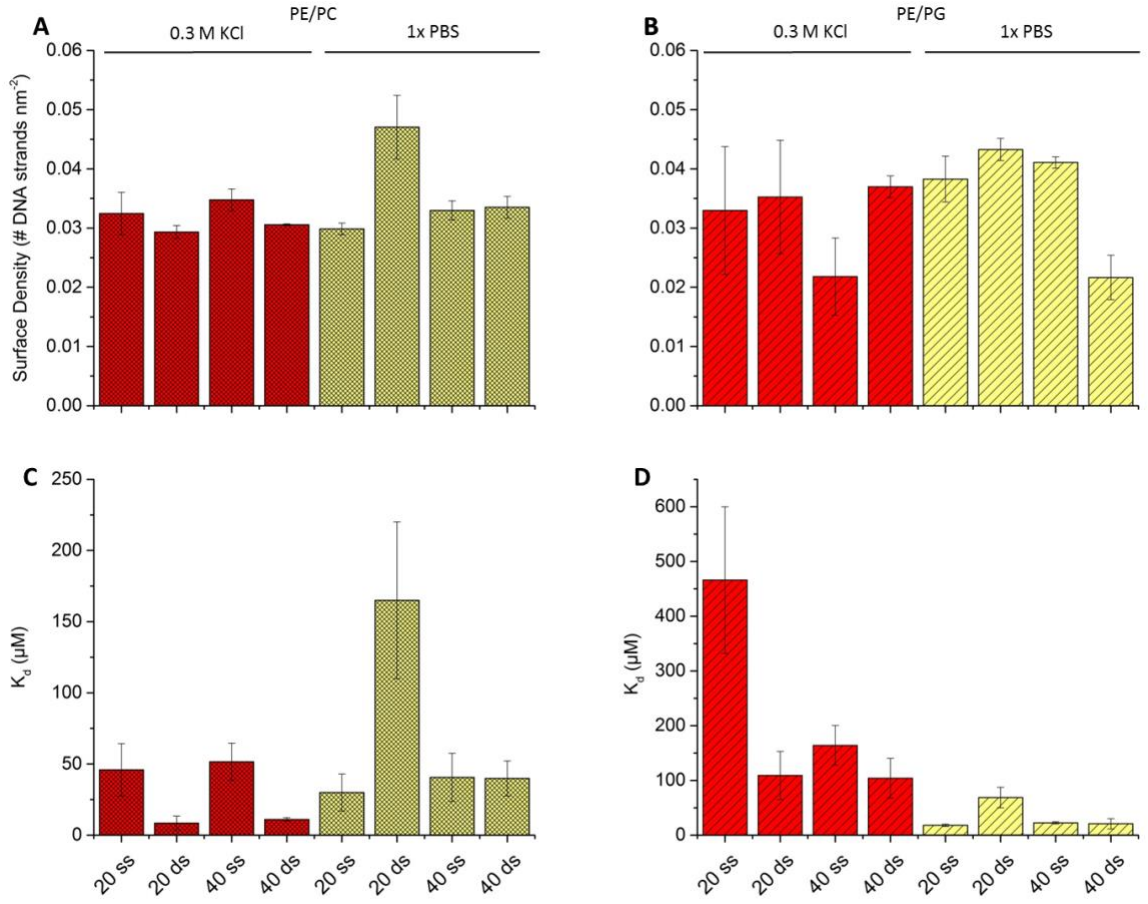


Figure S1: Maximum surface density and K_d values obtained from the gel shift assay. (A, B) Maximum surface density for DNA strands on PE/PC (A) and PE/PG SUVs (B) in buffers 0.3 M KCl (red columns) or PBS (yellow columns). (C, D) K_d for DNA strands on PE/PC (C) and PE/PG SUVs (D) in buffers 0.3 M KCl (red columns) or PBS (yellow columns). The bar charts visualize the data in Table S1.

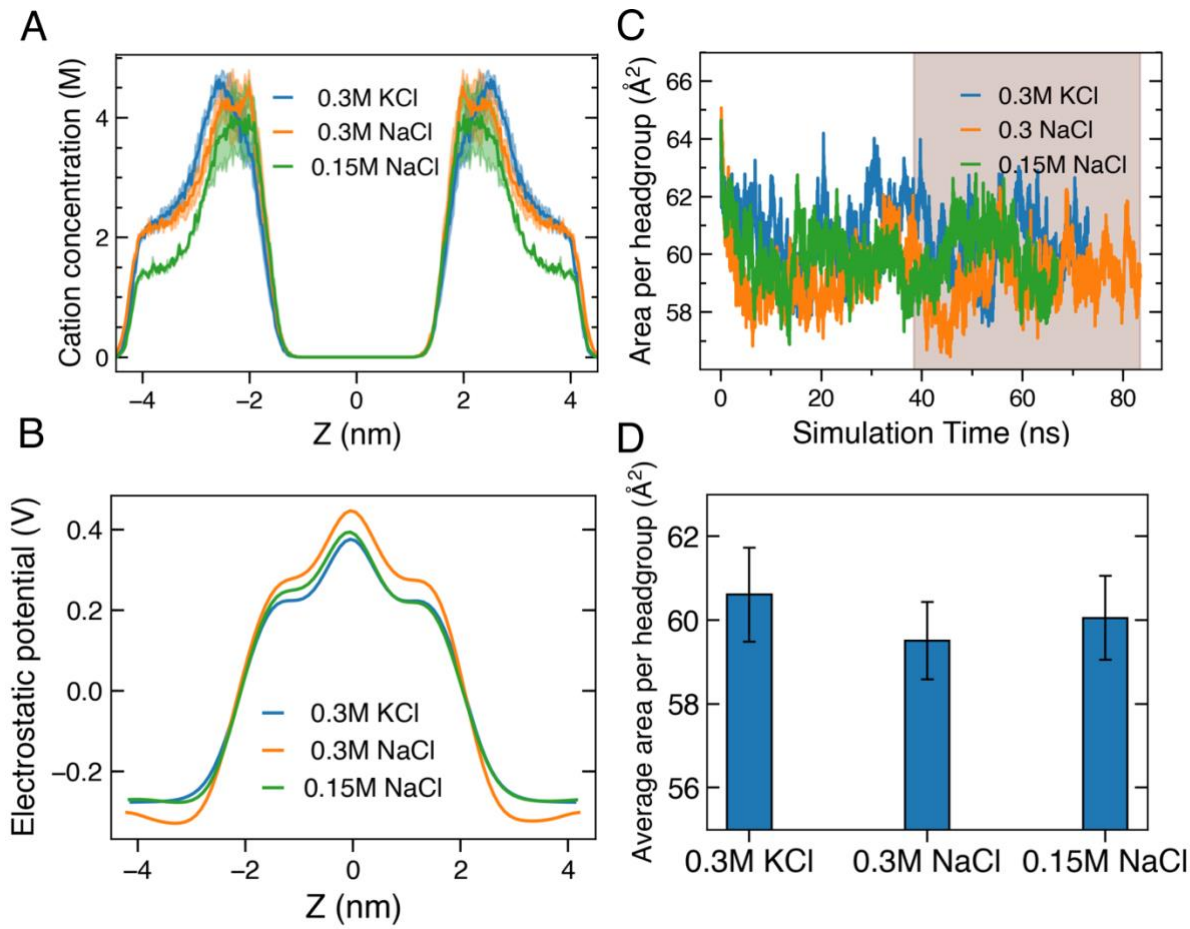


Figure S2: Ion type-dependent screening of PE/PG membrane. (A) The average concentration of K^+ and Na^+ cations versus distance from the center of a 50/50 PE/PG lipid bilayer for the specified three ion conditions. The values were averaged from the last 50 ns of an NPT equilibration. Additionally, we concentration profiles were averaged with respect to system's symmetry (reflection with respect to the bilayer midplane); the shaded region illustrates the error of the average. Na^+ ions are found to bind closely to the membrane then K^+ ions. **(B)** The average profile of the electrostatic potential along the bilayer normal computed using the VMD plugin PMEpot. The electrostatic potential for 0.3 M KCl matches closely with 0.15 M NaCl system. **(C)** The average area of a lipid head group under specified ion conditions. Due to their smaller size, the Na^+ ions interact stronger with the lipid head groups than K^+ ions and make the bilayer more compact. **(D)** Average area per headgroup at the three buffer conditions. The area has been averaged over the last 40 ns fragment of the equilibration trajectory (highlighted in panel C).

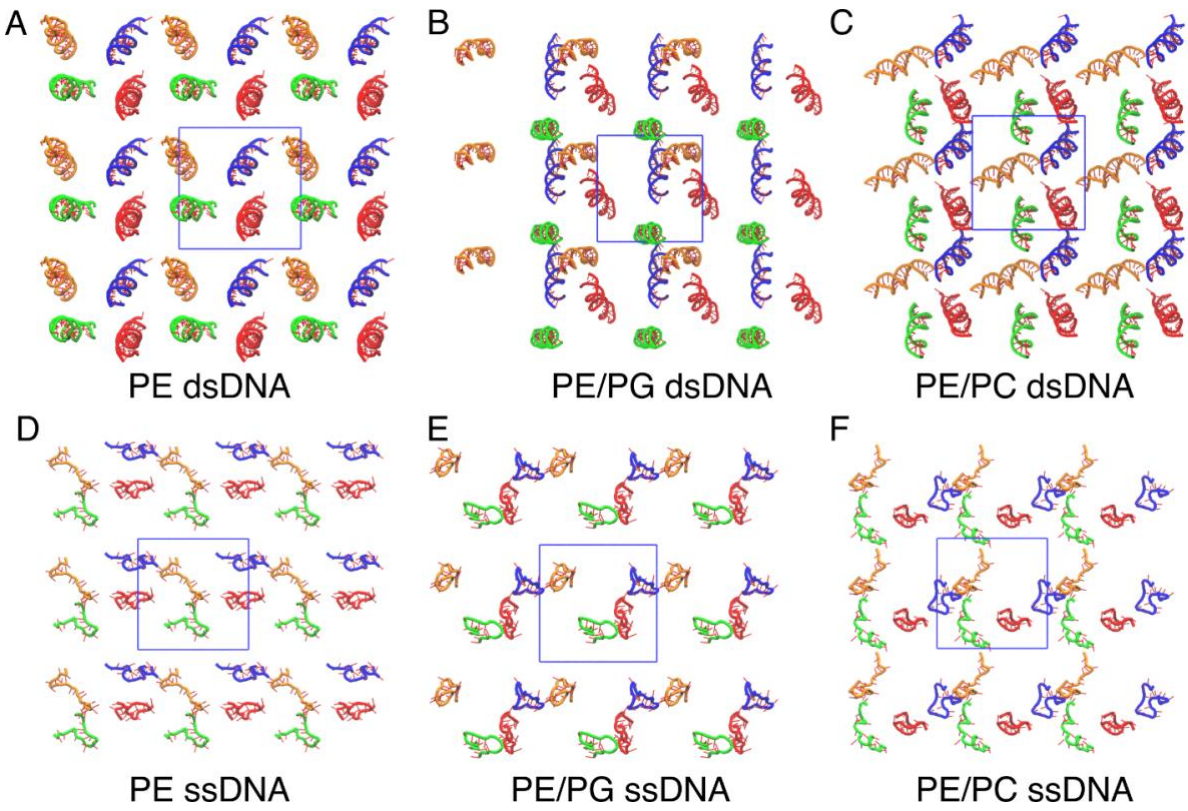


Figure S3: (A-F) Conformations of DNA molecules tethered to lipid bilayer membranes. Configuration of the DNA molecules at the end of the 300 ns MD trajectories viewed normal to the membrane plane. Lipid and solvent molecules are not shown for clarity. In addition to the periodic unit cell (highlighted by a blue square), each image shows the nearest periodic images of the unit cell within the membrane plan.

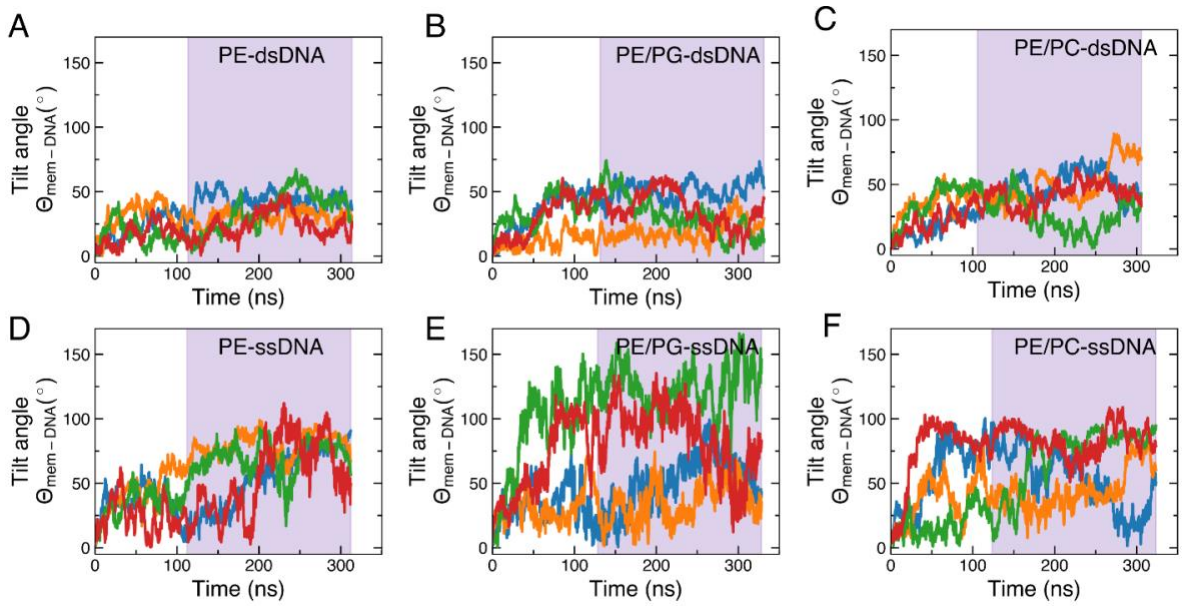


Figure S4: Tilt angle versus simulation time. The $\theta_{\text{mem-DNA}}$ angle was defined as the angle between the bilayer normal and the line joining the CoM of the first and the last basepair of dsDNA or the second and the last nucleotide of ssDNA. The highlighted region indicates the part of the MD trajectories used to determine the average values reported in Figure 5C.

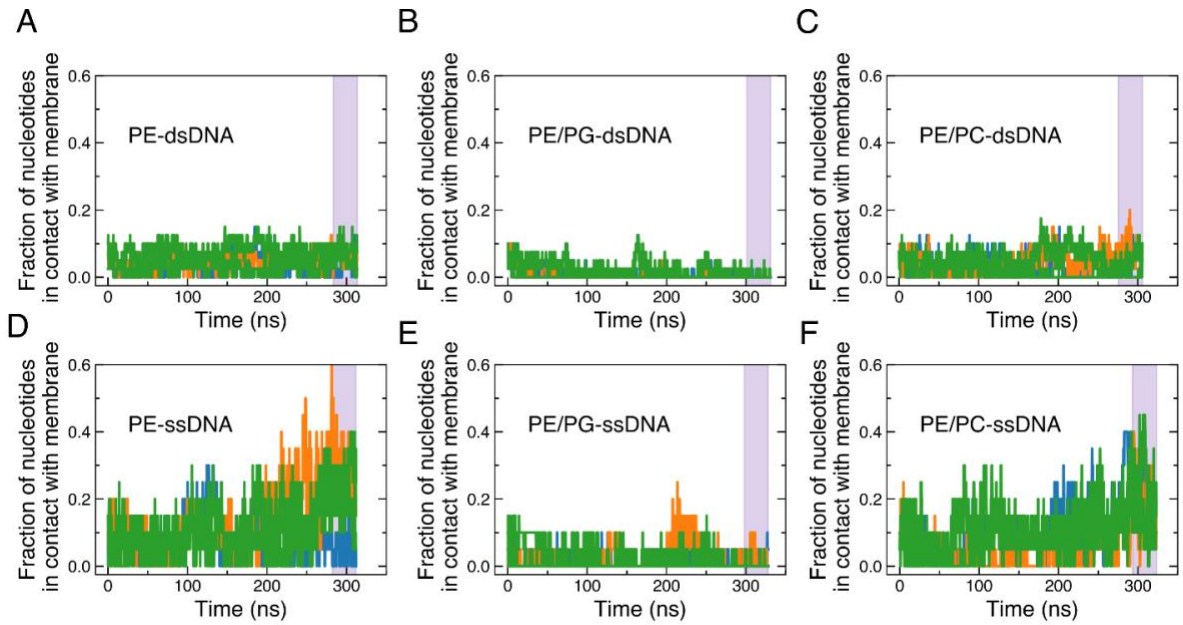


Figure S5: Fraction of DNA in contact with membrane: (A,B) Fraction of DNA nucleotides in contacts with the lipid bilayer as a function of simulation time. A contact was defined as a C3' atom of DNA backbone located within 5 Å of any non-hydrogen atoms of the membrane. The highlighted region indicates the part of the MD trajectories used to determine the average values reported in Figure 5D.

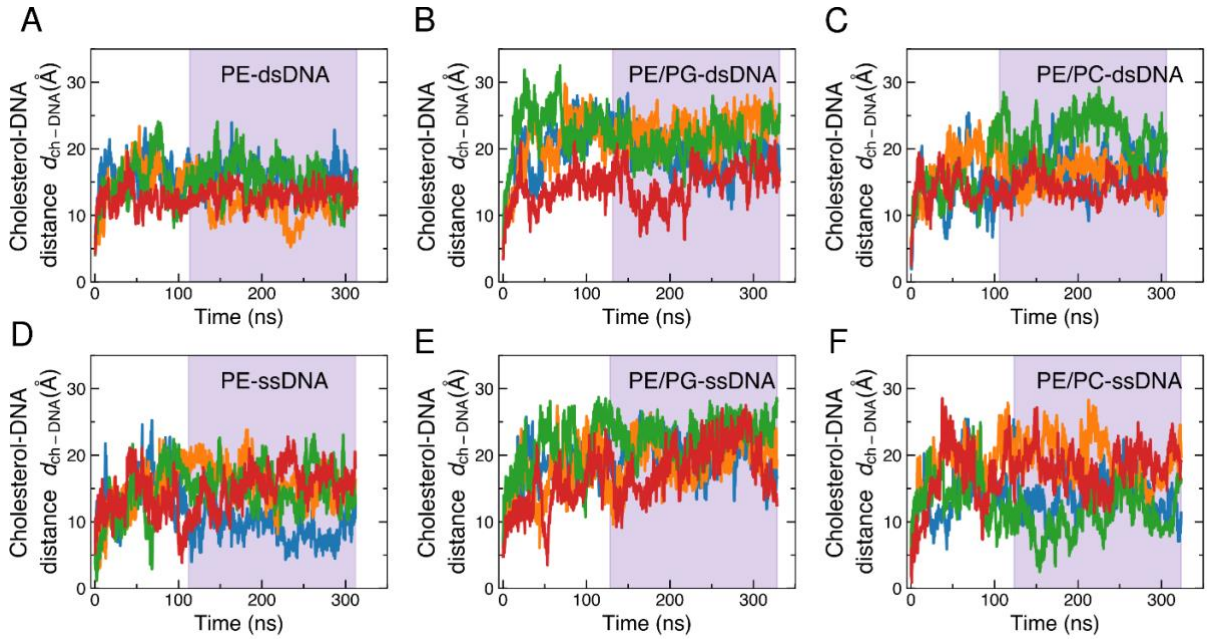


Figure S6: Distance between cholesterol and DNA as a function of simulation time. The $d_{\text{ch-DNA}}$ distance was computed along the bilayer normal using the CoM coordinates of the cholesterol and the nearest dsDNA basepair or the second nearest ssDNA nucleotide. The highlighted region indicates the part of the MD trajectories used to determine the average values reported in Figure 5E.

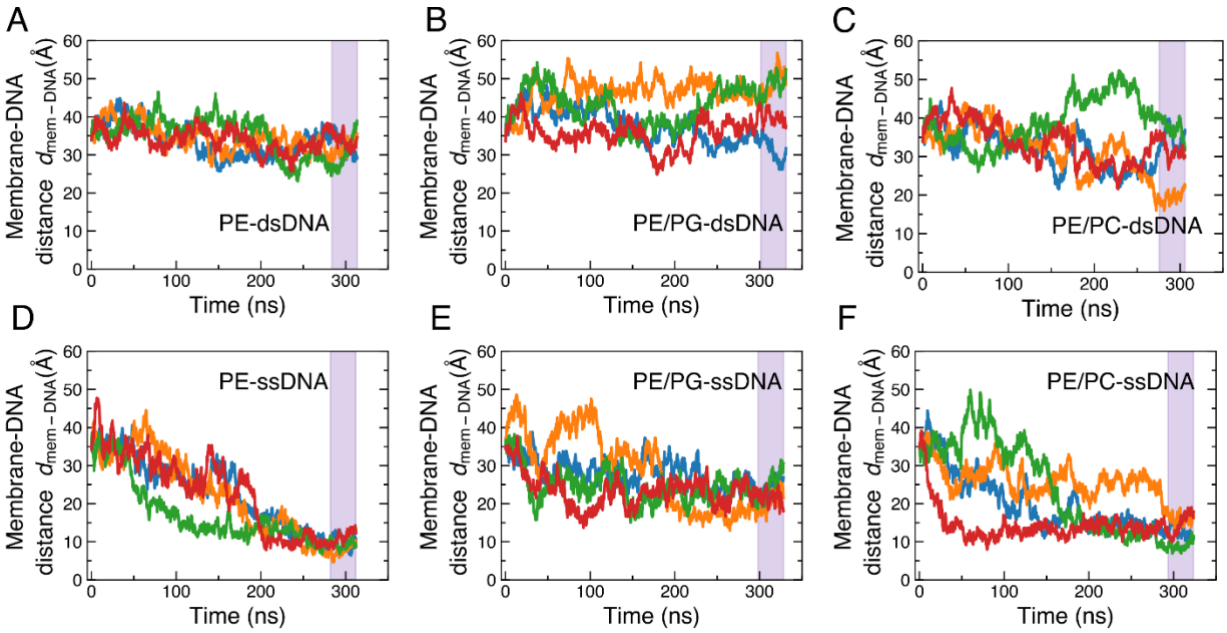


Figure S7: Distance between membrane and DNA as a function of simulation time. The $d_{\text{mem-DNA}}$ distance was computed along the bilayer normal using the CoM coordinates of the respective DNA molecules and of the phosphate groups of the nearest (upper in Figure 1A, B) membrane's leaflet. The highlighted region indicates the part of the MD trajectories used to determine the average values reported in Figure 5F.

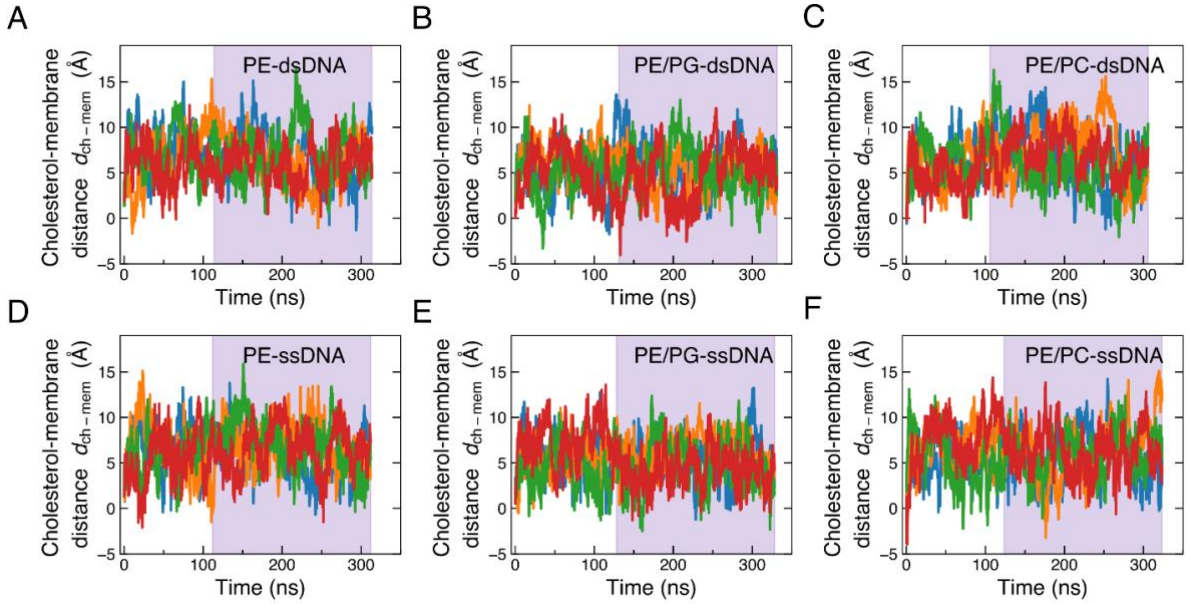


Figure S8: Distance between cholesterol and the membrane versus simulation time. The $d_{\text{ch-mem}}$ distance was computed along the bilayer normal using the CoM coordinates of the cholesterol and of the phosphate groups of the nearest (upper in Figure 1 A, B) membrane's leaflet. The highlighted region indicates the part of the MD trajectories used to determine the average values reported in Figure 5G.

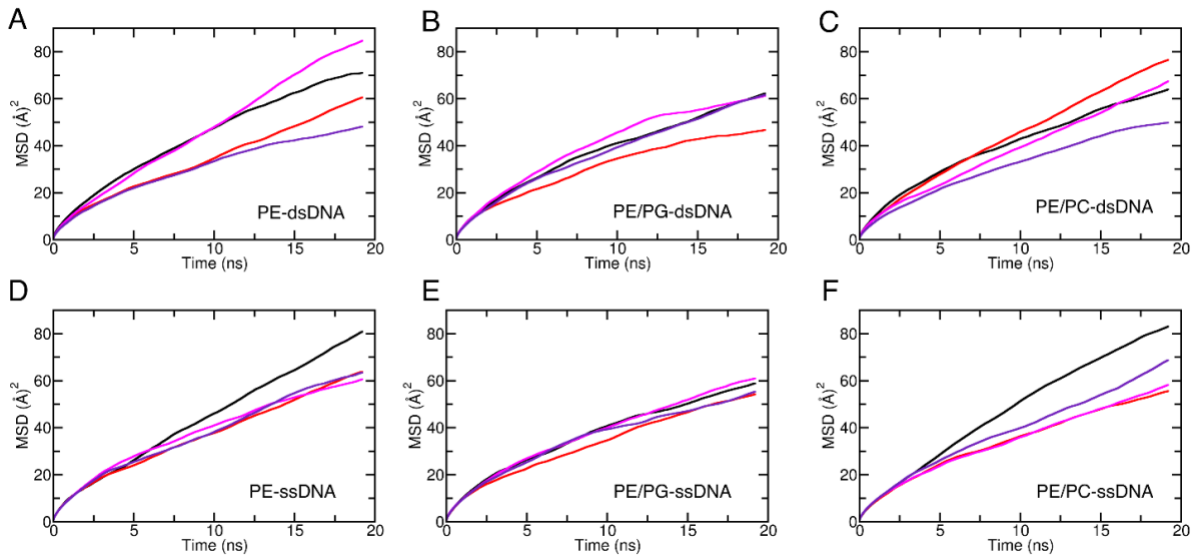
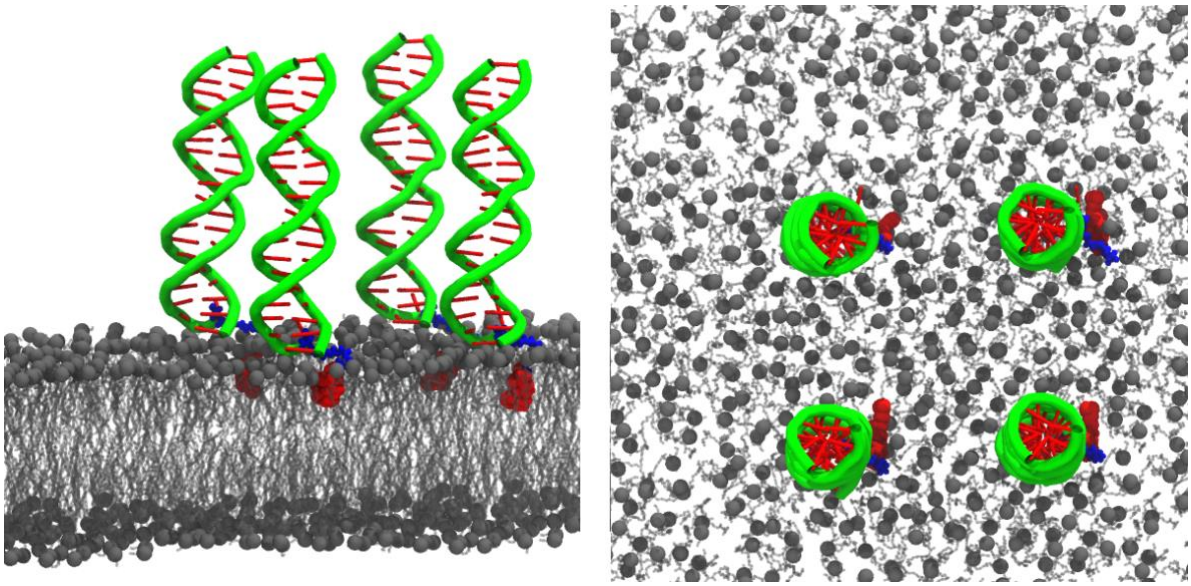
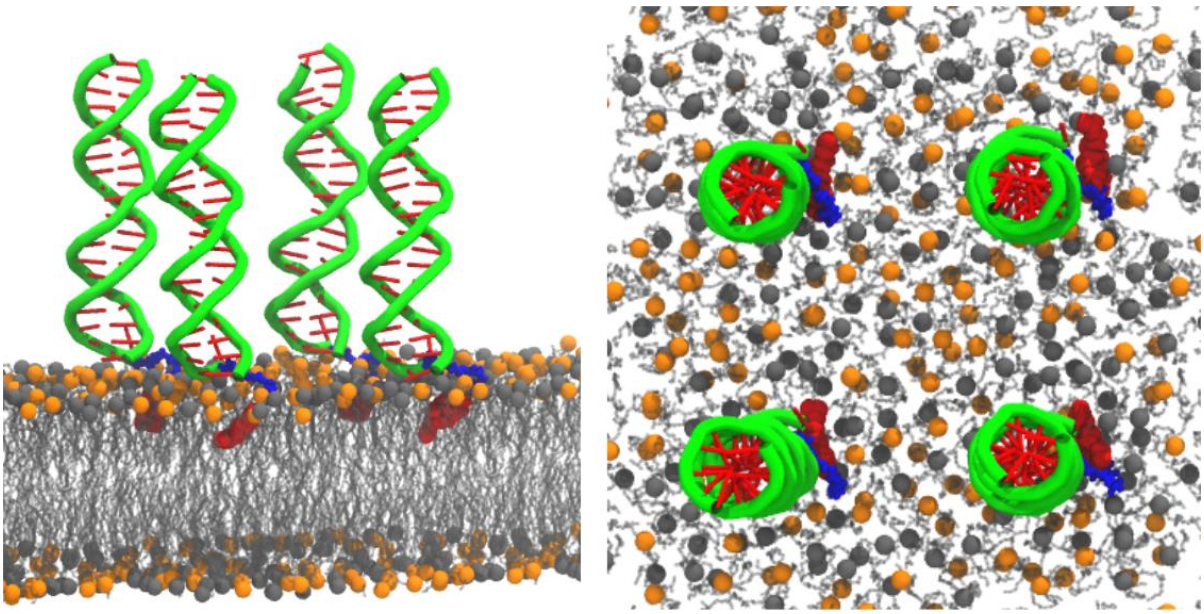


Figure S9: Mean square displacement (MSD) of the cholesterol anchor as a function of simulation time. The 20 ns MSD curves were extracted by averaging over 300 ns of the respective MD trajectories. The diffusion coefficients plotted in Figure 5H were computed as the least square fit to the MSD curves in the 7 to 20 ns range.

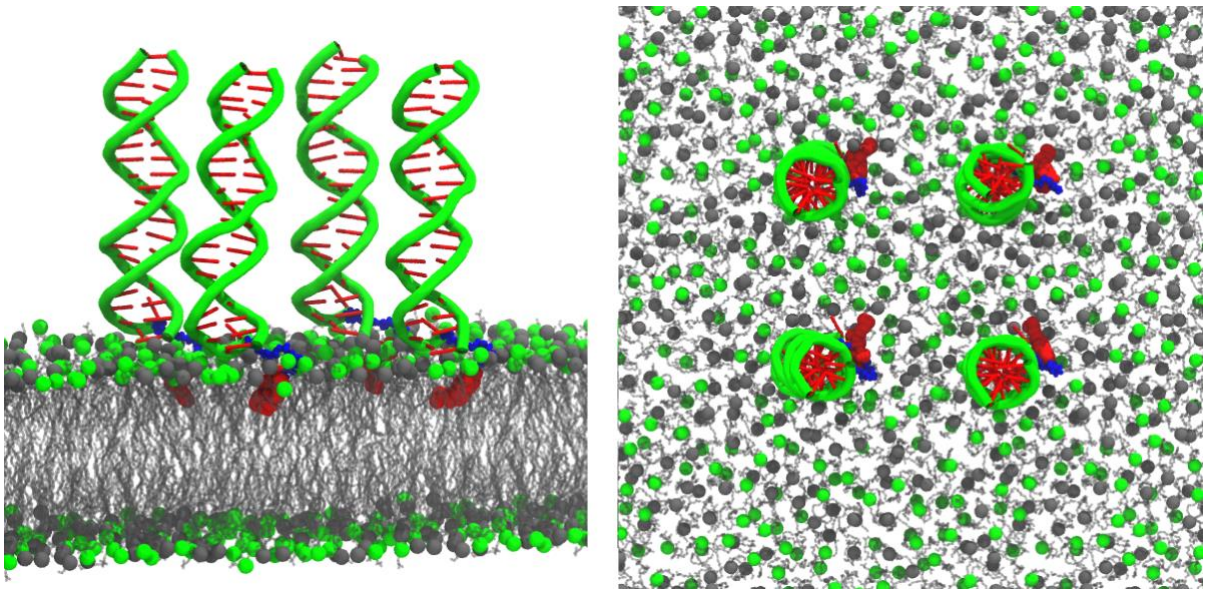
Captions to Supplementary Movies



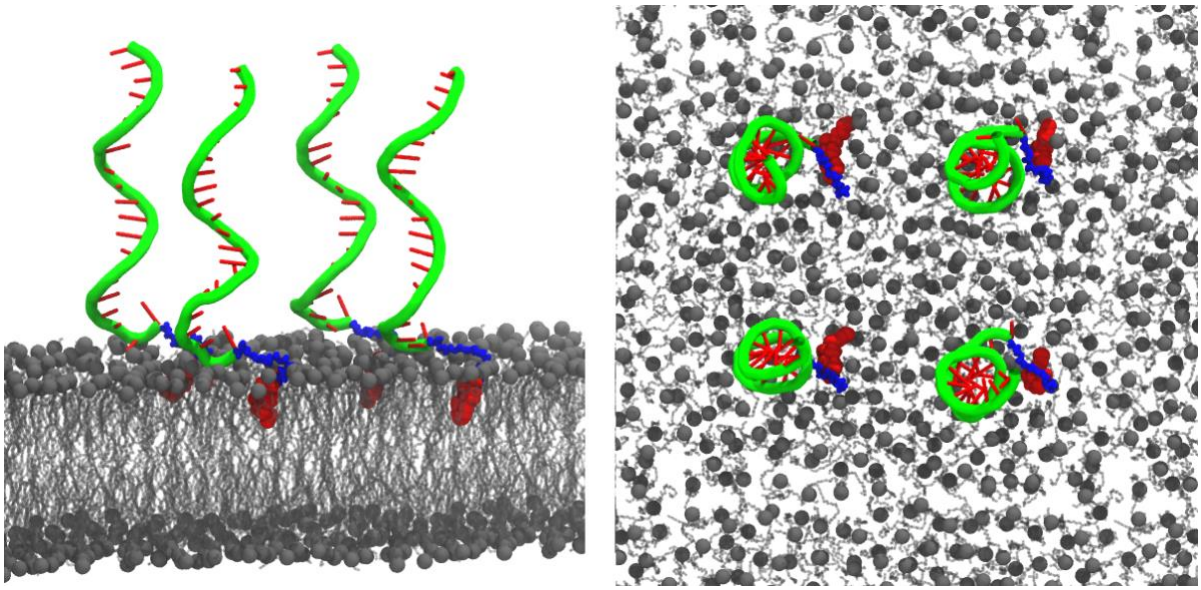
Supplementary Movie 1. All-atom molecular dynamics simulation of dsDNA molecules cholesterol-anchored to a POPE lipid bilayer membrane. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each headgroup highlighted as a vdW sphere. The lines define the simulation unit cell. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.



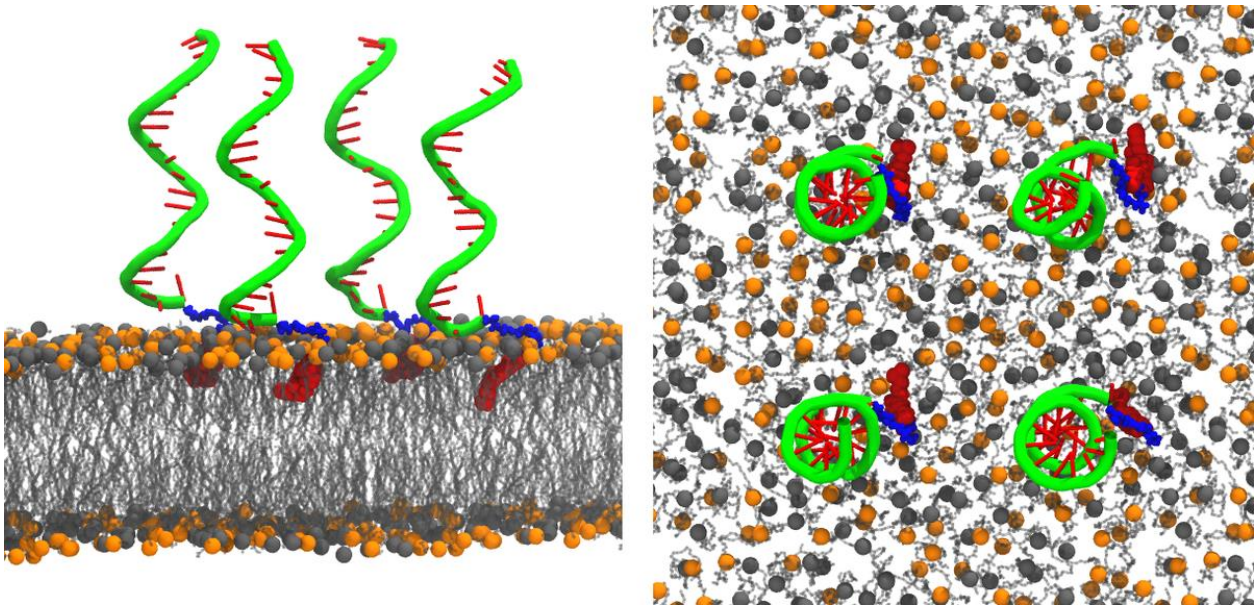
Supplementary Movie 2. All-atom molecular dynamics simulation of dsDNA molecules cholesterol-anchored to a lipid membrane composed of a 50/50 mixture of POPE and POPG lipids. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each PE and PG headgroup highlighted as a gray or orange vdW sphere, respectively. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.



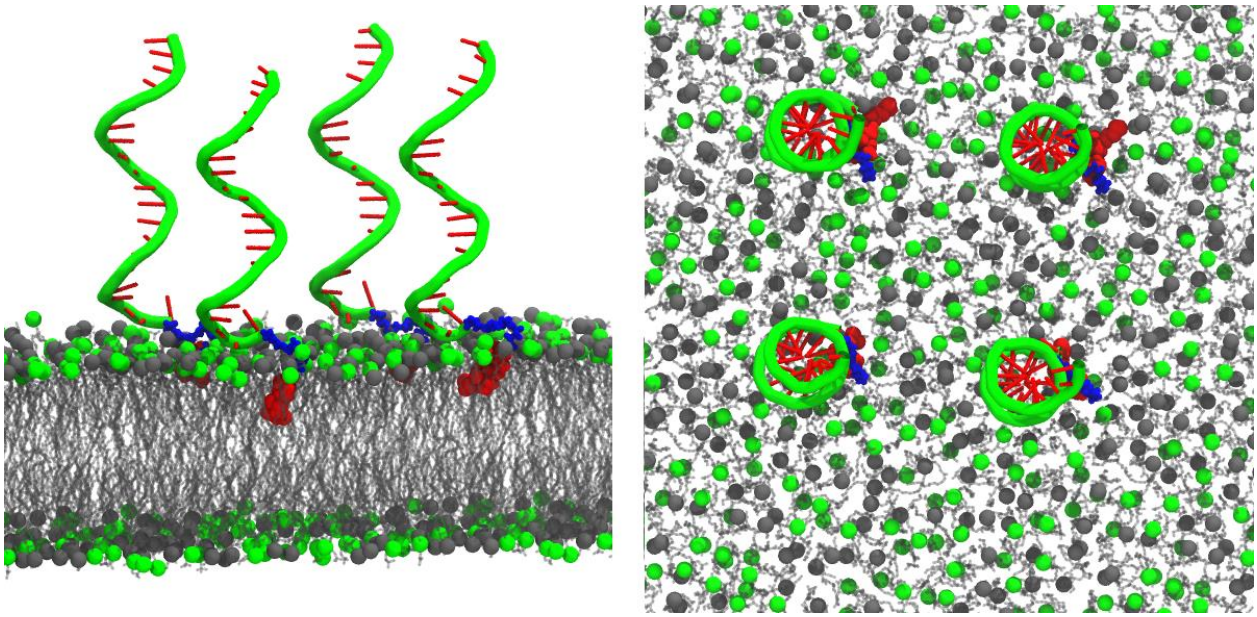
Supplementary Movie 3. All-atom molecular dynamics simulation of dsDNA molecules cholesterol-anchored to a lipid membrane composed of a 50/50 mixture of POPE and POPC lipids. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each PE and PC headgroup highlighted as a gray or green vdW sphere, respectively. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.



Supplementary Movie 4. All-atom molecular dynamics simulation of ssDNA molecules cholesterol-anchored to a POPE lipid bilayer membrane. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each headgroup highlighted as a vdW sphere. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.



Supplementary Movie 5. All-atom molecular dynamics simulation of ssDNA molecules cholesterol-anchored to a lipid membrane composed of a 50/50 mixture of POPE and POPG lipids. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each PE and PG headgroup highlighted as a gray or orange vdW sphere, respectively. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.



Supplementary Movie 6. All-atom molecular dynamics simulation of ssDNA molecules cholesterol-anchored to a lipid membrane composed of a 50/50 mixture of POPE and POPC lipids. The movie illustrates a 300 ns equilibration trajectory. The DNA backbone (green) and bases (red) are shown using a cartoon representation. Each cholesterol molecule (red vdW spheres) is attached to the DNA backbone via a triethylene glycol linker (blue lines). Lipid molecules are shown as gray lines with the phosphorous atom of each PE and PC headgroup highlighted as a gray or green vdW sphere, respectively. For clarity, water, ions and DNA from the neighboring periodic cells are not shown.