Electronic Supplementary Information

Re: Modulation of lipid vesicle-membrane interaction by cholesterol

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Table S1. POPC membrane area compressibility moduli and bending moduli as a function of cholesterol fraction.

% Chol	Area compresibility modulus, K_A (mN/m)	Bending modulus$^{\beta}$, k_C (k_BT)	$k_C/k_{C,0}$
0	463$^{\alpha}$	48.8	1.0
20	450	54.4	1.1
50	1100	161.4	3.3

$^{\alpha}$ Agrees with value estimated for "large membrane" for Dry Martini model by Arnarez *et al.*[1]

$^{\beta}$ Estimated as $K_A(h-1)^2/24$ where *h* is the membrane thickness, following Rawicz *et al.*[2]

Table S2. Lipid and cholesterol distribution in equilibrated vesicles.

	20% chol. vesicle		50% chol. vesicle	
	PC lipids	cholesterol	PC lipids	cholesterol
No. in outer leaflet	1764	317	1128	1006
No. in inner leaflet	1087	395	746	868
Inner/Outer	0.62	1.24	0.66	0.86

Table S3. Steady-state wrapping fractions obtained from our simulations.

Vesicle %Chol	Planar membrane %Chol		
	0	20	50
0	0.85	0.85	0.22
20	0.70	0.80	0.18
50	0.40	0.50	0.10

Table S4. Steady-state membrane fusion propensity obtained from our simulations. See Fig. 4 caption for definition of fusion propensity.

Vesicle %Chol	Planar membrane %Chol		
	0	20	50
0	0.26	0.09	1.00
20	0.06	0.22	0.22
50	0.78	0.42	0.14

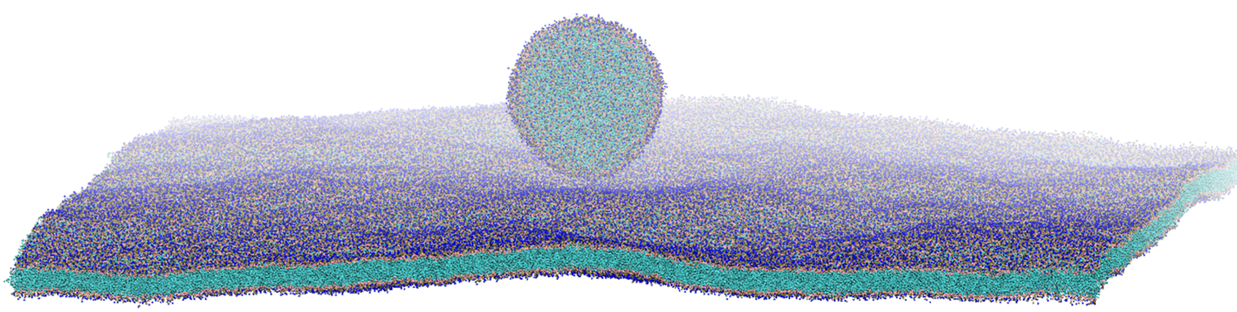

Fig. S1 A representative simulation snapshot of the entire simulation system showing a POPC vesicle placed on top of a POPC planar membrane.

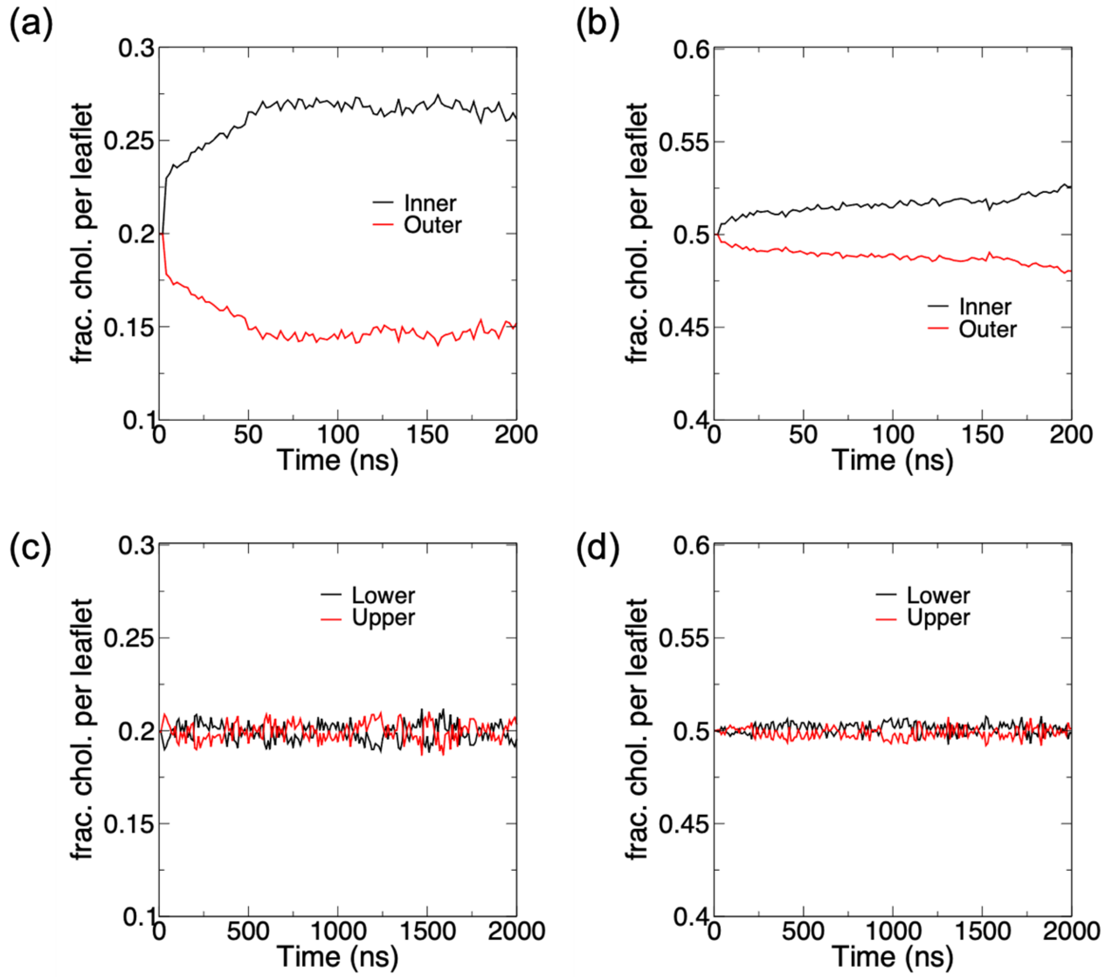

Fig. S2 The redistribution of cholesterol molecules in vesicle and planar membranes. (a-b) The temporal evolution of the fraction of cholesterol per leaflet for vesicles prepared with 20% (a) and 50% (b) cholesterol in both leaflets. (c-d) The temporal evolution of the fraction of cholesterol per leaflet for planar membranes prepared with 20% (a) and 50% (b) cholesterol in both leaflets.

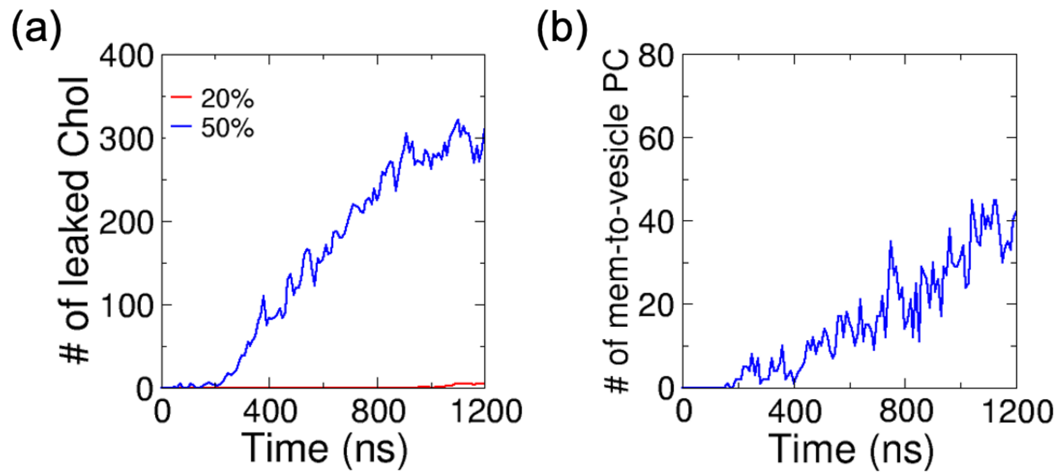

Fig. S3 Vesicle cholesterol leakage and exchange of PC lipids from planar membrane to vesicle for cholesterol-containing vesicles interacting with cholesterol-free planar membrane. (a) Number of leaked vesicle cholesterol with simulation time when POPC vesicles with 20% and 50% cholesterol fused onto cholesterol-free planar membrane. (b) Number of PC lipids migrating from planar membrane onto vesicle with simulation time.

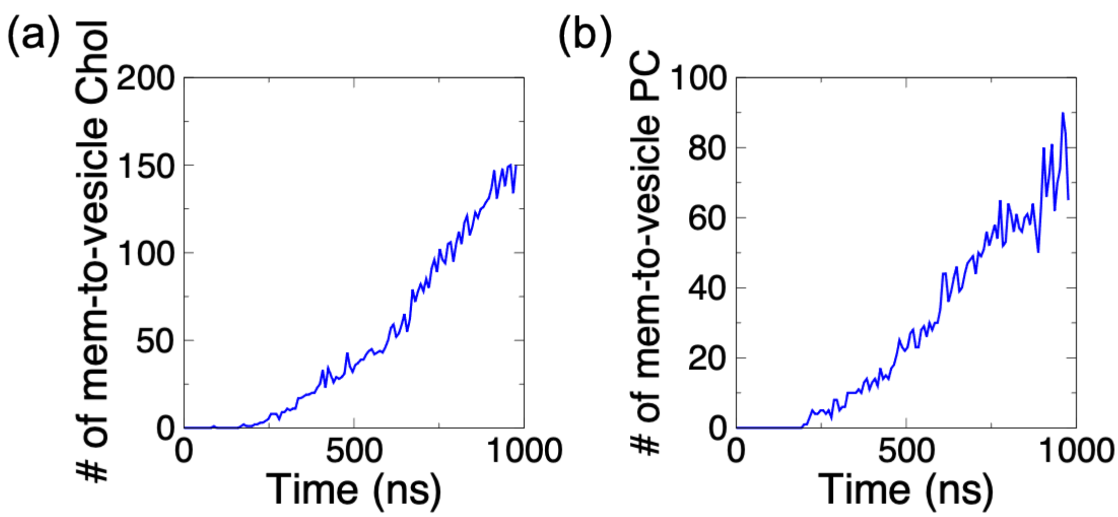

Fig. S4 Movement of cholesterol (a) and PC lipids (b) from 50% cholesterol planar POPC membrane onto cholesterol-free POPC vesicle.

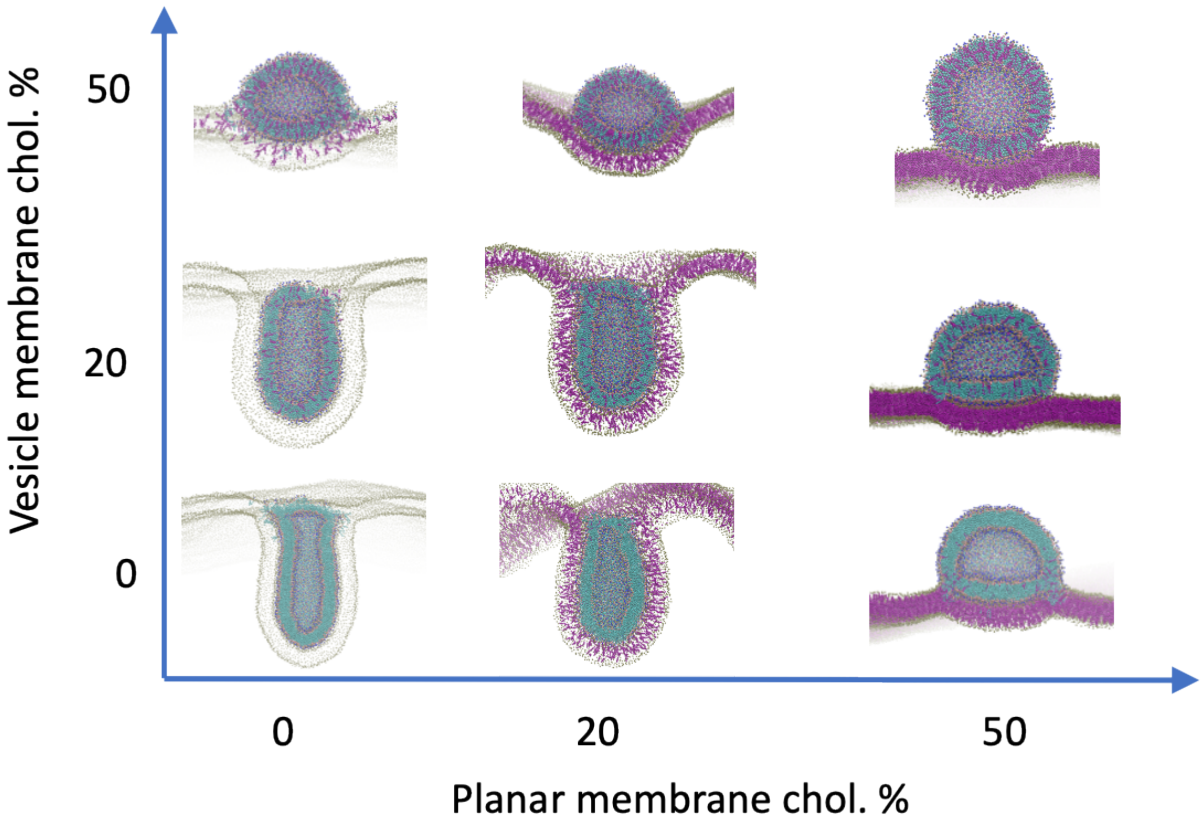

Fig. S5 Variation in the vesicle shape and wrapping degree by a planar membrane as a function of cholesterol levels in vesicle and planar membranes.

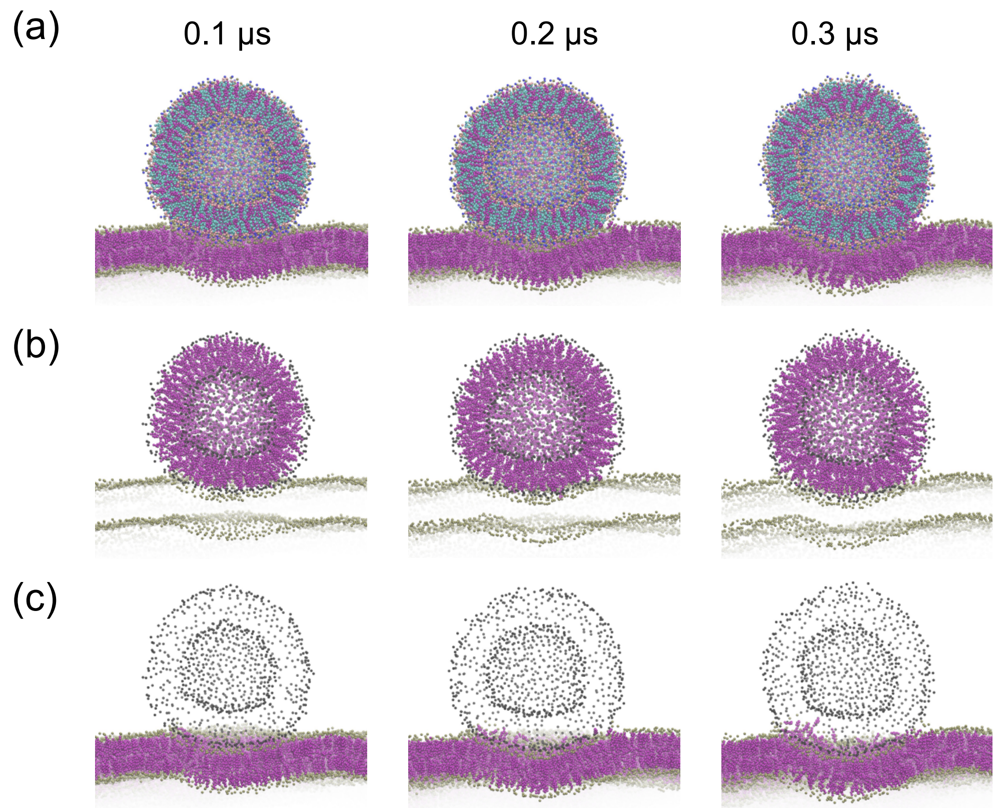

Fig. S6 Effect of high cholesterol content in both lipid vesicle and planar membranes on vesicle wrapping. (a) Simulation snapshots of vesicle-membrane interaction for POPC vesicle with 50% cholesterol on POPC planar membrane also with 50% cholesterol. (b) Same snapshots as (a) but only showing cholesterol molecules in vesicle and only vesicle PO_4 particles shown. (c) Same snapshots as (a) but only showing cholesterol molecules in membrane and only vesicle PO_4 particles shown.

References

(1) Arnarez, C.; Uusitalo, J. J.; Masman, M. F.; Ingólfsson, H. I.; de Jong, D. H.; Melo, M. N.; Periole, X.; de Vries, A. H.; Marrink, S. J. Dry Martini, a Coarse-Grained Force Field for Lipid Membrane Simulations with Implicit Solvent. *J. Chem. Theory Comput.* **2015**, *11*, 260–275.

(2) Rawicz, W.; Olbrich, K. C.; Mcintosh, T.; Needham, D.; Evans, E. Effect of Chain Length and Unsaturation on Elasticity of Lipid Bilayers. *Biophys. J.* **2000**, *79*, 328–339.