Supporting Information for "Complex nanoemulsion for vitamin delivery: droplet organization and interaction with skin membranes"

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Supporting Figures

Supporting Tables

Supporting Figures

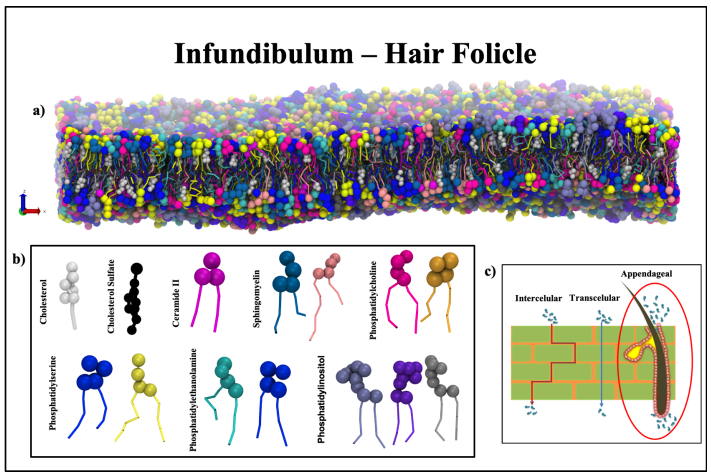


Figure S1 Hair follicle infundibulum membrane composition. The INF membrane based on Machado et al. 2016[1] with the lipids and the permeation pathways. The composition includes 14 different types of compounds (cholesterols, ceramide II NS, sphingomyelins and 9 different types of phospholipids). This membrane is similar to the plasma membrane model made by Ingólfsson et al. 2015[2] and preserves similar characteristics. (a) frontal view of the infundibulum model with the 14 components, among them cholesterol, ceramide, sphingomyelins and various types of phospholipids. (b) Legend of panel a. (c) The possible permeation pathways. The red circle indicates the pathway in which the INF membrane is involved.

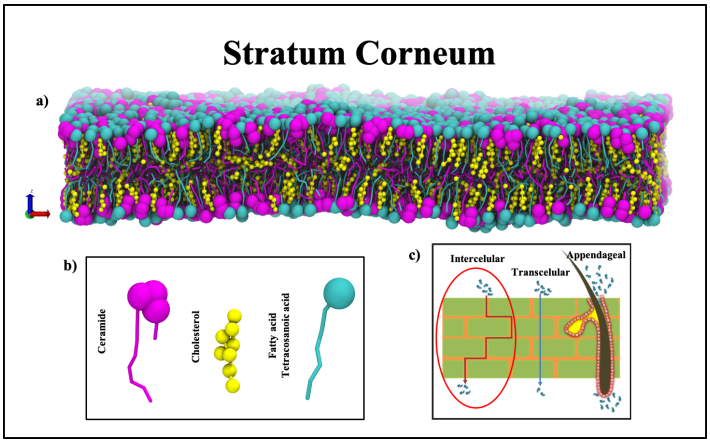


Figure S2 Stratum corneum membrane composition. The structure of the stratum corneum based on Machado et al. 2016[1] and the lipid models were taken from Ingólfsson et al. 2015[2]. (a) frontal view of the straum corneum model with 3 components (cholesterol, fatty acid, ceramide). (b) Legend of panel a. (c) The possible permeation pathways. This membrane represents the "mortar way in a model brick and mortar", as indicated by the red circle.

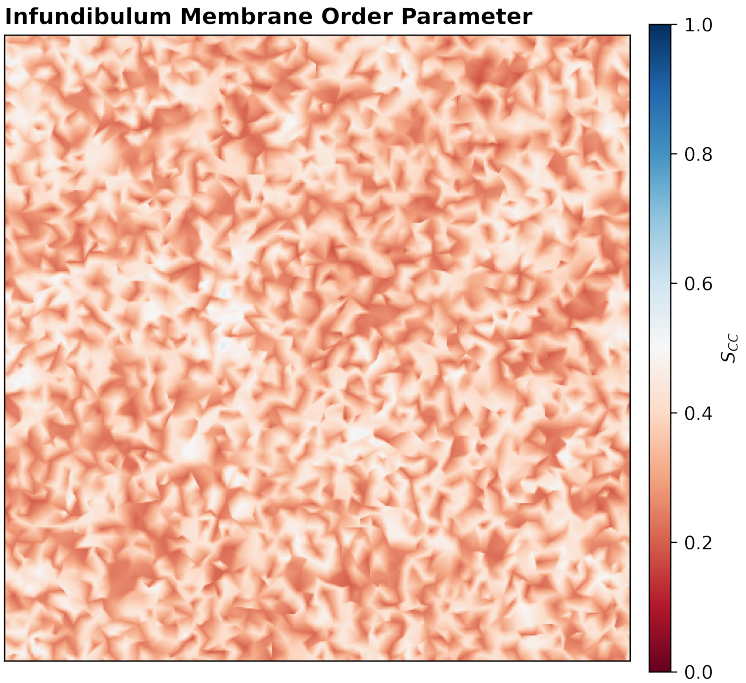


Figure S3 Averaged order parameter (S_{CC}) distributions of INF membrane over the last 100 ns trajectory in the 1000 ns MD run. The mean value is 0.362.

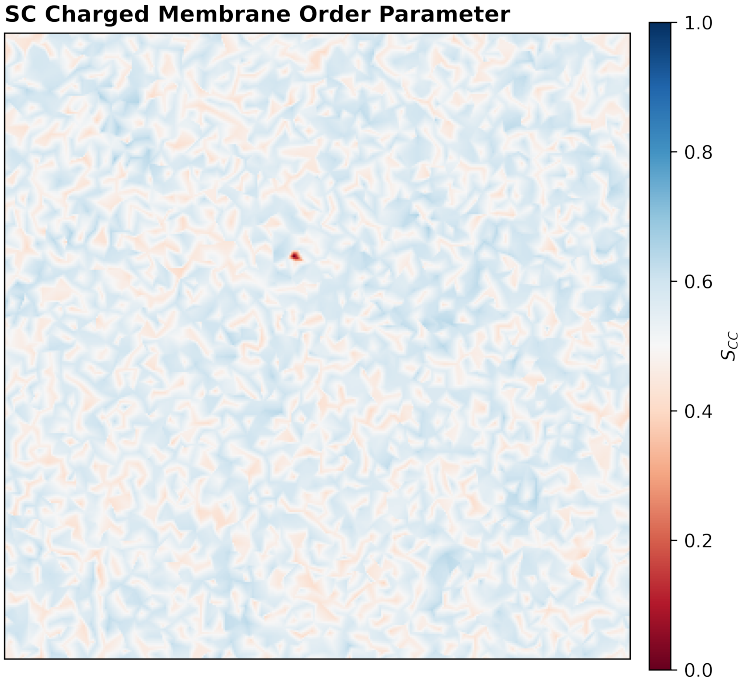


Figure S4 Averaged order parameter (S_{CC}) distributions of charged SC membrane over the last 100 ns trajectory in the 1000 ns MD run. The mean value is 0.528.

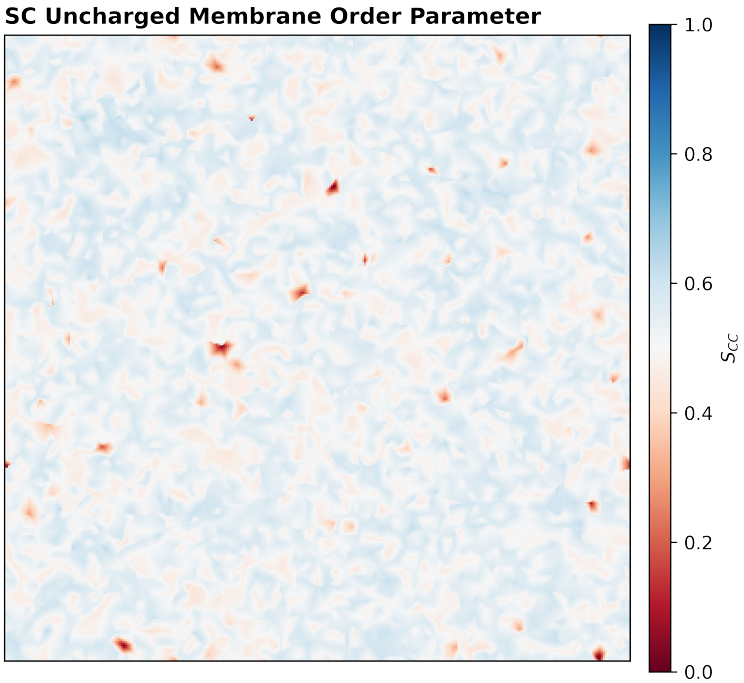


Figure S5 Averaged order parameter (S_{CC}) distributions of uncharged SC membrane over the last 100 ns trajectory in the 1000 ns MD run. The mean value is 0.525.

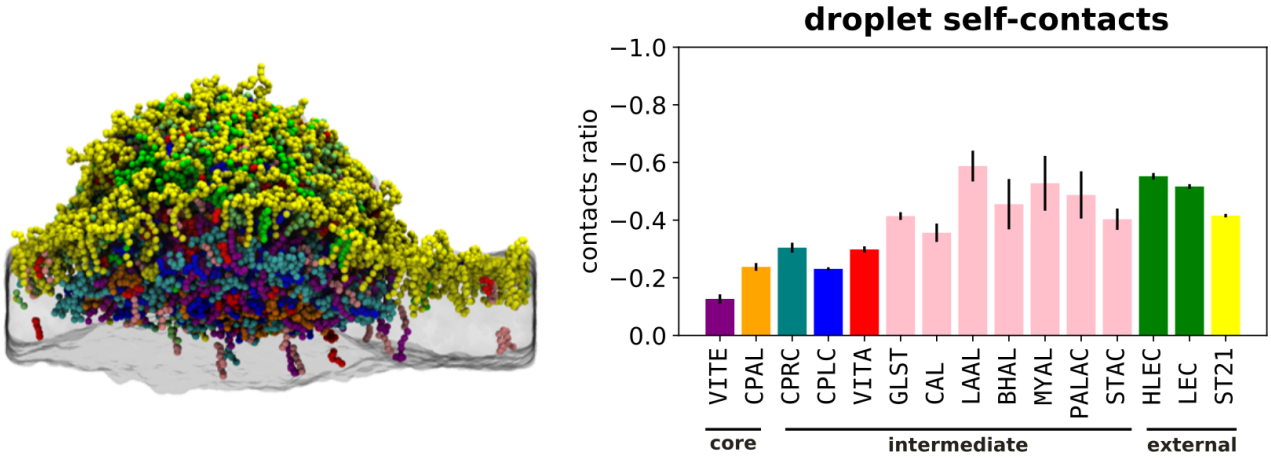


Figure S6 Nanodroplet fusion with neutral stratum corneum membrane. Snapshot of unbiased fusion at the final frame (1000 ns). The change in self-contacts of the bilayer between the initial (0 ns) and final (1000 ns) frame.

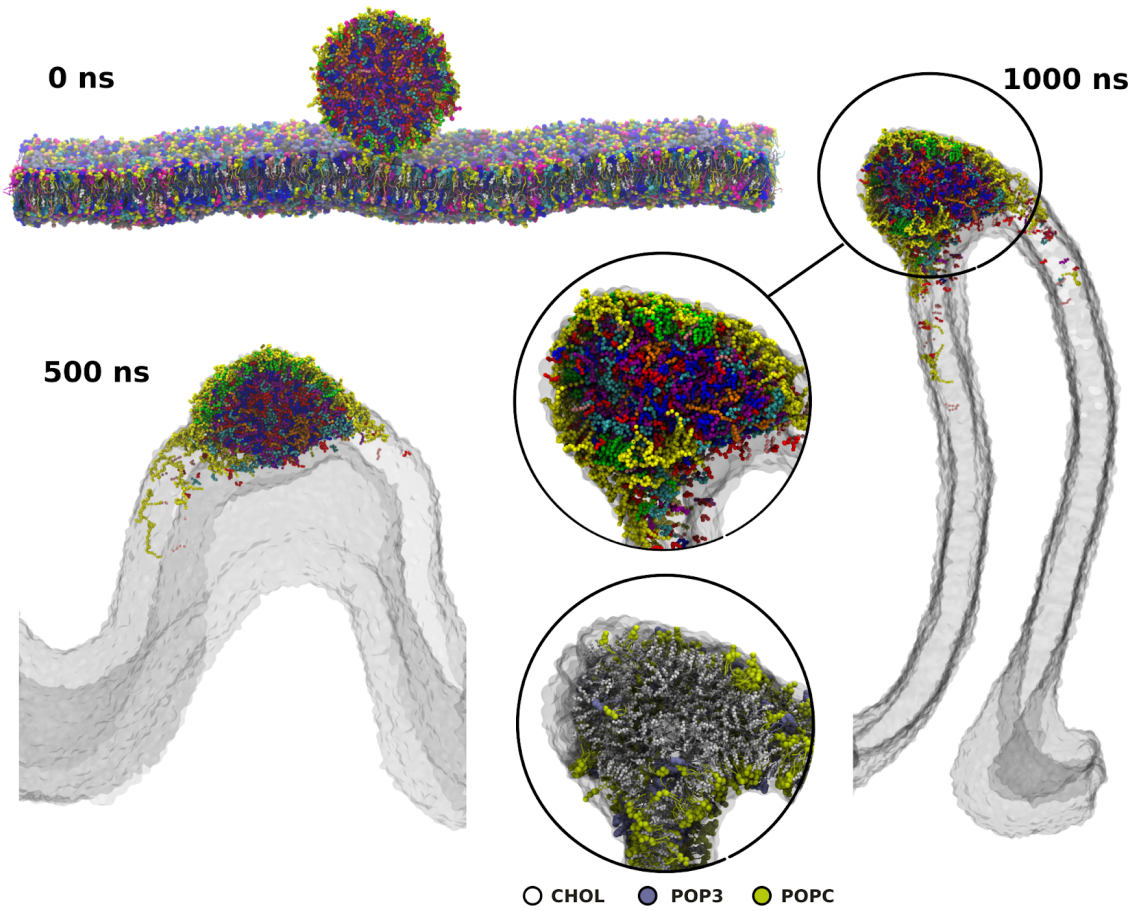


Figure S7 Nanodroplet fusion with a large infundibulum membrane. Snapshots of the nanodroplet with the infundibulum membrane model at different points in time during fusion (left). The zoom boxes show the fusion state at 1000ns, illustrating the relatively high amount of cholesterol compared to the other components.

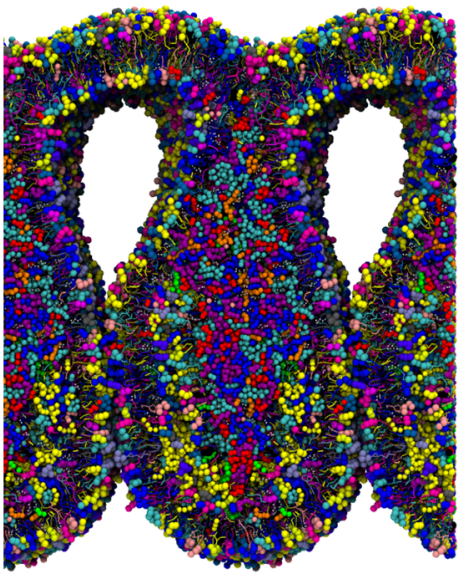
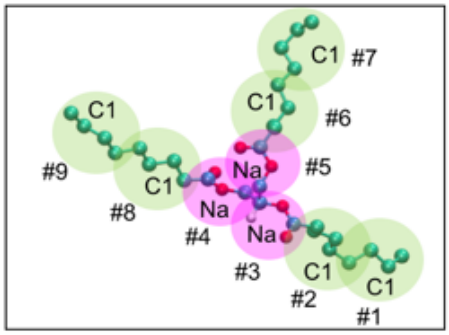
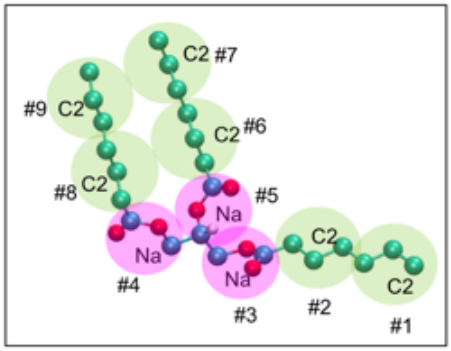
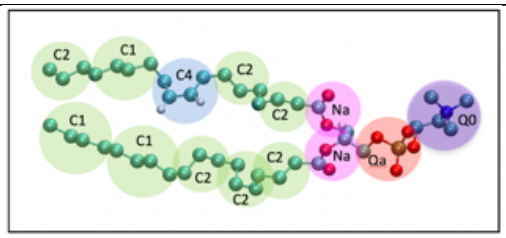
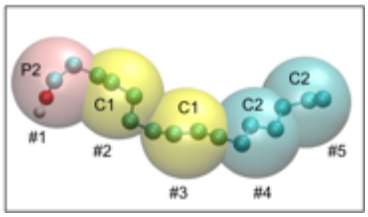
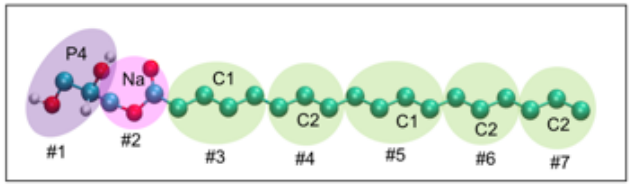
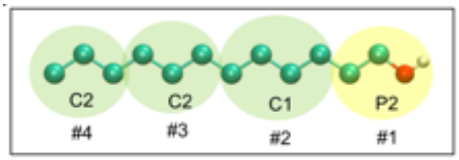
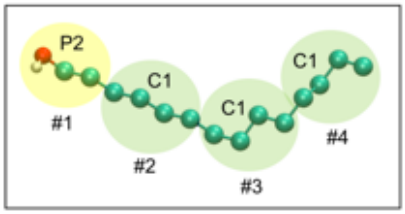
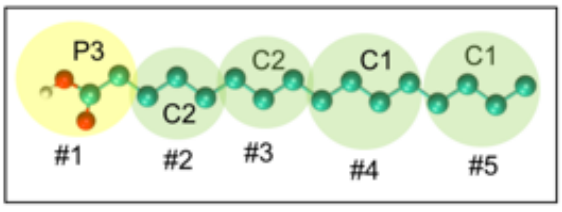
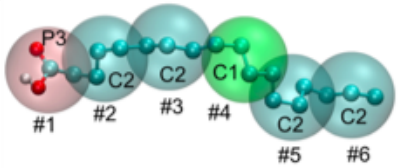
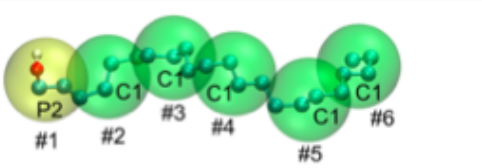
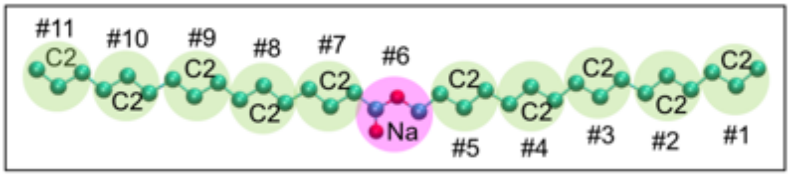


Figure S8 Example of unrealistic membrane folding observed for small INF membrane models caused by the periodic boundary conditions.

Supporting Tables

Table S1 Mappings and bead types of nanodroplet components. List of components of the nanodroplet, including molecule name, molecular formula and CG model, including mapping and bead types.

Mapping in CG representation	Molecule name and Molecular formula
	
Capric acid triglyceride $C_{33}H_{62}O_6$	Caprilic acid triglyceride $C_{27}H_{50}O_6$
	
Hidrogenated Lecithin $C_{44}H_{86}[NO]_8P$	Cetyl alcohol $C_{16}H_{34}O$
	
Gliceryl steareth $C_{21}H_{42}O_4$	Lauryl alcohol $C_{12}H_{26}O$
	
Miristyl $C_{14}H_{30}O$	Palmitic acid $C_{16}H_{32}O_2$
	
Stearic acid $C_{18}H_{36}O_2$	Behenyl alcohol $C_{22}H_{46}O$



Cetyl palmitate $C_{32}H_{64}O_2$

Table S2 Model validation for vitamins and Glycerin. The results of the computational partitioning free energy are compared to experimental values.

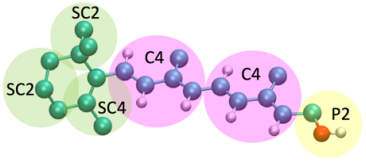
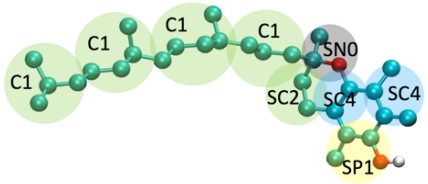
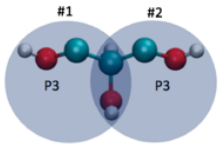
Molecule	Chemical structure	CG representation	Experimental ΔGpart octanol/water	CG MD ΔGpart octanol/water
Vitamin A (retinol)	$C_{20}H_{30}O$		32 kJ/mol	39 kJ/mol
Vitamin E (tocopherol)	$C_{29}H_{50}O_2$		71kJ/mol[3]	70 kJ/mol
Glycerin	$C_3H_8O_3$		-10 kJ/mol[4]	-10 kJ/mol

Table S3 Bonded parameters for glycerin and vitamin A/E.

Molecule	Bead ID	Bead type	Bond Value Constant	Angle Value Constant
Glycerin	1	P3	1-2 0.260 1250	.
.	2	P3	.	.
Vitamin A	1	SC2	1-2 0.289 5000	1-3-4 103 25.0
.	2	SC2	1-3 0.339 5000	2-3-4 145 25.0
.	3	SC4	2-3 0.338 5000	3-4-5 093 25.0
.	4	SC4	3-4 0.304 1250	4-5-6 115 25.0
.	5	SC4	4-5 0.403 1250	.
.	6	P2	5-6 0.316 1250	.
Vitamin E	1	SP1	1-2 0.330 5000	1-2-3 052 25.0
.	2	SC4	1-3 0.270 5000	1-3-4 115 25.0
.	3	SC4	2-3 0.270 5000	1-3-5 171 25.0
.	4	SC2	3-4 0.210 5000	2-3-4 168 25.0
.	5	SN0	3-5 0.270 5000	2-4-5 111 25.0
.	6	C1	4-5 0.240 5000	3-4-5 071 25.0
.	7	C1	5-6 0.310 1250	3-5-6 103 25.0
.	8	C1	6-7 0.350 1250	4-5-6 078 25.0
.	9	C1	7-8 0.420 1250	5-6-7 162 25.0
.	.	.	8-9 0.460 1250	6-7-8 157 25.0
.	.	.	.	7-8-9 162 25.0

References

1 N. Machado, L. dos Santos, B. Carvalho, P. Singh, C. T. Soto, N. Azoia, A. Cavaco-Paulo, A. Martin and P. Favero, *Computers in Biology and Medicine*, 2016, **75**, 151–159.

2 H. I. Ingólfsson, M. N. Melo, F. J. van Eerden, C. Arnarez, C. A. Lopez, T. A. Wassenaar, X. Periole, A. H. de Vries, D. P. Tieleman and S. J. Marrink, *Journal of the American Chemical Society*, 2014, **136**, 14554–14559.

3 *Vitamin E*, ed. E. Niki, Royal Society of Chemistry, 2019.

4 *Physical and thermodynamic properties of pure chemicals: data compilation*, 1990.