SUPPORTING INFORMATION

Simulations of Pure Ceramide and Ternary Lipid Mixtures as Simple Interior *Stratum Corneum* Models

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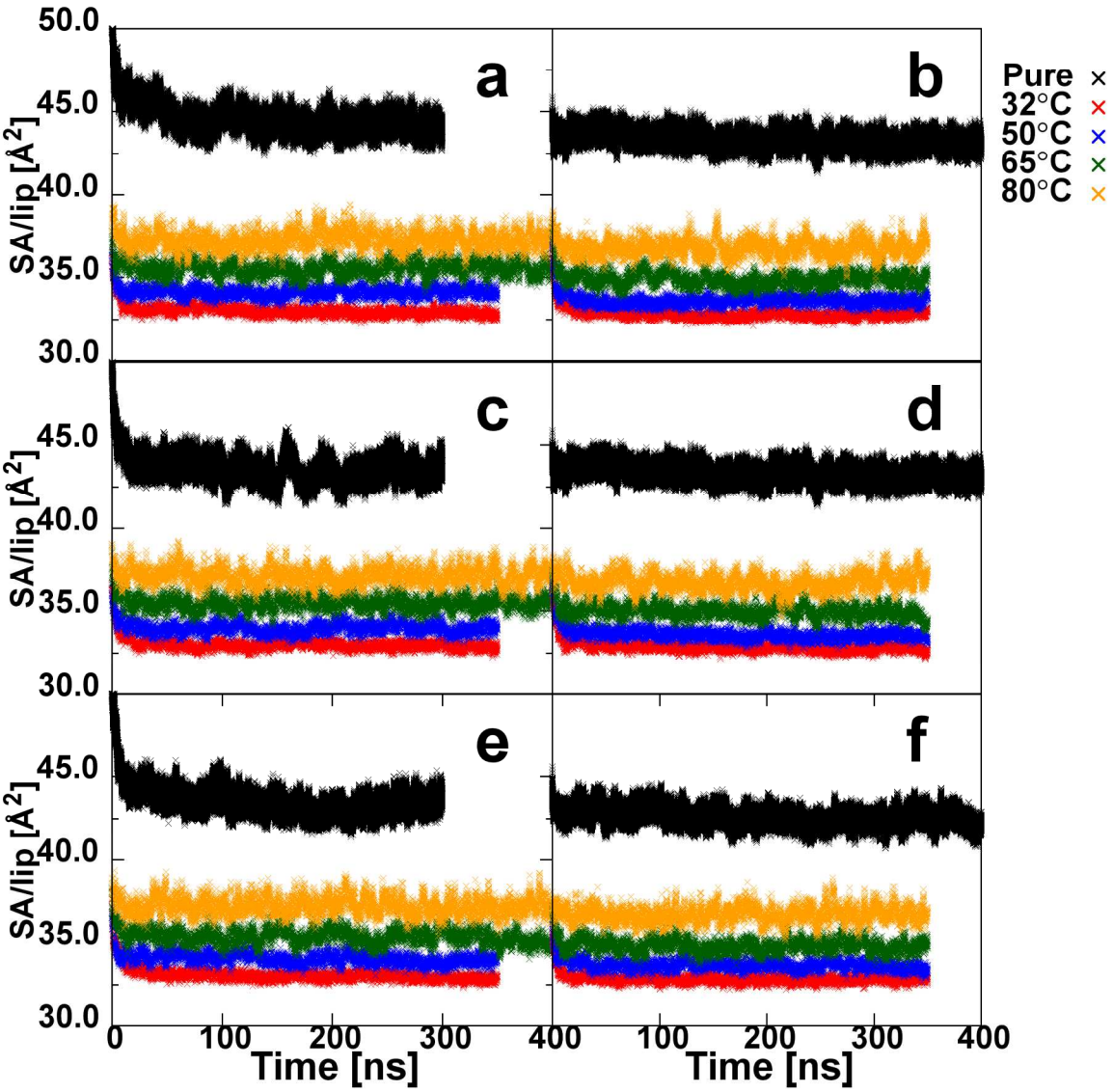

Figure S1. Comparison of overall SA/lip as a function of time for various systems using triplicate replicas for (a,c,e) Cer16 systems and (b,d,f) Cer24 systems. (a,b) represent replica 1, (c,d) represent replica 2, and (e,f) represent replica 3. Systems with a reported temperature are ternary mixtures while "Pure" are systems of pure Cer.

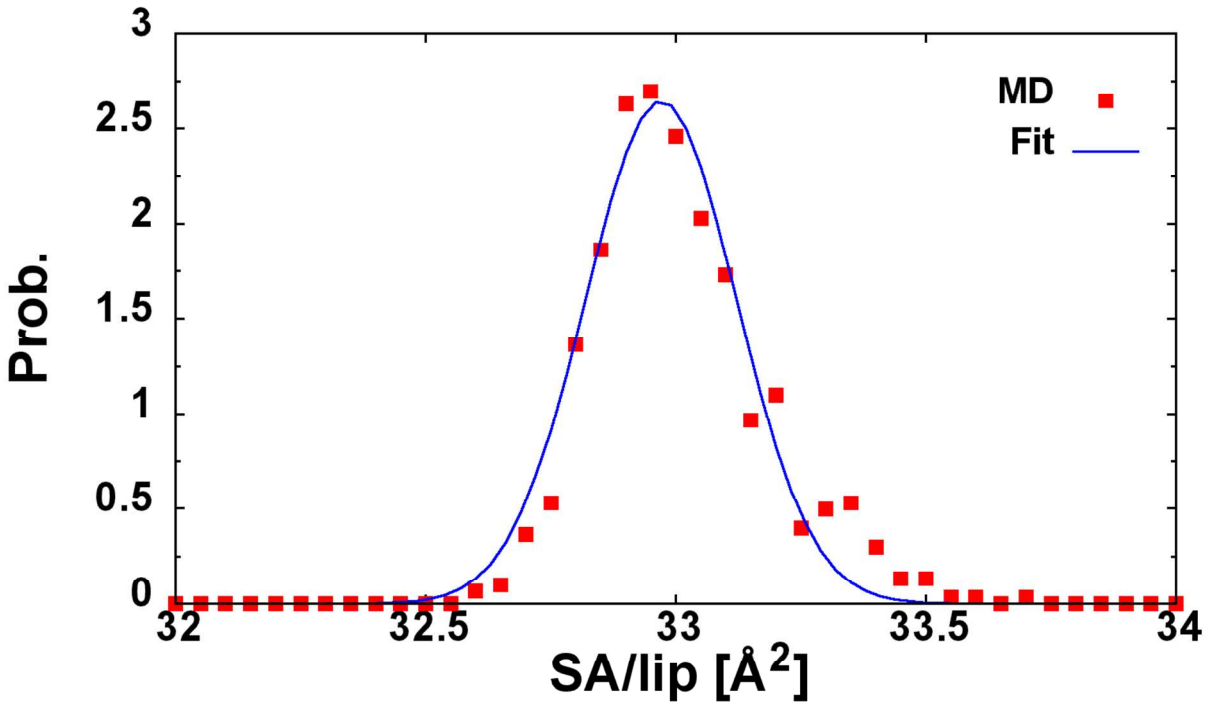

Figure S2. Probability distribution of overall SA/lip for Cer16/Chol/FFA at 32ºC using 0.5 ns blocks of the last 300 ns of data. "MD" refers to simulation data and "Fit" refers to a Gaussian fit with parameters μ=32.97±0.02 Å^2, σ=0.151±0.007 Å^2, and R^2=0.97.

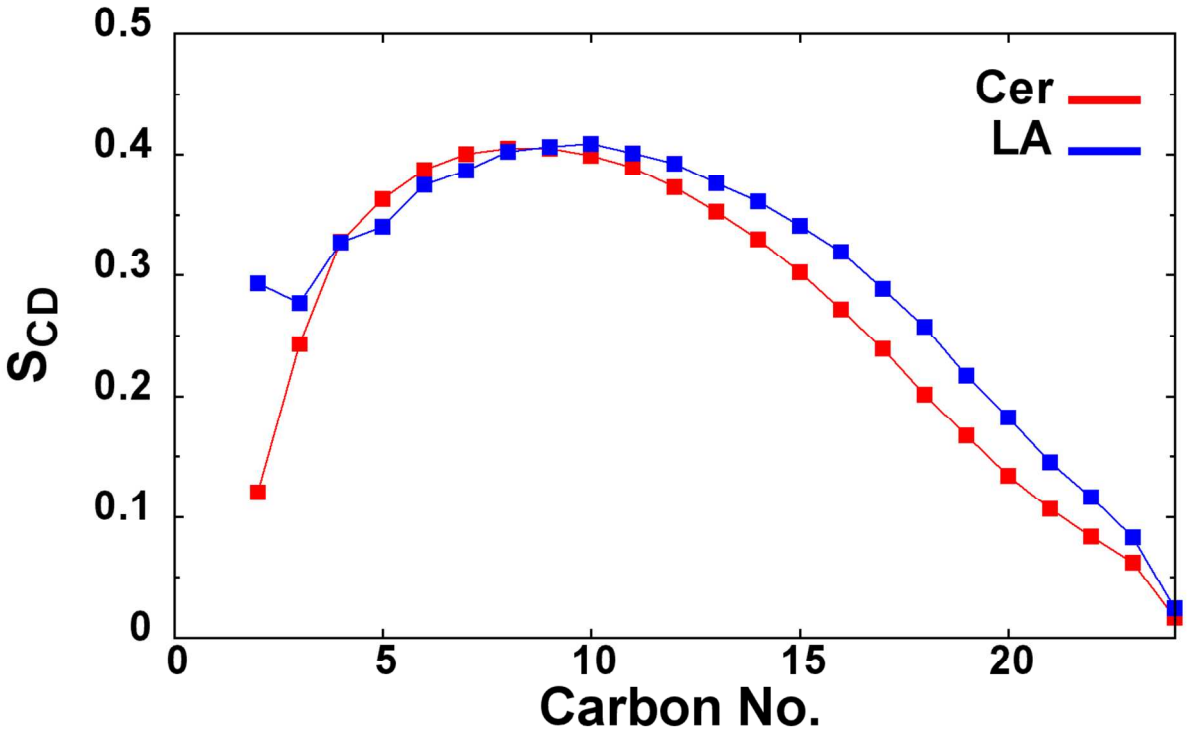

Figure S3. Comparison of S_{CD} between the fatty acid chain of Cer24 and LA in Cer24/Chol/LA at 65ºC.

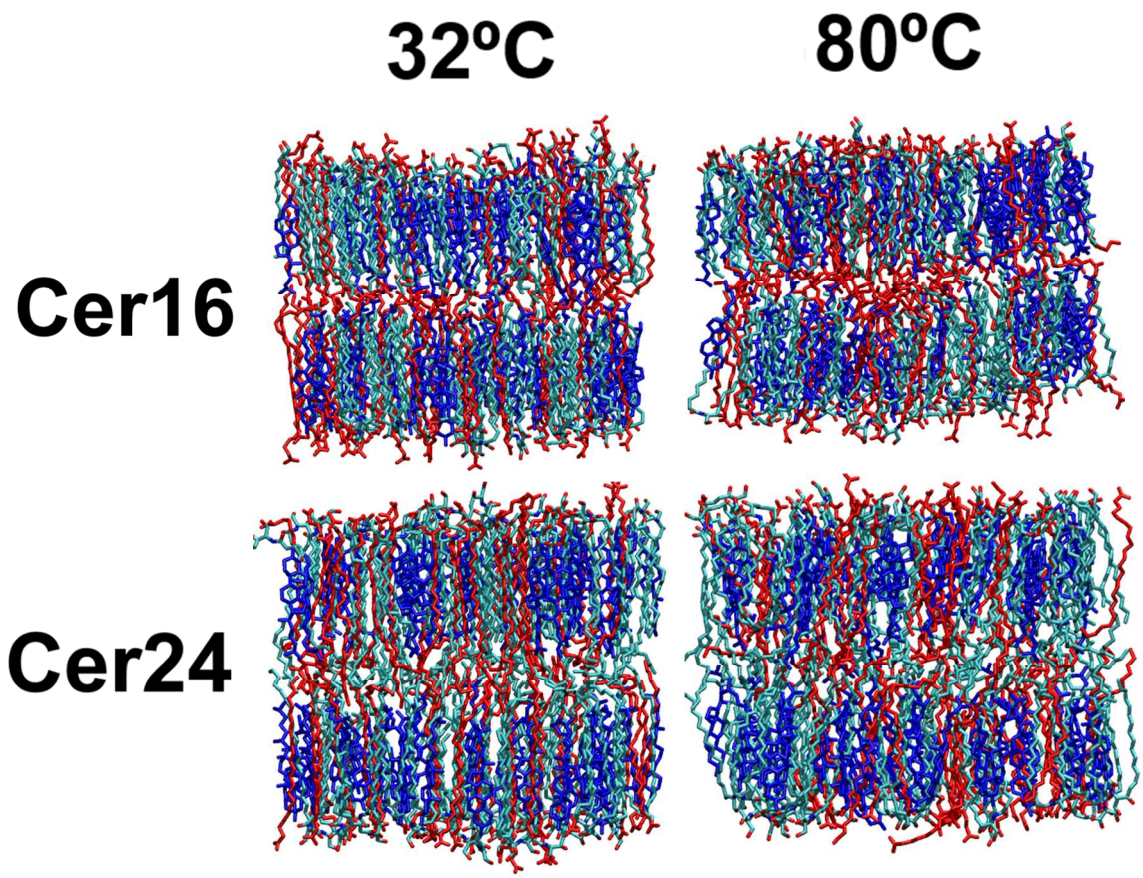

Figure S4. Snapshots of Cer/Chol/LA bilayers taken from the end of simulation.

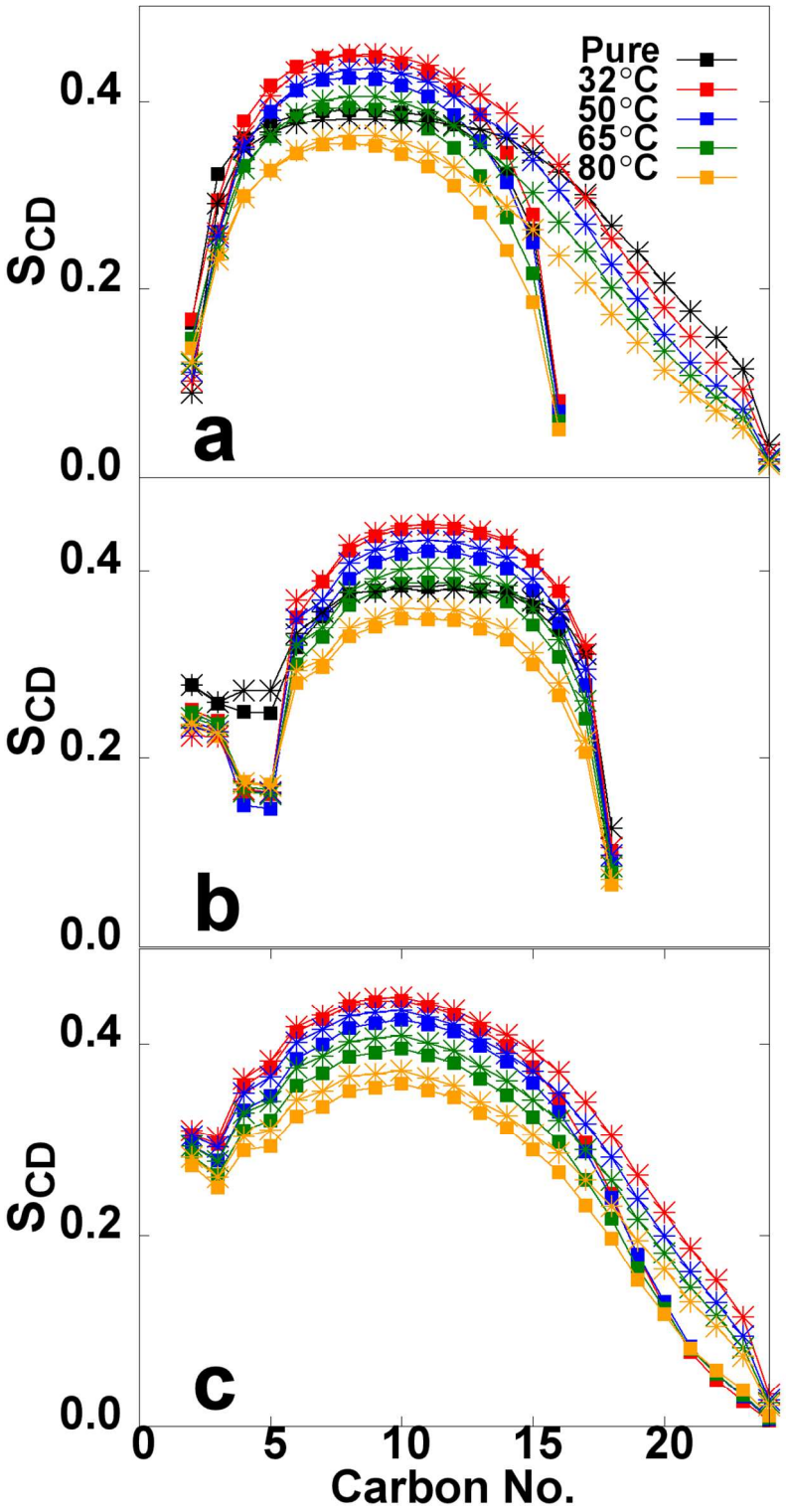

Figure S5. S_{CD} of various systems for a) fatty acid chain of Cer b) sphingosine chain of Cer, and c) fatty acid chain of LA. Systems with a reported temperature are ternary mixtures while "Pure" are systems of pure Cer. Filled boxes represent Cer16 while crosses represent Cer24 systems.

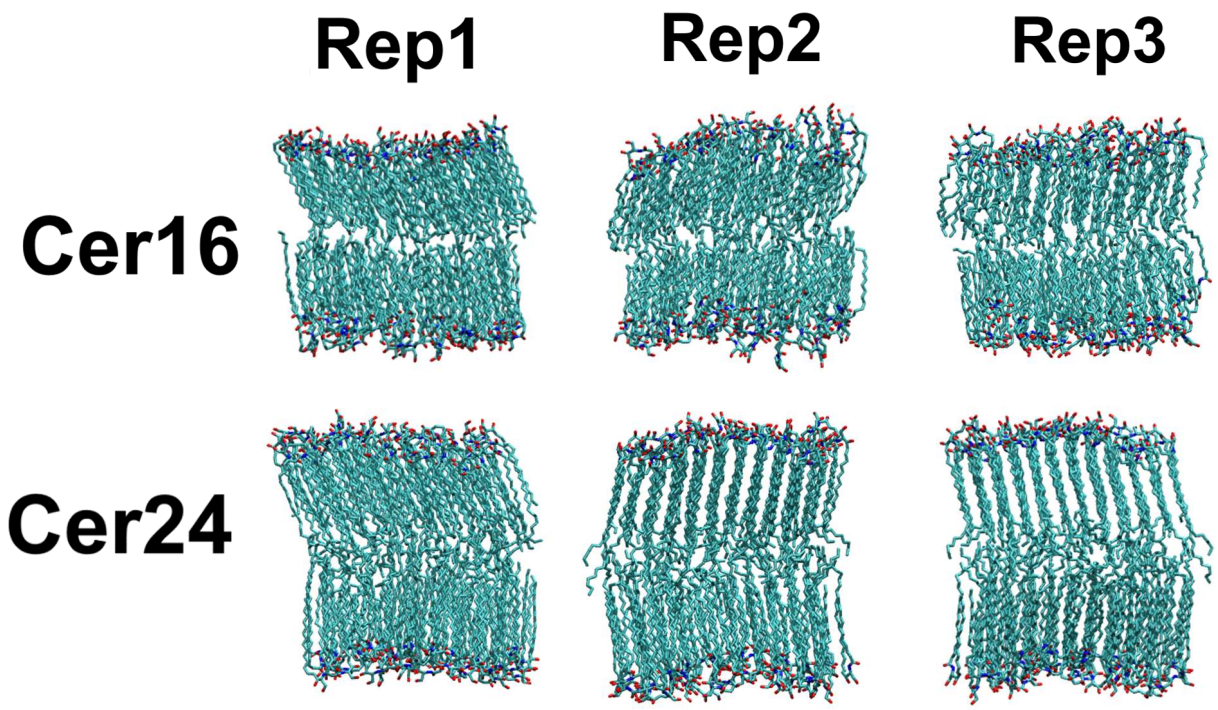

Figure S6. Snapshots of pure Cer bilayers taken from the end of simulation.

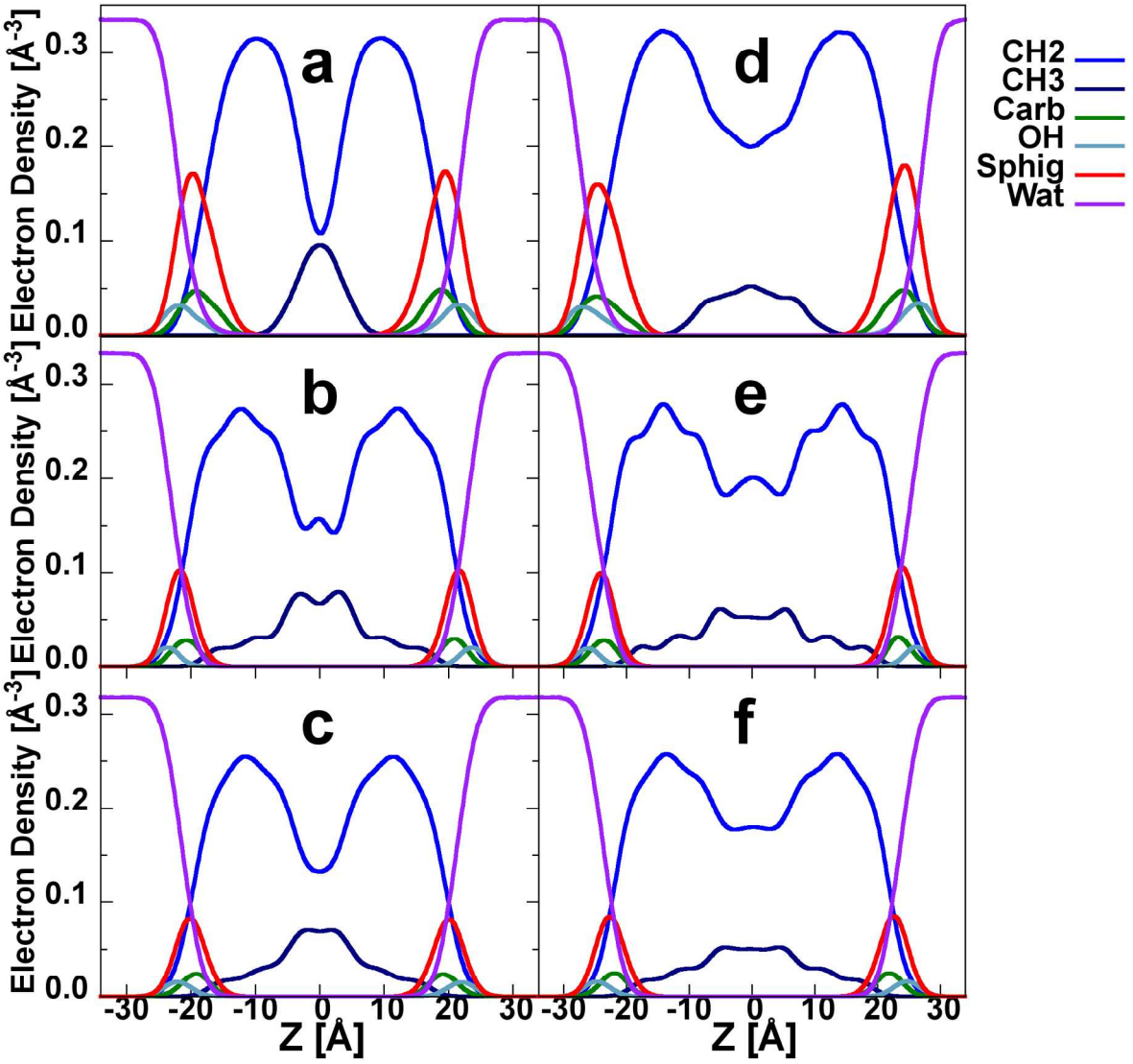

Figure S7. Comparison of Cer component EDPs for (a,d) pure Cer, (b,e) Cer/Chol/LA at 32ºC, and (c,f) Cer/Chol/LA at 80ºC. (a-c) represent Cer16 systems while (d-f) represent Cer24 systems. Groups represented are methylene (CH2), methyl (CH3), carbonyl (Carb), hydroxyl (OH), sphingosine (Sphig), and water (Wat).

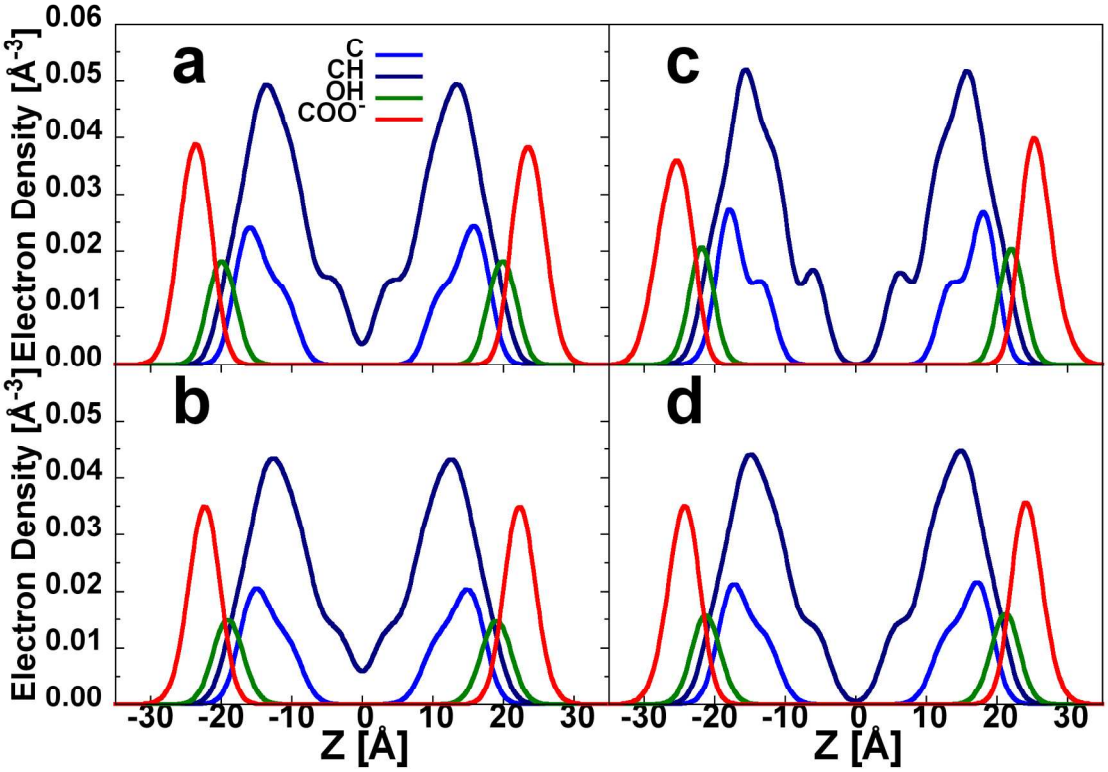

Figure S8. Comparison of Chol and LA component EDPs for (a,c) Cer/Chol/LA at 32ºC, and (b,d) Cer/Chol/LA at 80ºC. (a,b) represent Cer16 systems while (c,d) represent Cer24 systems. Groups represented are hydrogen-lacking carbons (C), methine (CH), Chol hydroxyl (OH), and LA carboxylate (COO^-).

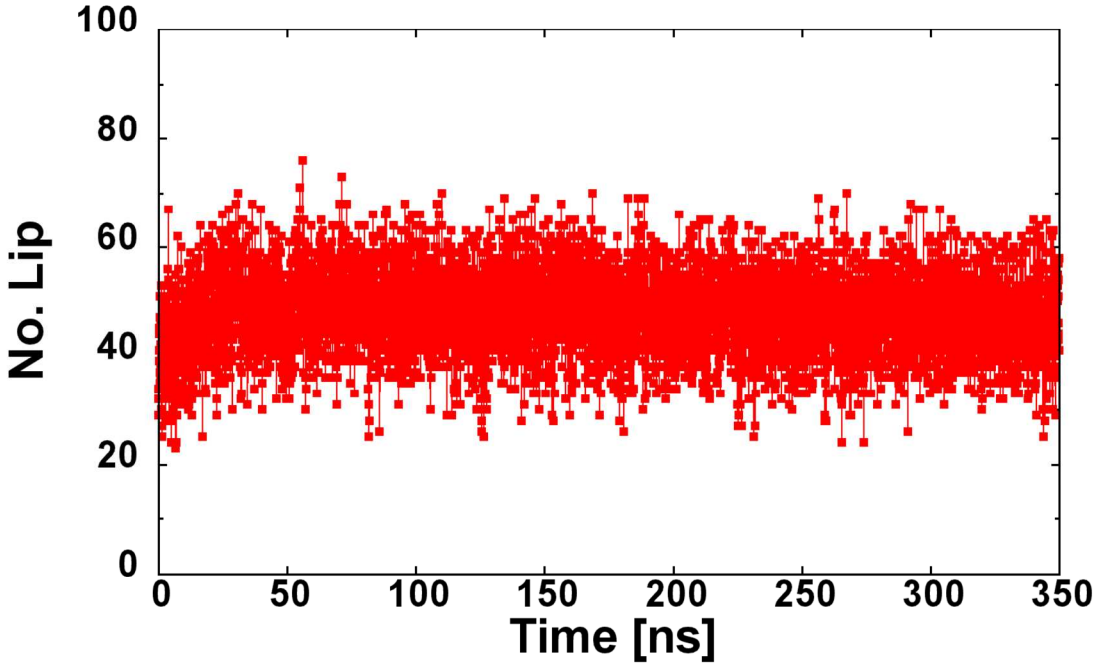

Figure S9. Number of clustered lipids as a function of time for Cer16/Chol/LA at 32ºC. All lipids are considered for clustering analysis.

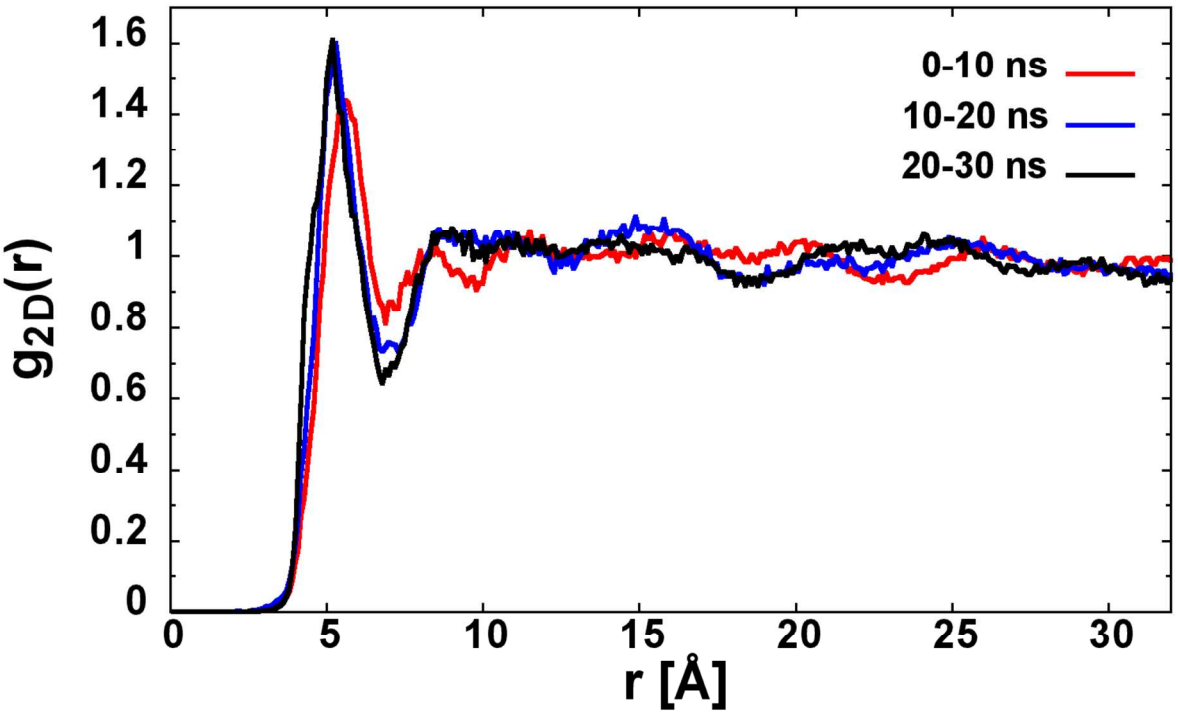

Figure S10. Comparison of Cer ($C2_S$-$C2_S$) self 2D RDFs at different time intervals for Cer16/Chol/LA at 32ºC.

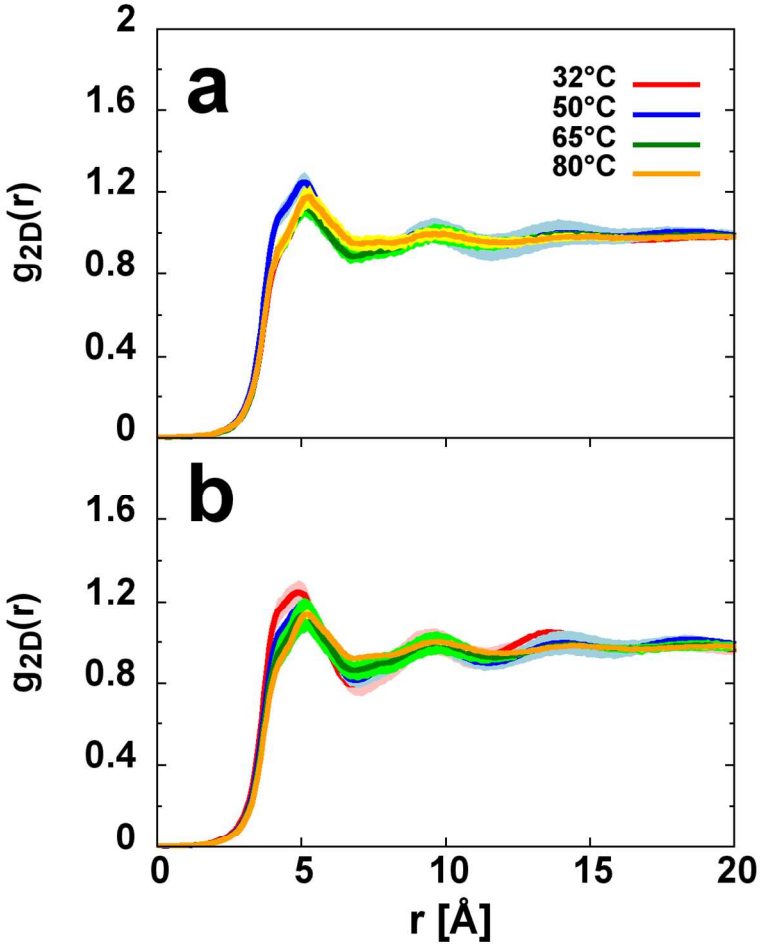

Figure S11. Comparison of LA (C1-C1) self 2D RDFs at different temperatures for a) Cer16 systems and b) Cer24 systems. Lighter shades of each color represent the standard error interval.

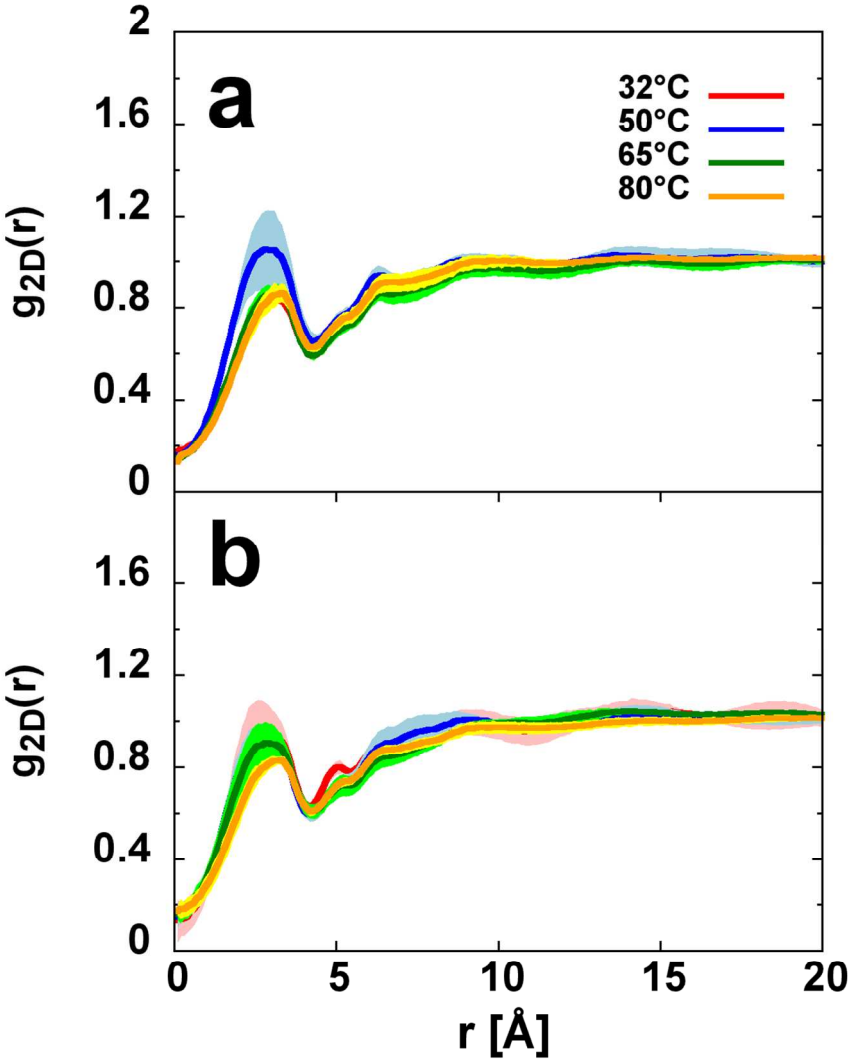

Figure S12. Comparison of Cer-Chol 2D RDFs at different temperatures for a) Cer16 systems and b) Cer24 systems. Atoms are selected based on self RDFs (Cer $C2_S$ and Chol O3). Lighter shades of each color represent the standard error interval.

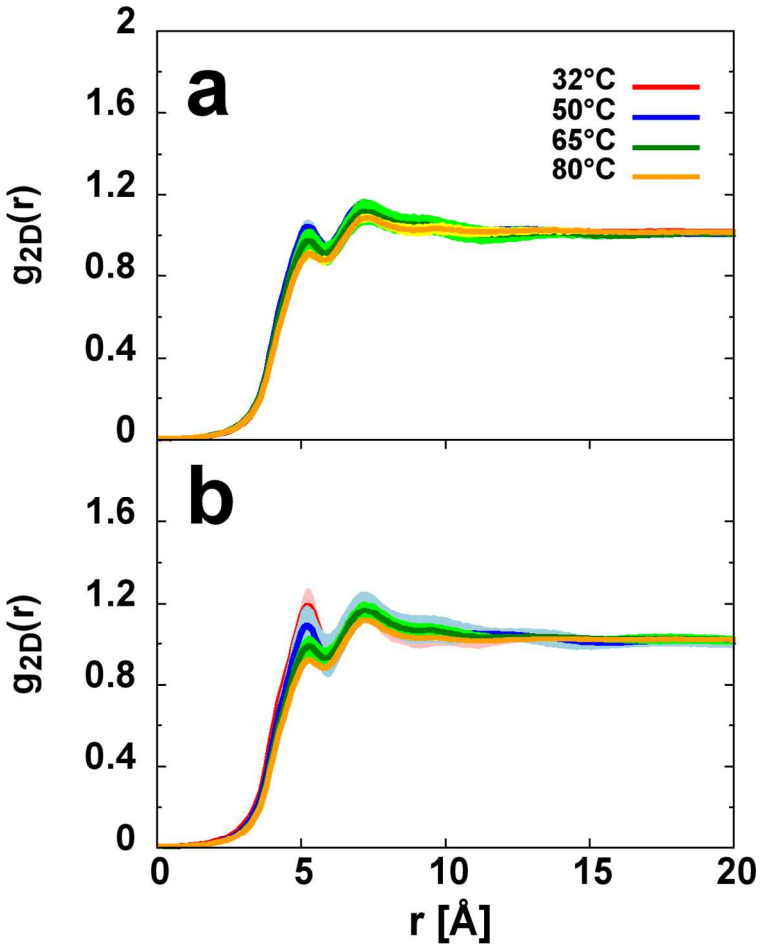

Figure S13. Comparison of Cer-LA 2D RDFs at different temperatures for a) Cer16 systems and b) Cer24 systems. Atoms are selected based on self RDFs (Cer $C2_S$ and LA C1). Lighter shades of each color represent the standard error interval.

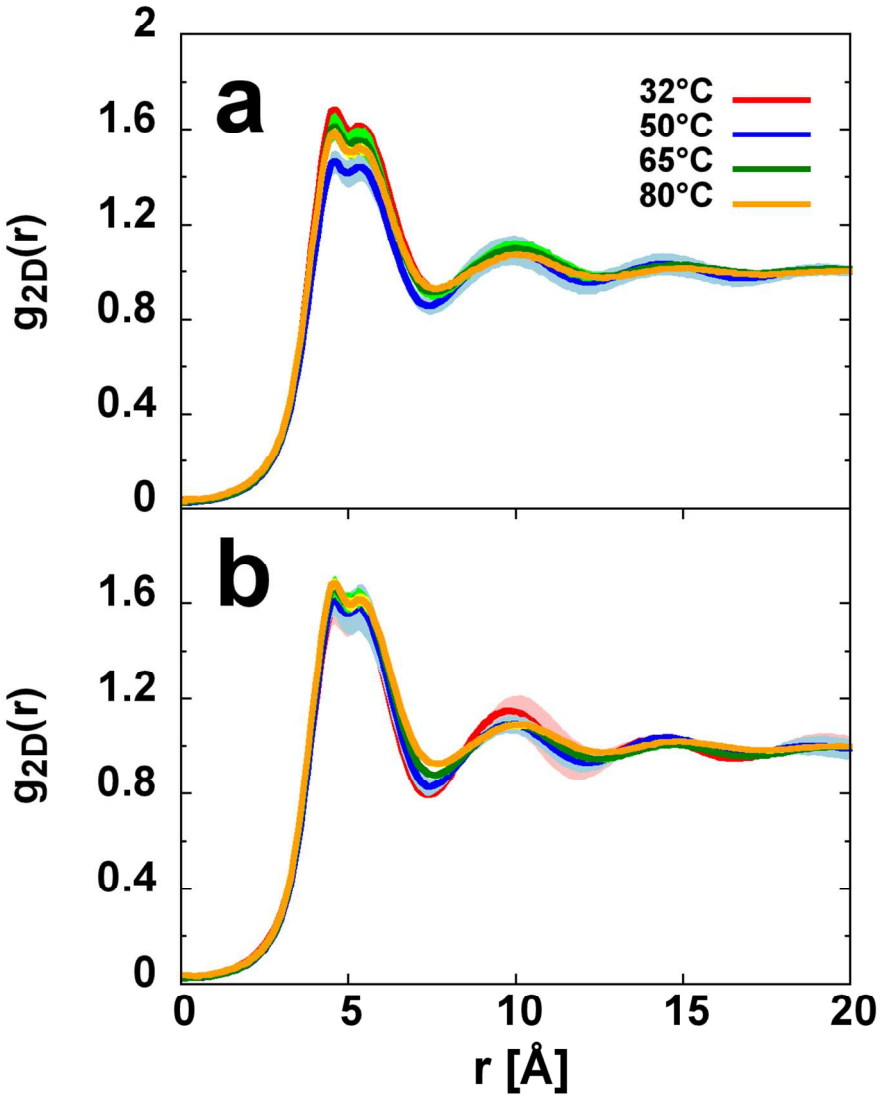

Figure S14. Comparison of Chol-LA 2D RDFs at different temperatures for a) Cer16 systems and b) Cer24 systems. Atoms are selected based on self RDFs (Chol O3 and LA C1). Lighter shades of each color represent the standard error interval.

Table S1. Hydrogen bond (defined as when the distance between donor and acceptor is less than 2.4 Å and the angle is greater than 150º) count for significant groups/ hydrogen bond pairs involving Cer donors. Subscript LA refers to LA acceptor groups.

Bond	System	T (ºC)	N_{HB}/lip
N-H::O=C	Cer16	32	0.328±0.009
	Cer16/Chol/LA	32	0.149±0.009
	Cer16/Chol/LA	50	0.147±0.009
	Cer16/Chol/LA	65	0.181±0.005
	Cer16/Chol/LA	80	0.151±0.003
	Cer24	32	0.362±0.007
	Cer24/Chol/LA	32	0.126±0.023
	Cer24/Chol/LA	50	0.152±0.010
	Cer24/Chol/LA	65	0.156±0.015
	Cer24/Chol/LA	80	0.147±0.004
N-H::O$^-$C$_{LA}$	Cer16	32	--
	Cer16/Chol/LA	32	0.056±0.009
	Cer16/Chol/LA	50	0.038±0.002
	Cer16/Chol/LA	65	0.031±0.001
	Cer16/Chol/LA	80	0.026±0.0004
	Cer24	32	--
	Cer24/Chol/LA	32	0.056±0.006
	Cer24/Chol/LA	50	0.052±0.005
	Cer24/Chol/LA	65	0.036±0.001
	Cer24/Chol/LA	80	0.031±0.001
N-H::O=C$_{LA}$	Cer16	32	--
	Cer16/Chol/LA	32	0.057±0.009
	Cer16/Chol/LA	50	0.037±0.001
	Cer16/Chol/LA	65	0.030±0.001
	Cer16/Chol/LA	80	0.026±0.001
	Cer24	32	--
	Cer24/Chol/LA	32	0.058±0.007
	Cer24/Chol/LA	50	0.052±0.005
	Cer24/Chol/LA	65	0.036±0.002
	Cer24/Chol/LA	80	0.032±0.001

Table S2. Hydrogen bond (defined as when the distance between donor and acceptor is less than 2.4 Å and the angle is greater than 150º) count for significant groups/ hydrogen bond pairs involving Chol donors. Subscript LA refers to LA acceptor groups.

Bond	System	T (ºC)	N_{HB}/lip
O-H::O=C	Cer16	32	--
	Cer16/Chol/LA	32	0.104±0.006
	Cer16/Chol/LA	50	0.128±0.014
	Cer16/Chol/LA	65	0.103±0.002
	Cer16/Chol/LA	80	0.097±0.003
	Cer24	32	--
	Cer24/Chol/LA	32	0.105±0.009
	Cer24/Chol/LA	50	0.097±0.003
	Cer24/Chol/LA	65	0.104±0.003
	Cer24/Chol/LA	80	0.090±0.002
O-H::O^{-}C$_{LA}$	Cer16	32	--
	Cer16/Chol/LA	32	0.044±0.001
	Cer16/Chol/LA	50	0.040±0.001
	Cer16/Chol/LA	65	0.046±0.001
	Cer16/Chol/LA	80	0.044±0.0001
	Cer24	32	--
	Cer24/Chol/LA	32	0.045±0.001
	Cer24/Chol/LA	50	0.047±0.001
	Cer24/Chol/LA	65	0.048±0.001
	Cer24/Chol/LA	80	0.048±0.0005
O-H::O=C$_{LA}$	Cer16	32	--
	Cer16/Chol/LA	32	0.045±0.001
	Cer16/Chol/LA	50	0.041±0.001
	Cer16/Chol/LA	65	0.046±0.001
	Cer16/Chol/LA	80	0.044±0.0002
	Cer24	32	--
	Cer24/Chol/LA	32	0.045±0.001
	Cer24/Chol/LA	50	0.048±0.001
	Cer24/Chol/LA	65	0.048±0.0002
	Cer24/Chol/LA	80	0.048±0.0003

Table S3. Clustering fractions for Cer, Chol, and LA. N_C is the number of lipids per cluster, R_C is the fraction of the particular lipid in clusters, and R_N is the fraction of the particular lipid in the membrane.

Lipid	System	T (ºC)	N_C	R_C	R_N*	R_C-R_N
Cer	Cer16	32	3.73±0.02	--	--	--
	Cer16/Chol/LA	32	1.57±0.02	0.387±0.003	0.34	0.047±0.003
	Cer16/Chol/LA	50	1.60±0.02	0.401±0.005	0.34	0.061±0.005
	Cer16/Chol/LA	65	1.56±0.02	0.398±0.005	0.34	0.058±0.005
	Cer16/Chol/LA	80	1.50±0.01	0.392±0.001	0.34	0.052±0.001
	Cer24	32	3.91±0.03	--	--	--
	Cer24/Chol/LA	32	1.56±0.01	0.381±0.004	0.34	0.041±0.004
	Cer24/Chol/LA	50	1.55±0.01	0.389±0.003	0.34	0.049±0.003
	Cer24/Chol/LA	65	1.53±0.01	0.387±0.004	0.34	0.047±0.004
	Cer24/Chol/LA	80	1.49±0.004	0.386±0.001	0.34	0.046±0.001
Chol	Cer16	32	--	--	--	--
	Cer16/Chol/LA	32	1.30±0.04	0.320±0.008	0.33	-0.010±0.008
	Cer16/Chol/LA	50	1.29±0.02	0.324±0.005	0.33	-0.006±0.005
	Cer16/Chol/LA	65	1.26±0.004	0.322±0.002	0.33	-0.008±0.002
	Cer16/Chol/LA	80	1.26±0.003	0.329±0.001	0.33	-0.001±0.001
	Cer24	32	--	--	--	--
	Cer24/Chol/LA	32	1.32±0.02	0.322±0.004	0.33	-0.008±0.004
	Cer24/Chol/LA	50	1.31±0.004	0.329±0.003	0.33	-0.001±0.003
	Cer24/Chol/LA	65	1.30±0.01	0.330±0.001	0.33	0.000±0.001
	Cer24/Chol/LA	80	1.28±0.01	0.331±0.002	0.33	0.001±0.002
LA	Cer16	32	--	--	--	--
	Cer16/Chol/LA	32	1.18±0.02	0.292±0.007	0.33	-0.038±0.007
	Cer16/Chol/LA	50	1.10±0.02	0.276±0.006	0.33	-0.054±0.006
	Cer16/Chol/LA	65	1.10±0.01	0.280±0.003	0.33	-0.050±0.003
	Cer16/Chol/LA	80	1.07±0.002	0.279±0.001	0.33	-0.051±0.001
	Cer24	32	--	--	--	--
	Cer24/Chol/LA	32	1.21±0.02	0.297±0.004	0.33	-0.033±0.004
	Cer24/Chol/LA	50	1.13±0.03	0.282±0.006	0.33	-0.048±0.006
	Cer24/Chol/LA	65	1.12±0.01	0.283±0.003	0.33	-0.047±0.003
	Cer24/Chol/LA	80	1.09±0.004	0.283±0.001	0.33	-0.047±0.001

* Value is exact