Supporting Information

Mesoporous silica as a matrix for photocatalytic titanium dioxide nanoparticles: Lipid membrane interactions

*Elisa Parra-Ortiz[1], Lucrezia Caselli[1], Monica Agnoletti[1], Maximilian W. A. Skoda[2], Xiaomin Li[3], Dongyuan Zhao[3], and Martin Malmsten[1,4]**

[1]Department of Pharmacy, University of Copenhagen, DK-2100 Copenhagen, Denmark

[2]ISIS Pulsed Neutron and Muon Source, Rutherford Appleton Laboratory, OX11 0QX Harwell, Oxfordshire, UK

[3]Department of Chemistry, Collaborative Innovation Center of Chemistry for Energy Materials, State Key Laboratory of Molecular Engineering of Polymers, Fudan University, 200433 Shanghai, P. R. China

[4]Department of Physical Chemistry 1, University of Lund, SE-22100 Lund, Sweden

*Corresponding author (martin.malmsten@sund.ku.dk)

KEYWORDS: Lipid membrane, lipid oxidation, mesoporous, photocatalysis, silica, TiO_2

Table S1. Scattering length densities (SLD) of the different materials used in the neutron reflectivity experiments, calculated using the Neutron Activation and Scattering Calculator and the Biomolecular Scattering Length Density Calculator.[1, 2]

Material	SLD ($\cdot 10^{-6}$ Å^{-2})
Silicon (Si)	2.07
Silicon oxide (SiO_2)	3.47
Titanium oxide (TiO_2)	2.42
Head groups in h-buffer	2.00[a]
Head groups in CM-buffer	2.06[a]
Head groups in d-buffer	2.17[a]
Hydrogenated acyl tails (2/1/1 palmitoyl/arachidonoyl/oleyl)	-0.231[b]
h-buffer	-0.56
CM-buffer	2.07
d-buffer	6.10-6.25[d]

[a] Calculated assuming a 3/1 PC/PG (mol/mol) head group composition, which varies due to partial hydrogen exchange of the PG groups.

[b] Calculated as the arithmetic mean of the SLD of palmitoyl, arachidonoyl and oleyl chains by the formula: $SLD = \frac{\Sigma(N_i \cdot b_i)}{V_m}$

[c] Calculated from the amino acid sequence using the Biomolecular Scattering Length Density Calculator, and allowing the default 90% labile hydrogen exchange.

[d] 10 mM Tris buffer made using 99% D_2O; SLD value adjusted manually from the critical edge position in each neutron reflectivity sample curve.

Table S2. Summary of structural data obtained from the neutron reflectivity fits of 50/25/25 (molar ratio) POPC/PAPC/POPG bilayers before and after incubation with the samples indicated, all in 10 mM Acetate buffer, pH 3.4. Values in bold were fixed and assumed constant. An extra outermost layer was also included in the analysis for the final bilayer after incubation the nanoparticles and 2 h of UV exposure in order to obtain good fits, and its resulting parameters are listed in **Table S3**. Errors were calculated using the Bootstrap Error Estimate function in RasCAL.[3,4] Error analysis showed less than 1 Å error for thickness and roughness, 2% for hydration, and $0.1 \cdot 10^{-6}$ Å^{-2} for SLD, unless otherwise specified.

- **Virus-like Mesoporous SiO_2 Nanoparticles**

Sample		Initial bilayer					Final bilayer				
		Thick (Å)	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**	**Thick (Å)**	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**
100 ppm Virus-like SiO_2 + 25 ppm TiO_2	**Heads**	**7.5**	4	34	63	44	**7.5**	8	71	146	42
	Tails	29	6	0			27	11	52		
100 ppm Virus-like SiO_2	**Heads**	**7.5**	4	30	60	46	**7.5**	4	39	68	44
	Tails	31	5	0			29	5	7		

- **Smooth Mesoporous SiO_2 Nanoparticles**

Sample		Initial bilayer					Final bilayer				
		Thick (Å)	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**	**Thick (Å)**	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**
100 ppm Smooth SiO_2 + 25 ppm TiO_2	**Heads**	**7.5**	4	32	62	45	**7.5**	8	77	181	45
	Tails	30	5	0			30	5	66		

- **TiO_2 Nanoparticles**

Sample		Initial bilayer					Final bilayer				
		Thick (Å)	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**	**Thick (Å)**	**Rough (Å)**	**Hyd (%)**	**APM (Å²)**	**Total thick (Å)**
25 ppm TiO_2	**Heads**	**7.5**	5	30	60	46	**7.5**	5	78	185	43
	Tails	31	5	0			28	10	64		

Table S3. Structural parameters obtained for the outermost region in the neutron reflectivity fits of 50/25/25 (molar ratio) POPC/PAPC/POPG bilayers after incubation with the different nanoparticles and 2 h of UV exposure at pH 3.4, characterized in 3 contrasts.

Final outermost layer	**100 ppm Virus-like SiO_2 + 25 ppm TiO_2**	**100 ppm Smooth SiO_2 + 25 ppm TiO_2**	**25 ppm TiO_2**
Thickness (Å)	17 ± 2	16 ± 1	29 ± 1
Roughness (Å)	29 ± 2	10 ± 2	23 ± 2
Hydration (%)	47 ± 2	71 ± 2	64 ± 2
SLD (· 10^{-6} $Å^{-2}$)	1.7 ± 0.1	2.4 ± 0.1	1.6 ± 0.1

Figure S1. Size distribution of 25 ppm bare TiO_2 nanoparticles at pH 3.4 (A), and corresponding correlation coefficient for TiO_2 nanoparticles at pH 3.4 (B), from which the distribution function of Figure S1A is calculated. The correlation coefficients measured for TiO_2 nanoparticles at pH 5.4 and 7.4 are also shown, while reliable distribution functions cannot be calculated with conventional models (e.g. Contin and cumulants algorithms) due to the severe aggregation of the samples.

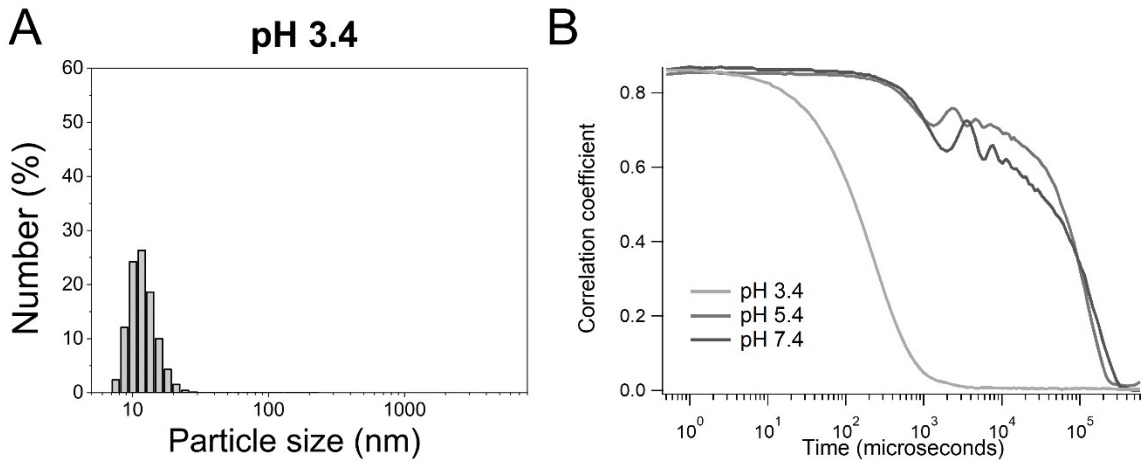


Figure S2. Size distributions of 100 ppm free *smooth* SiO_2 at pH 3.4, 5.4 and 7.4 (top), 100/25 ppm smooth SiO_2/TiO_2 obtained by direct mixing at pH 3.4, 5.4 or 7.4 (middle), and 100/25 ppm smooth SiO_2/TiO_2 obtained by mixing at pH 3.4 followed by pH increase and rinsing (bottom).

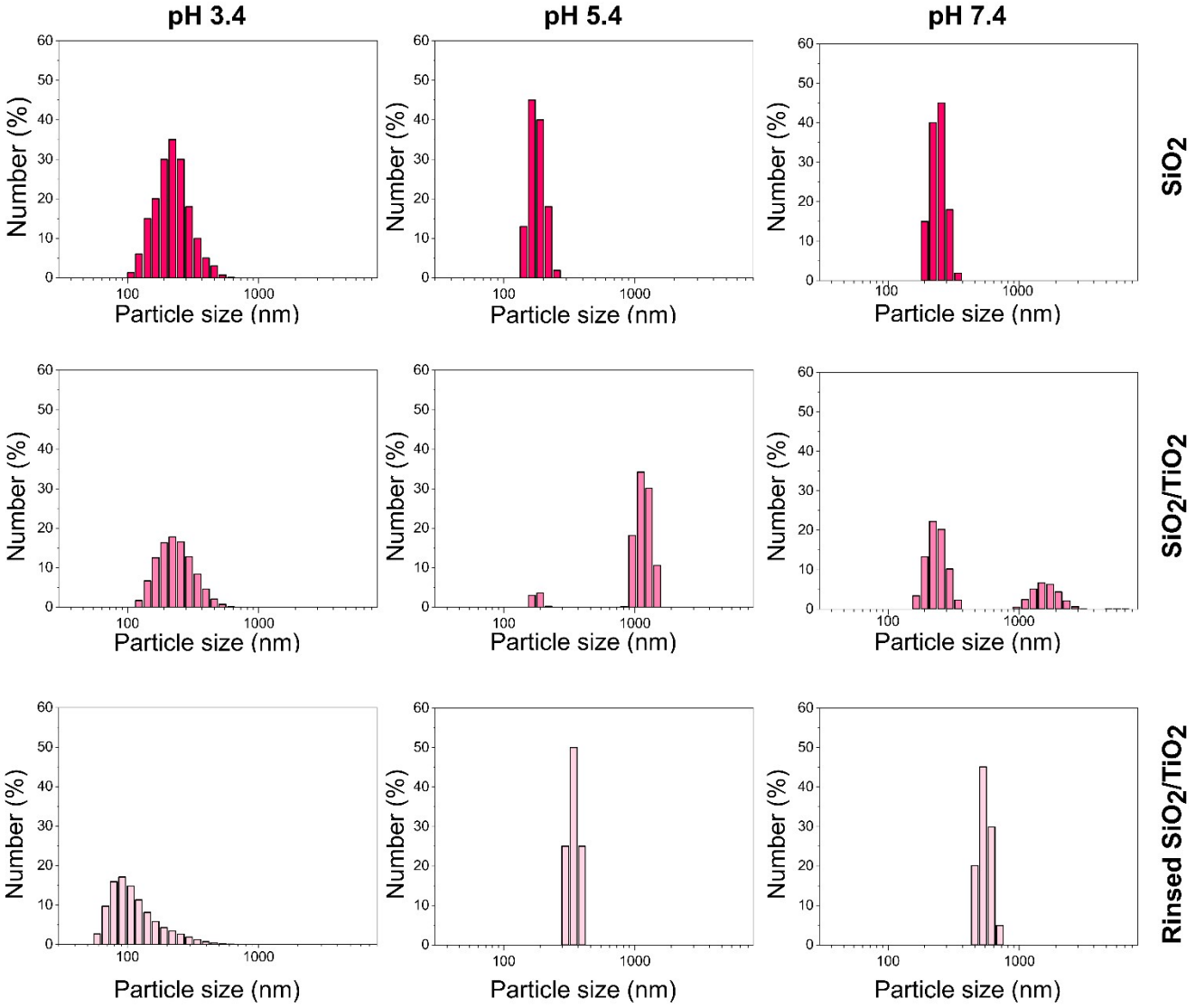


Figure S3. Size distributions of 100 ppm free *virus-like* SiO_2 at pH 3.4, 5.4 and 7.4 (top), 100/25 ppm virus-like SiO_2/TiO_2 obtained by direct mixing at pH 3.4, 5.4 or 7.4 (middle), and 100/25 ppm virus-like SiO_2/TiO_2 obtained by mixing at pH 3.4 followed by pH increase and rinsing (bottom).

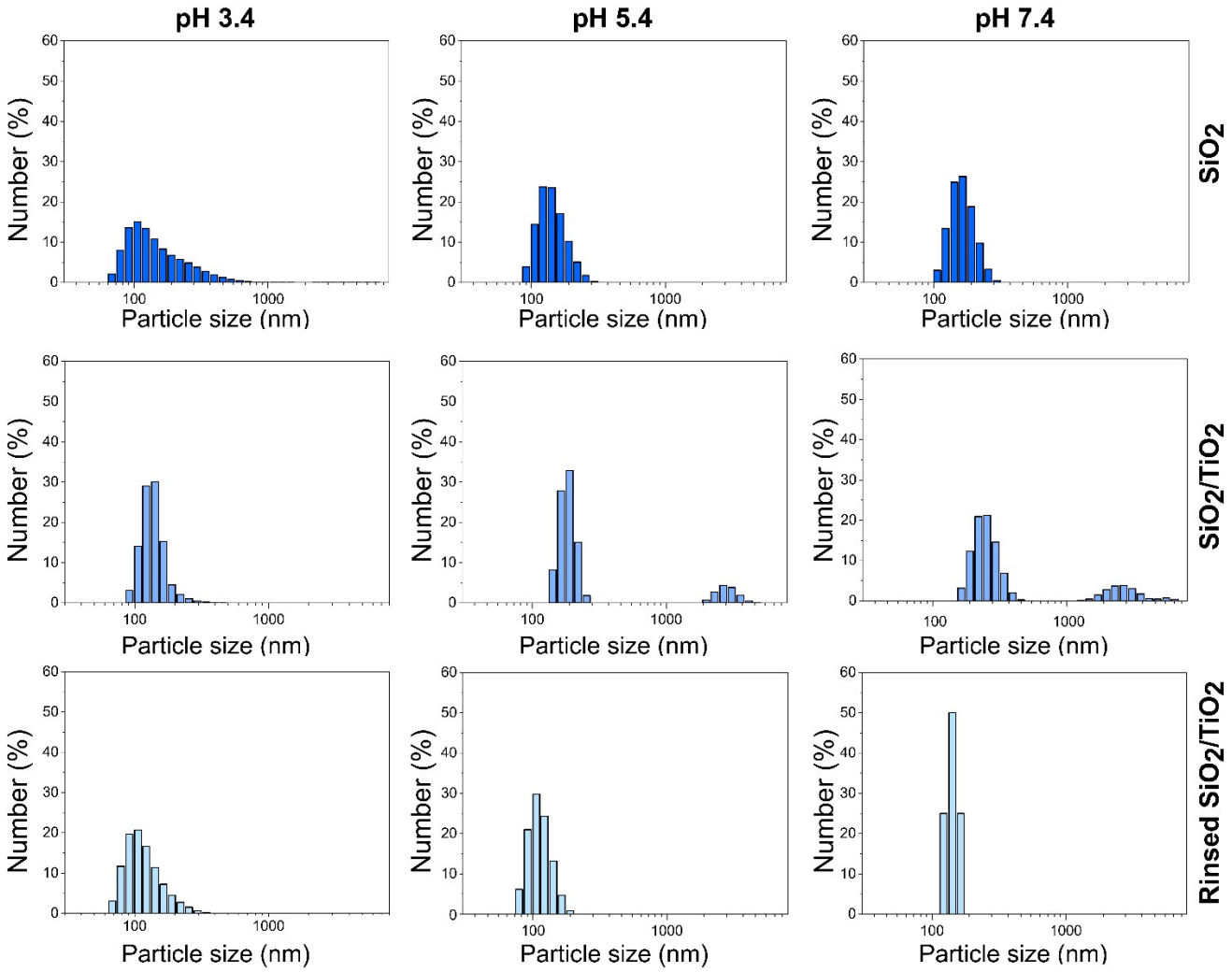


Figure S4. CryoTEM images of TiO_2 nanoparticles (25 and 100 ppm) at pH 3.4 (top) and 7.4 (bottom).

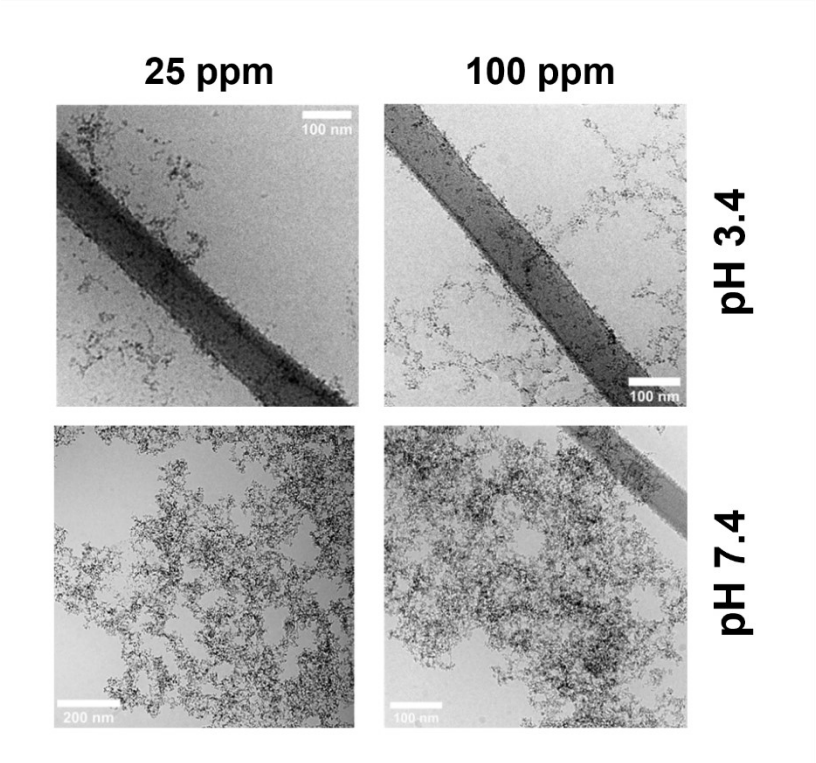


Figure S5. Oxidation curves, obtained from C_{11}-BODIPY oxidation assays, showing the effect of SiO_2/TiO_2 combinations, consisting of 100 ppm of either virus-like or smooth SiO_2 with increasing TiO_2 concentrations (0-100 ppm), as well as the corresponding TiO_2 controls, on POPC/PAPC/POPG (50/25/25) unilamellar liposomes subjected to *in situ* UV exposure in 10 mM buffer at pH 3.4 (top) and pH 7.4 (bottom).

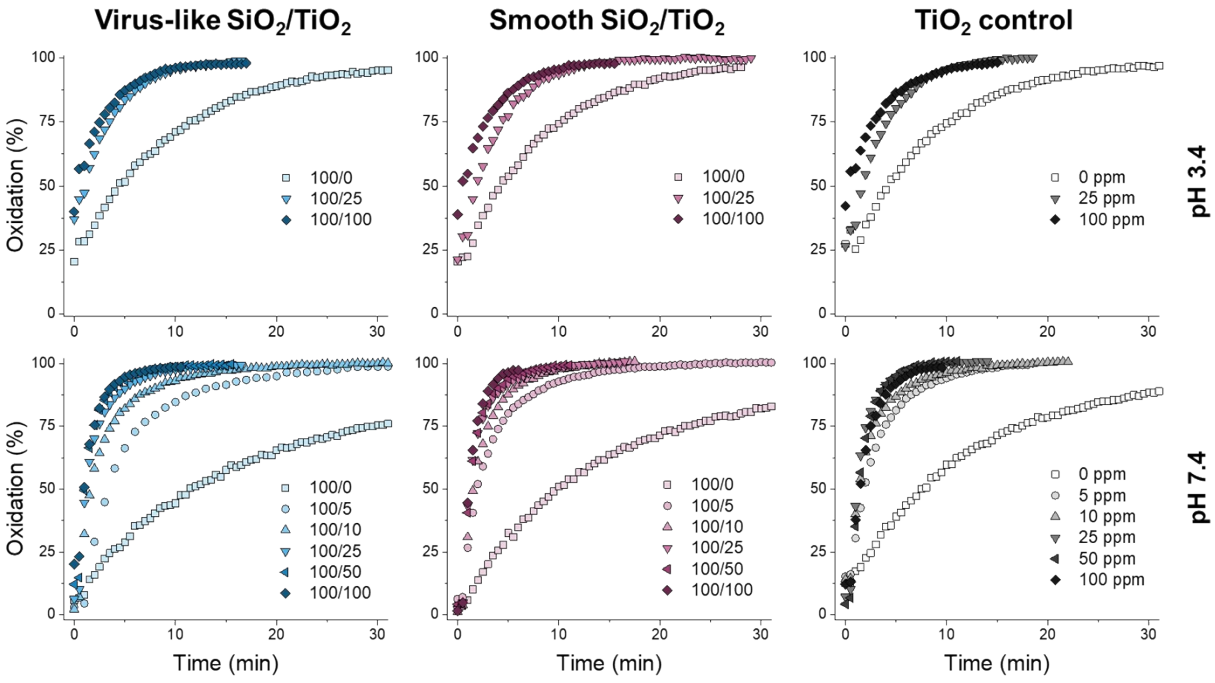


Figure S6. Oxidation curves obtained from C_{11}-BODIPY oxidation assays in the presence of D-mannitol (•OH scavenger, 100 mM) and SOD (superoxide inhibitor, 10 U/mL), showing the effect of 100/25 ppm SiO_2/TiO_2 combinations of either virus-like or smooth SiO_2, as well as the corresponding TiO_2 control on POPC/PAPC/POPG (50/25/25) unilamellar liposomes subjected to *in situ* UV exposure in 10 mM buffer at pH 3.4 (top) and pH 7.4 (bottom).

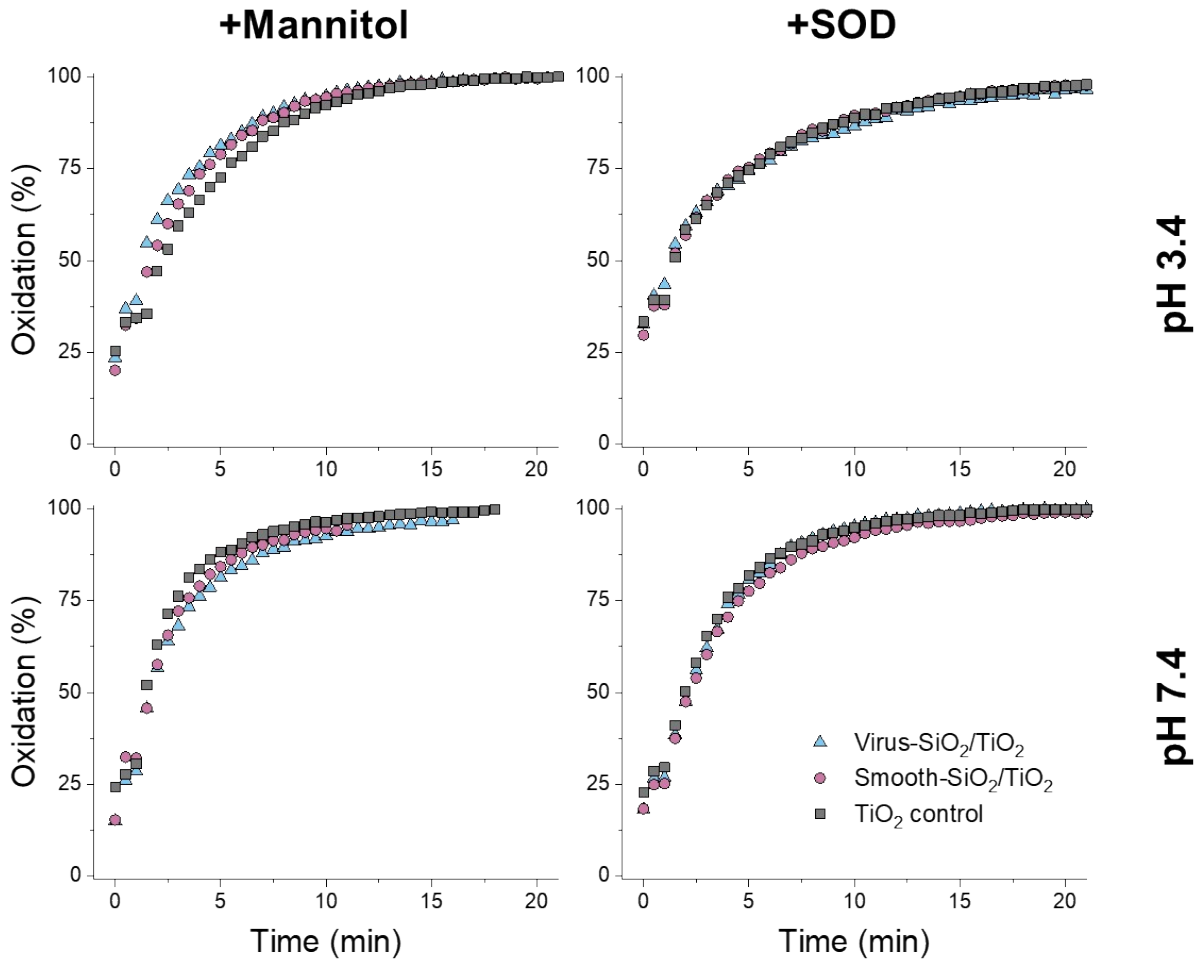


Figure S7. Neutron reflectivity curves with best model fits (left) and SLD profiles (right) obtained for supported POPC/PAPC/POPG bilayers before and after incubation with 100 ppm non-loaded virus-like SiO_2 nanoparticles, 2 h of *in situ* UV exposure and final rinsing, performed in 10 mM Acetate buffer at pH 3.4. Curves are shown for two different buffer contrasts, dAcet and hAcet, with the data for the latter offset by 10^{-1} for clarity. The grey box in the SLD profiles indicates the position of the silicon block and reflecting interface, consisting of bulk Si and a SiO_2 layer.

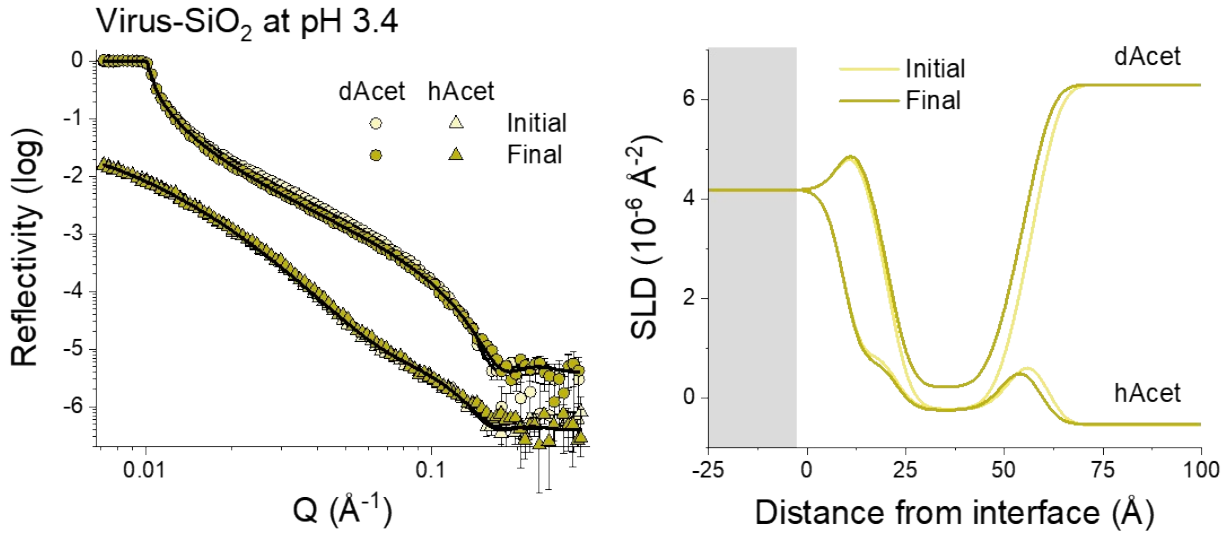
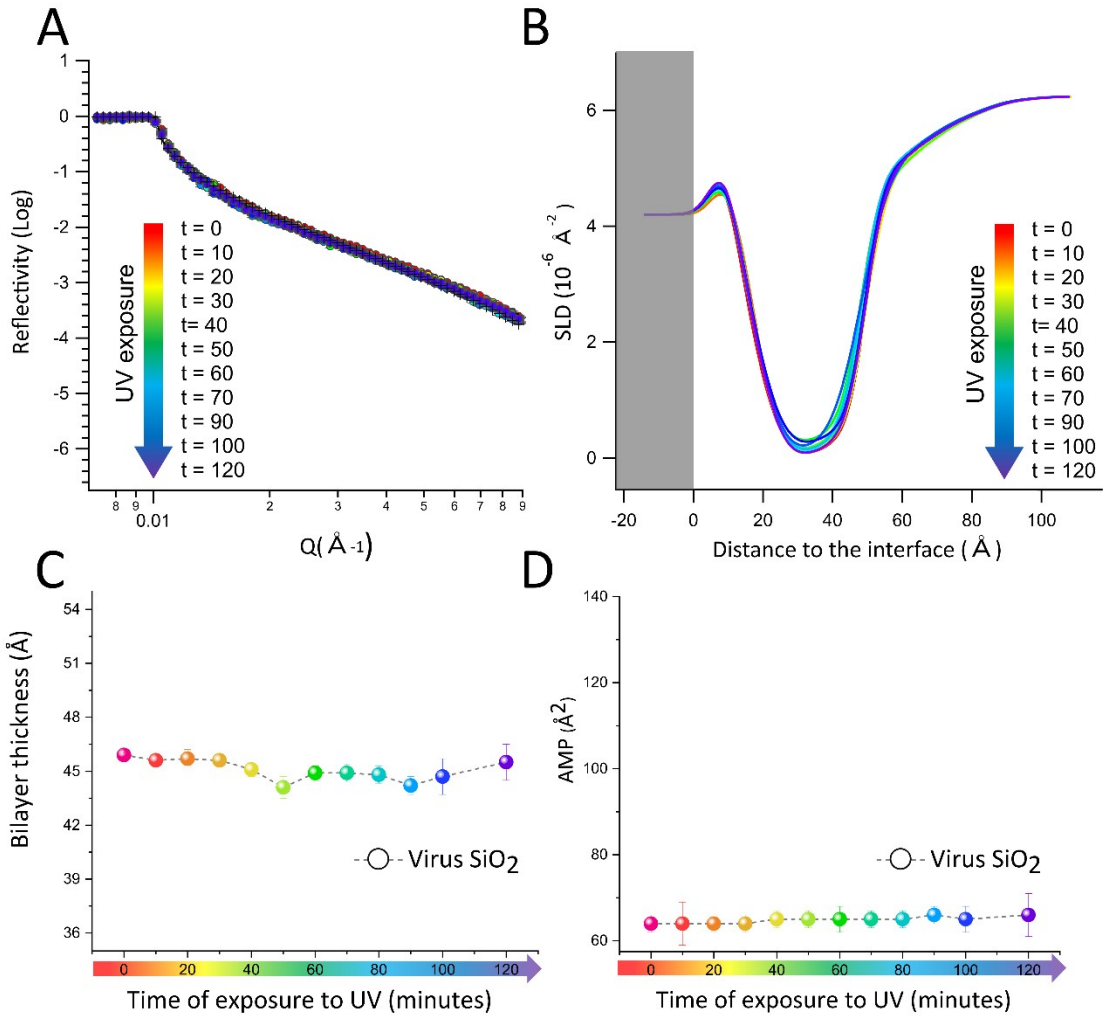
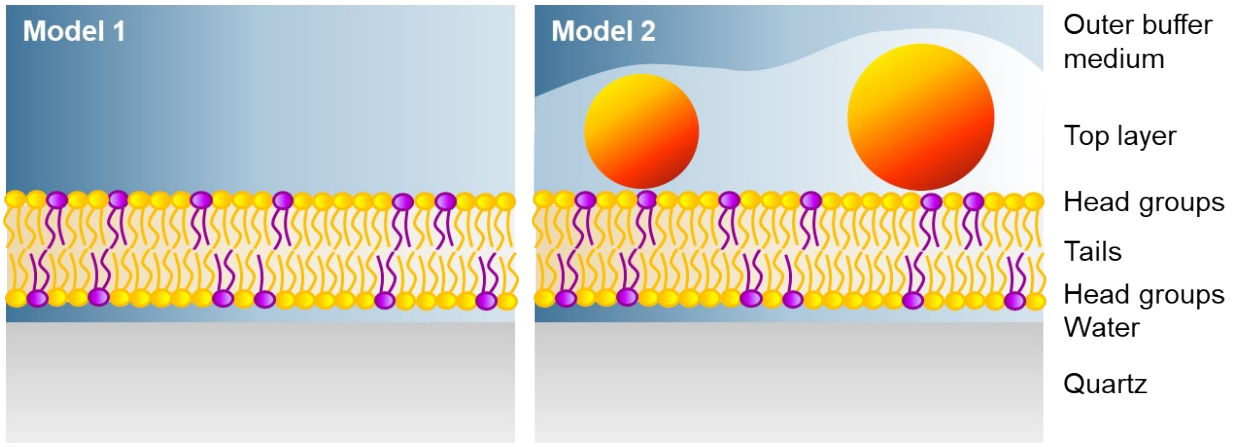


Figure S8. Neutron reflectivity curves and best fits (A) for non-loaded virus-like silica nanoparticles (100 ppm) measured as a function of UV irradiation time, as well as corresponding SLD kinetics (B). Shown also are the calculated bilayer thickness (C) and area per molecule (APM; D) before, during UV exposure.



Scheme S1. Schematic illustration of the different fitting models applied to the neutron reflectivity data, which assumes a homogeneous lateral (i.e., over the bilayer plane) and distal (i.e., between both bilayer leaflets) distribution of the different lipid species, the presence of a water layer in between the bilayers and the quartz surface, and (after UV exposure) the formation of a thick, hydrated and rough top layer with an intermediate SLD in between the different types of nanoparticles and the lipids.



REFERENCES

1. Research NCfN. Neutron activation and scattering calculator [Available from: https://www.ncnr.nist.gov/resources/activation/.
2. Council ISaTF. Biomolecular Scattering Length Density Calculator [Available from: http://psldc.isis.rl.ac.uk/Psldc/index.html/.
3. Parratt LG. Surface studies of solids by total reflection of X-rays. Physical Review. 1954;95(2):359-69.
4. Efron B. Bootstrap methods: Another look at the jackknife. In: Kotz S, Johnson NL, editors. Breakthroughs in statistics: Methodology and distribution. New York, NY: Springer New York; 1992. p. 569-93.