Supporting Information for

Lipidomic analysis probes lipid coronas on hydrophilic nanoparticles from natural lung surfactant

Xuan Bai [a, #], Sin Man Lam [b, c, #], Pengcheng Nie[d, e], Ming Xu[e, f], Sijin Liu[e, f], Guanghou Shui [b, e, *], Guoqing Hu [a, *]

a Department of Engineering Mechanics, State Key Laboratory of Fluid Power and Mechatronic Systems, Zhejiang University, Hangzhou, China;

b State Key Laboratory of Molecular Developmental Biology, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China;

c LipidALL Technologies Company Limited, Changzhou, China;

d State Key Laboratory of Nonlinear Mechanics, Institute of Mechanics, Chinese Academy of Sciences, Beijing, China;

e University of the Chinese Academy of Sciences, Beijing, China;

f State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Sciences, Beijing, China.

 # These authors contributed equally;

** Correspondence: ghu@zju.edu.cn; ghshui@genetics.ac.cn.*

Table S1 Characterization of NPs used in the present experiments including their chemical composition, surface property, hydrodynamic diameter measured by dynamic light scattering (n=3), geometric diameter measured by transmission electron microscope (TEM) (n=10), and zeta potential (n=3).

NP	Chemical composition	Surface property	Hydrodynamic diameter (nm)	Geometric diameter (nm)	Zeta potential (mV)
Negatively charged	SiO_2	None	152.5 ± 4.2	113.9 ± 2.9	-34.1 ± 0.5
Neutral	SiO_2	Amine	276.3 ± 6.0	114.3 ± 3.9	2.5 ± 0.4
Positively charged	SiO_2	Amine	146.8 ± 3.4	108.4 ± 6.9	32.0 ± 3.2

Table S2 Composition of the Curosurf® determined by LC-MS. Data represents mean ± SD (n = 3).

Species	PC	SM	PI	PE	PG	PS	PA
Proportion in total lipids (%)	71.2±1.2	20.5±1.1	3.6±0.2	1.9±0.1	1.7±0.1	0.7±0.0	0.3±0.0
Number of total lipids detected	30	11	22	39	16	7	24
Number of lyso-lipid detected	4	0	4	0	0	2	5
Most abundant species	32:0	42:2	38:4	34:1	34:1	36:1	18:1
(Proportion (%))	40.2±4.2	33.7±1.3	16.4±3.9	8.7±2.2	25.6±1.1	30.9±0.3	23.4±0.2
	34:1	34:1	34:1	38:4	32:0	18:1	18:2
	12.1±1.3	29.7±2.6	15.4±0.3	8.3±1.5	23.5±2.2	28.0±1.1	16.5±2.7
	32:1	42:1	36:2	34:2	34:2	18:0	16:0
	9.4±0.3	15.7±1.0	9.8±0.8	8.2±0.8	9.7±1.6	22.3±3.0	16.1±0.5

Table S3. Hydrodynamic size and zeta potential of LS at 37 °C (n=3).

Sonication time (minute)	Hydrodynamic diameter (nm)	Zeta potential (mV)
0	2825.0 ± 204.1	-44.5 ± 2.53
5	852.3 ± 46.9	-
15	584.1 ± 21.8	-

Table S4 Detailed composition of the LS lipids used in CGMD simulations.

Species	Ratio (%)
PC (32:0, 34:0, 36:0)	38
PC (32:1, 34:1, 36:1)	18
PC (32:2, 34:2, 36:2)	7
PC (36:4)	5
Lyso PC (16:0)	2
SM (d18:1/16:0, d18:1/18:0)	14
SM (d20:1/24:1)	8
PI (32:1, 34:1, 36:1)	1
PI (32:2, 34:2, 36:2)	1
PI (36:4)	1
PG (32:0, 34:0, 36:0)	1
PG (32:1, 34:1, 36:1)	1
PE (32:1, 34:1, 36:1)	1
PE (32:2, 34:2, 36:2)	1
PS (34:1, 36:1)	1

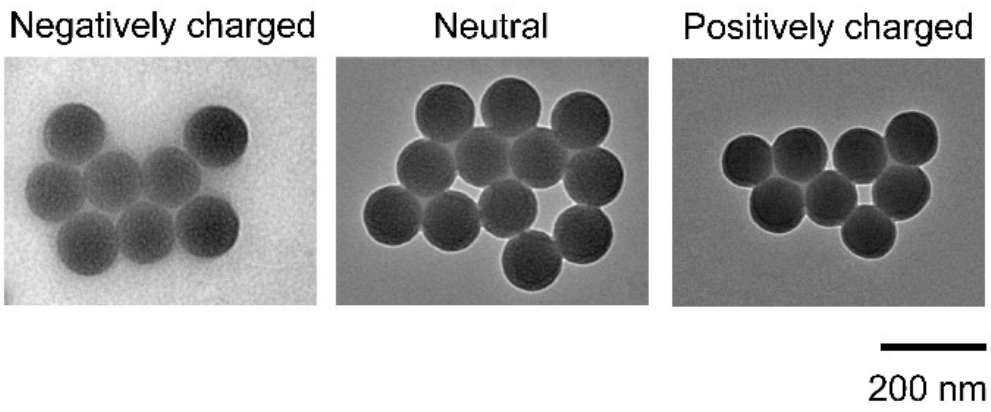

Figure. S1 TEM images of silica NPs with different surface charges. Scale bar, 200nm.

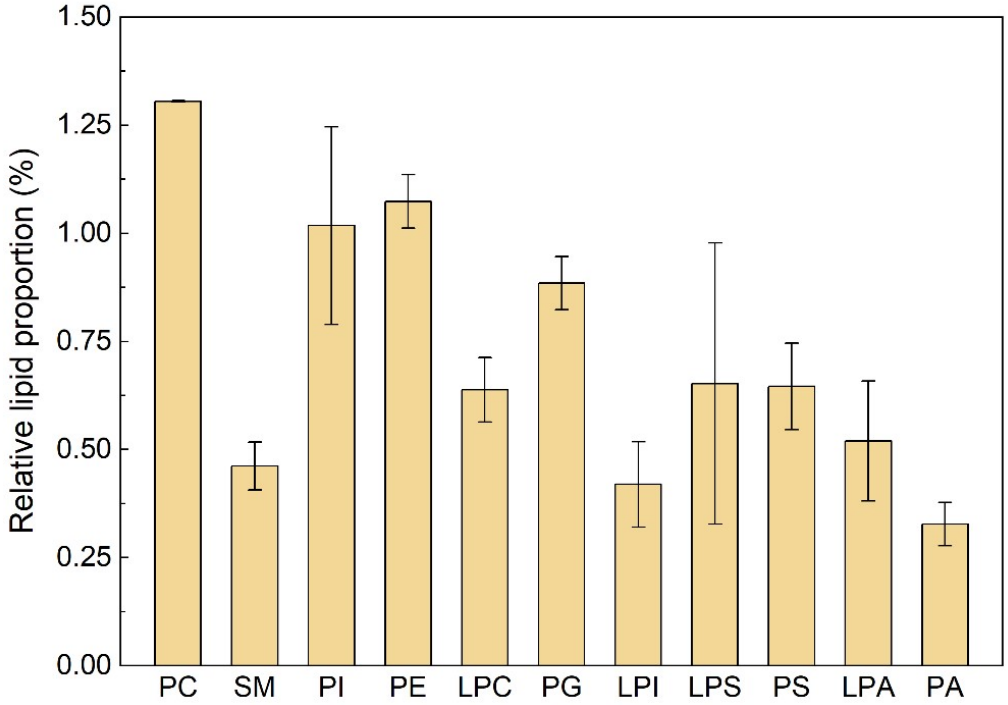

Figure S2. Relative lipid distribution in the corona on neutral NPs based on lipid species after 1-hour incubation with sonication.

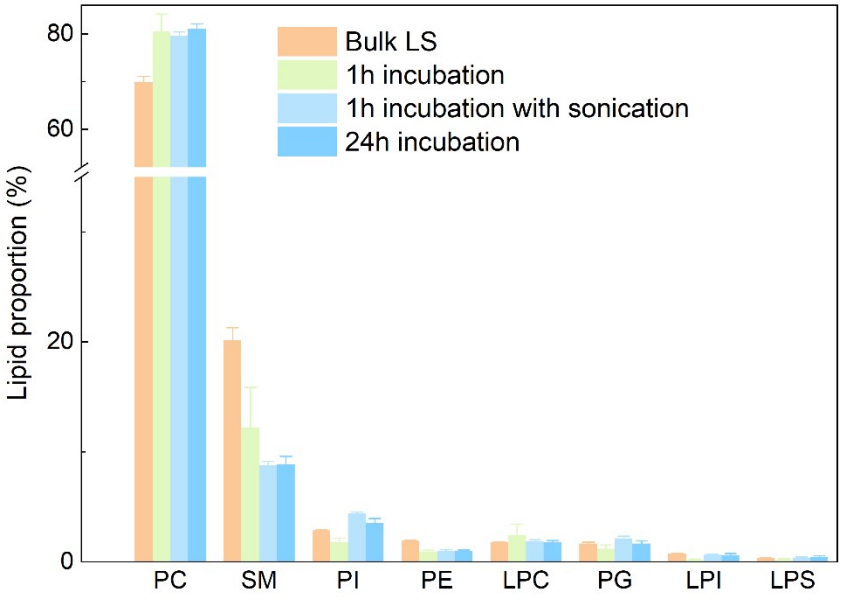

Figure S3. Absolute lipid distribution in bulk LS and the corona on positively charged NPs under 1-hour incubation, 1-hour incubation with sonication and 24-hour incubation.

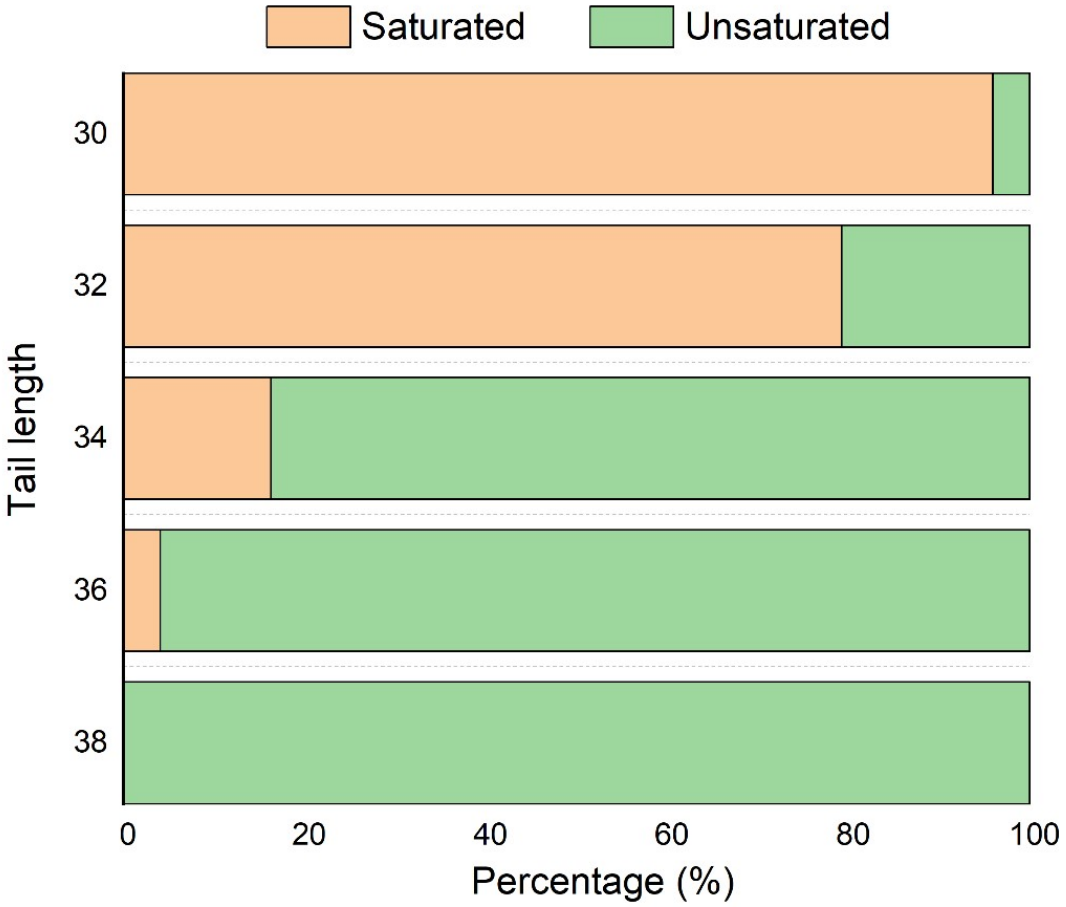

Figure S4. Proportion of saturated and unsaturated lipids with different tail length in the bulk LS.

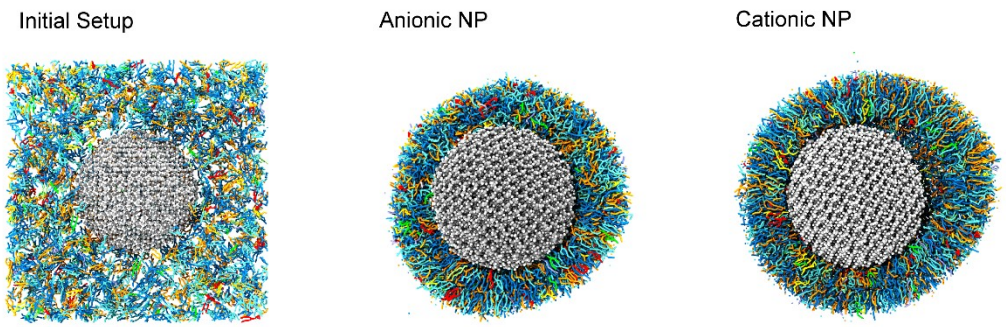

Figure S5. Snapshots for the interactions between NPs and dispersed LS, including the initial setup, and the equilibrated structure of the LS with anionic and cationic NPs.

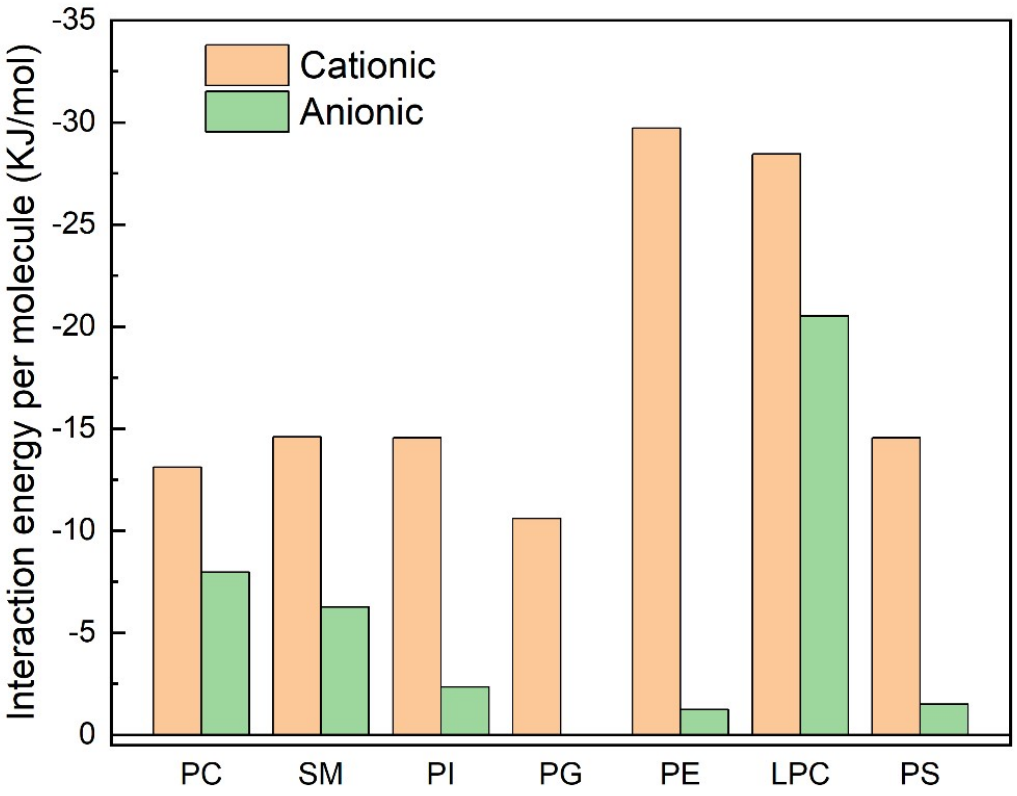

Figure S6. Interaction energy per molecule of the cationic and anionic NPs with the LS species including electrostatic and Van der Waals interactions.

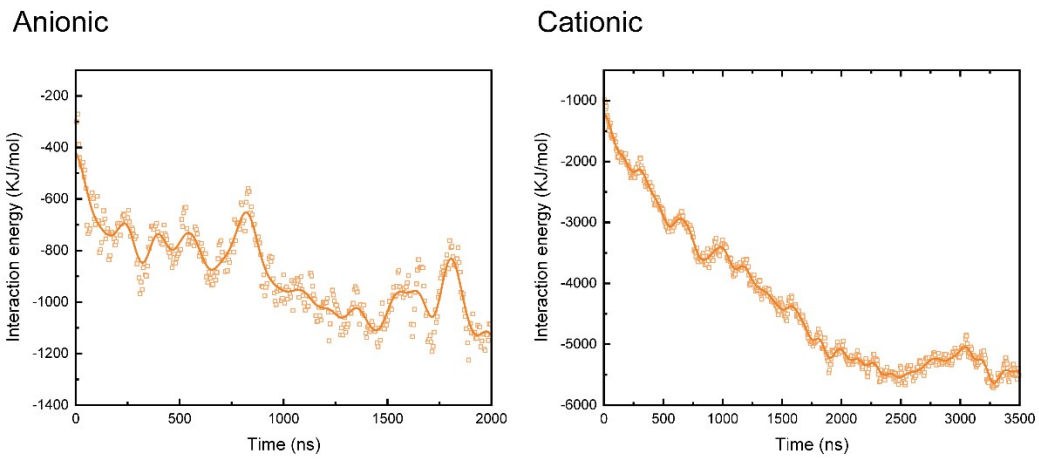

Figure S7. Time evolution of the interaction energy of the NPs with the LS bilayer including electrostatic and Van der Waals interactions.

Note S1

Calculation of the amount and density of adsorbed lung surfactant (LS) lipids

Number of total NPs (N_{NP}):

$$N_{NP} = \frac{M_{NP}}{m_{NP}} = \frac{V_{sol} c_{NP}}{\rho_{NP} v_{NP}}$$

where M_{NP} is the mass of total NPs, m_{NP} is the mass of an individual NP, $V_{sol} = 0.4\ ml$ is the volume of the NP solution, $c_{NP} = 0.5\ mg/ml$ is the density of the concentration of the NP solution, $\rho_{NP} = 2.2\ g/cm^3$ is the density of the NP, and v_{NP} is the volume of an individual NP.

Surface of total NPs (S_{NP}):

$$S_{NP} = N_{NP} s_{NP} = \frac{3 V_{sol} c_{NP}}{\rho_{NP} r_{NP}}$$

where s_{NP} is the surface of an individual NP, and r_{NP} is the geometric radius of the NP. Thus, we can obtain the $S_{NP-neutral} = 4.79 \times 10^{-3}\ m^2$ for the neutral NPs, and $S_{NP-positively\ charged} = 5.03 \times 10^{-3}\ m^2$ for the positively charged NPs.

Density of the adsorbed LS for fully wrapping total NPs is,

$$D_{LS}^{0} = \frac{2 M_{LS}}{A_{LS} NA} = 4.02\ mg/cm^2$$

where NA is the Avogadro constant, and $A_{LS} = 0.62\ nm^2$ is the area per lipid of the equilibrated LS bilayer obtained by molecular simulations, and M_{LS} is the mole mass of the LS that can be approximated as,

$$M_{LS} = 0.8 \times M_{DPPC} + 0.2 \times M_{PNSM} \approx 750\ g/mol$$

Density of adsorbed lipids on NPs is,

$$D_{LS} = \frac{M_{LS} n_{LS}}{S_{NP}}$$

where n_{LS} is the amount of the adsorbed lipids on NPs.

Therefore, the density of the adsorbed lipid on the neutral NPs after after 1-hour incubation with sonication is $2.83 mg/cm^2$, that on the positively charged NPs after 1-hour incubation is $5.83 mg/cm^2$, that on the positively charged NPs after 1-hour incubation with sonication is $2.79 mg/cm^2$, and that on the positively charged NPs after 24-hour incubation is $3.13 mg/cm^2$.