Supplementary Information

1. Size Distribution of Lipid Vesicles

The size distribution of lipid vesicles is constructed based on available information regarding vesicular size in mammalian alveolar fluid. There are generally three broad types of vesicles based on size: small unilamellar vesicles (SUVs), large unilamellar vesicles (LUVs) and giant unilamellar vesicles (GUVs). The available information has been summarized in Table S1.

The upper and lower limits of the size ranges are taken as the 95% and 5% values of a log-normal distribution for vesicular size. Then, the subsequent mean and standard deviation for each type of vesicle are estimated. The measures for the respective log-normal distributions are combined with the respective percent compositions to construct an overall population of vesicles having SUVs, LUVs and GUVs with a size distribution representative of mammalian alveolar fluid. The figure shows the overall size distribution of lipid vesicles.

Table S1. Properties of surfactant lipid vesicles.

Vesicle type	Percent composition *	Size range **	Mean, SD (nm)
SUV	43%	20–50 nm	35, 7.5
LUV	48%	50–500 nm	275, 112.5
GUV	9%	>1000 nm	1000, 0

***** From Goerke, 1998 [1]; ****** From Notter, *Lung Surfactants* [2].

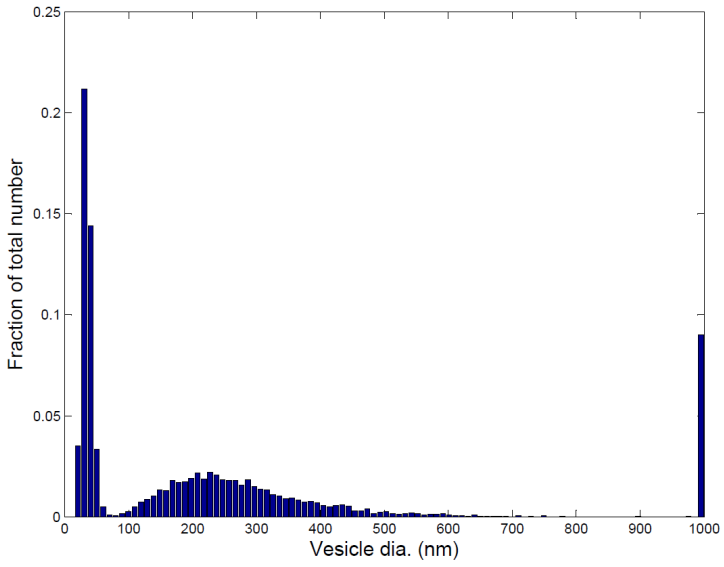

Figure S1. Size distribution of surfactant lipid vesicles.

2. Estimation of Steric Stabilization

Steric effects have been considered for coating molecules using the method shown by Damodaran [3], who used the following equation to estimate the repulsive energy due to steric effects:

$$E_{st} = \left(kTn_m L / s\right).\left[\left(2L/d\right)^{2.25} - \left(d/2L\right)^{0.75}\right] \quad \text{(S1)}$$

where k is Boltzmann's constant, T is the absolute temperature, n_m is the number of coating molecules per unit surface area of the ENM, L is the chain length of the coating molecule, s is the mean distance

between coating molecules and d is the mean distance between interacting ENMs. Here, the mean distance between coating molecules, s, is given by $s = \sqrt{1/n_m}$. The distance between interacting ENMs, d, varies as two ENMs approach each other, and hence, the total interaction energy is estimated by integrating over the entire distance, as was done by Mukherjee *et al*. [4] for attractive and repulsive electrical potentials.

Parameters L and n_m in Equation (S1) for citrate and PVP molecules are summarized in Table S2. The number of coating molecules per unit ENM surface area (n_m) is generally known to vary with ENM size. The values of n_m for various sizes of ENMs have been estimated by Mukherjee *et al*. [4]. The molecular lengths of citrate and PVP molecules are taken from the literature (PVP from Zeng *et al*. [5] and citrate from Appelblat and Manzurola [6]).

Table S2. Coating molecule densities for different NPs.

Parameters	C20	C110	P20	P110
L	6.73 A° *	6.73 A° *	16 nm **	64 nm **
n_m (molecules/m^2)	8.94×10^{18}	4.92×10^{19}	4.36×10^{19}	2.9×10^{19}

* Based on an apparent molar volume of 96.24 cm^3/mol for trisodium citrate from Appelblat and Manzurola [6]; ** Based on 10 kDa and 40 kDa PVP chain length from Zeng *et al*. [5].

The steric repulsive potential estimated from Equation (S1) is normalized by the steric potential created by an uncoated Ag ENM. The molar volume of Ag is 10.335 cm^3 per mole. Considering an Avogadro number of molecules making up that volume and assuming an Ag atom as roughly spherical, the mean radius of the Ag atom, r_{Ag}, can be estimated as 1.6 A°. Empirical and calculated values of the atomic radius of Ag are also reported to be around 160 pm or 1.6 A° (Source: Webelements [7]). Number of Ag atoms present on the surface of an uncoated Ag ENM can be estimated as $n_m = 1/\pi r_{Ag}^2$.

Therefore, using L = 3.2 A° and $n_m = 1.24 \times 10^{19}$ atoms/m^2, we can get from Equation (S1) the value of E_{Ag}. The steric effect is quantified as $\lambda_{ST} = \frac{|E_{Ag}|}{|E_{coat}|}$.

The mutual interaction of ENMs consists of an attractive van der Waals' interaction potential and a repulsive interaction potential. Detailed expressions for these interaction potentials are provided in the original ADSRM article (Mukherjee *et al*. [4]). The repulsive interaction potential between the agglomerates can be expressed via the electric double layer (EDL) interaction potential equation that was developed using the linear superposition principle by Gregory [8] as:

$$\phi_R(h) = 128\varepsilon\pi\left(\frac{k_B T}{Ze}\right)^2\left(\frac{r_i r_j}{r_i + r_j}\right)\gamma^2 \exp(-\kappa h) \quad \text{(S2)}$$

Here, ε is the permittivity of the medium, Z is the valence of ions in the medium, e is the elementary charge, k_B is the Boltzmann's constant, κ is the Debye–Hückel parameter and γ is the reduced surface potential, which is a function of the surface zeta potential ζ of the particles. The effective repulsive potential, φ_e, is obtained by adjusting the electric repulsive potential φ_R by the steric effect represented by λ_{ST} as:

$$\phi_e(h) = \phi_R(h).\lambda_{ST}(h) \quad \text{(S3)}$$

3. Estimation of Zeta Potentials

The zeta potential of lipid-adsorbed ENMs has been estimated using a weighed function as:

$$\zeta = \zeta_L.\theta + \zeta_0\left(1-\theta\right) \tag{S4}$$

where ζ_0 is the zeta potential of the ENM without lipid adsorption, ζ_L is the reduced zeta potential due to lipid adsorption and θ is the fractional surface coverage of the ENM by lipids. Allam *et al*. [9] measured zeta potentials of nanoparticles, with and without the presence of lipids.

Table S3. Surface zeta potential (in mV) for NPs.

ζ for uncoated NPs	**−32.4**	**−40.7**	**−47.1**	**−11.2**	**−12.3**	**−23.3**	**−10.3**	**−10.8**	**−22.5**
ζ for lipid coated NPs	−11.9	−15.6	−19.1	−4.5	−5.5	−7.4	−2.2	−3.4	−5.2

Measured values of zeta potential for coated and uncoated NPs from Allam *et al*. [9]; From these measurements, the average value of ζ_L/ζ_0 was estimated as 0.34; Zeta potentials of various types of uncoated ENMs are summarized in the main article.

4. Protein Adsorption and Desorption

Zhdanov and Kasemo [10] modeled protein adsorption and desorption on lipid bilayers and how the adsorption and desorption rates (k_a and k_d) varied with lipid surface coverage. The measurements for adsorption and desorption were used to fit a function for k_a and k_d as follows:

$$k_a = k_a^0.(1+\beta_a\theta^{n_a}) \tag{S5}$$

$$k_d = k_d^0.(1+\beta_d\theta^{n_d}) \tag{S6}$$

Here, k_a^0 and k_d^0 are the values of k_a and k_d obtained by extrapolation of the data shown above for θ = 0. Without the presence of lipids (θ = 0), there would be no preference for any of the proteins regarding adsorption, and hence, the values of k_a^0 and k_d^0 would be the same. The exact values do not matter here, as they are normalized in the model and used as relative probabilities. The values of the fitted parameters for the four surfactant proteins are shown below:

Table S4. Adsorption and desorption parameters for surfactant proteins.

Protein	***L***	k_a^0	k_d^0	β_a	β_d	k_a	k_d
SP-A	2	3.16×10^{-4}	2×10^{7}	1.5×10^{4}	2.5×10^{-7}	1.79	−3.2
SP-B	4	3.16×10^{-4}	2×10^{7}	4.58×10^{7}	2.3×10^{-3}	3.92	−1.09
SP-C	4	3.16×10^{-4}	2×10^{7}	4.58×10^{7}	2.3×10^{-3}	3.92	−1.09
SP-D	2	3.16×10^{-4}	2×10^{7}	1.5×10^{4}	2.5×10^{-7}	1.79	−3.2

5. Calculation of Protein Diffusion Coefficients

The estimation of diffusion coefficients of proteins involves multiple parameters, such as the molecular weight *M*, partial specific volume $\bar{V}$ and the sedimentation coefficient, *s*, which are related by the Svedberg equation [11] as shown below:

$$D = \frac{RTs}{M(1-\bar{V}\rho)} \quad \text{(S7)}$$

The sedimentation parameter, s, is given by: $s = v/a$, where v/a is the ratio of the volume-to-area of the protein molecule concerned. Young *et al.* [11] used the Svedberg equation to derive an empirical correlation for proteins, which can be written as:

$$D = (7.51\times10^{-8})\cdot T\bar{V}^{-1/3}/\eta \quad \text{(S8)}$$

where $\bar{V}$ is the partial specific volume of the protein under consideration, η is the viscosity of the medium and T is the absolute temperature.

References

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