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Size dependency of gold nanoparticles interacting with model membranes

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Relevance

- Insights for the work on effect of arsenic on skin substitute.

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Arsenic (V) induces a fluidization of algal cell and liposome membranes

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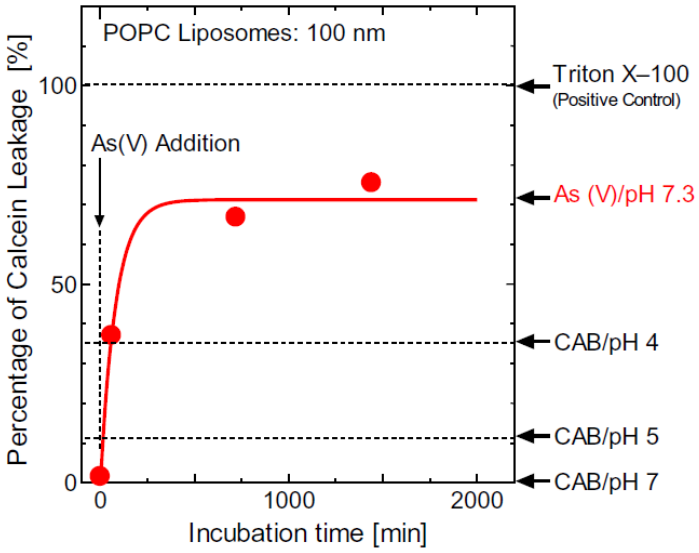


Introduction

- Nanotoxicity
  - Nanomaterials are used in a wide range of sectors including medicine, technology, cosmetics and food. It is important to understand the events occurring at bio-nano interfaces.
  - Key event: interaction of nanomaterials with phospholipid membranes.
- Known:
  - Citrate-stabilised AuNPs (<15 nm) strongly interact with phosphocholine (PC) lipids and the formation of AuNPs aggregates on liposomes surface depends on the fluidization of the lipid membrane.
- New insight:
  - Fate of citrate-stabilised AuNPs on interaction with lipid model membranes and the size dependency of this interaction.

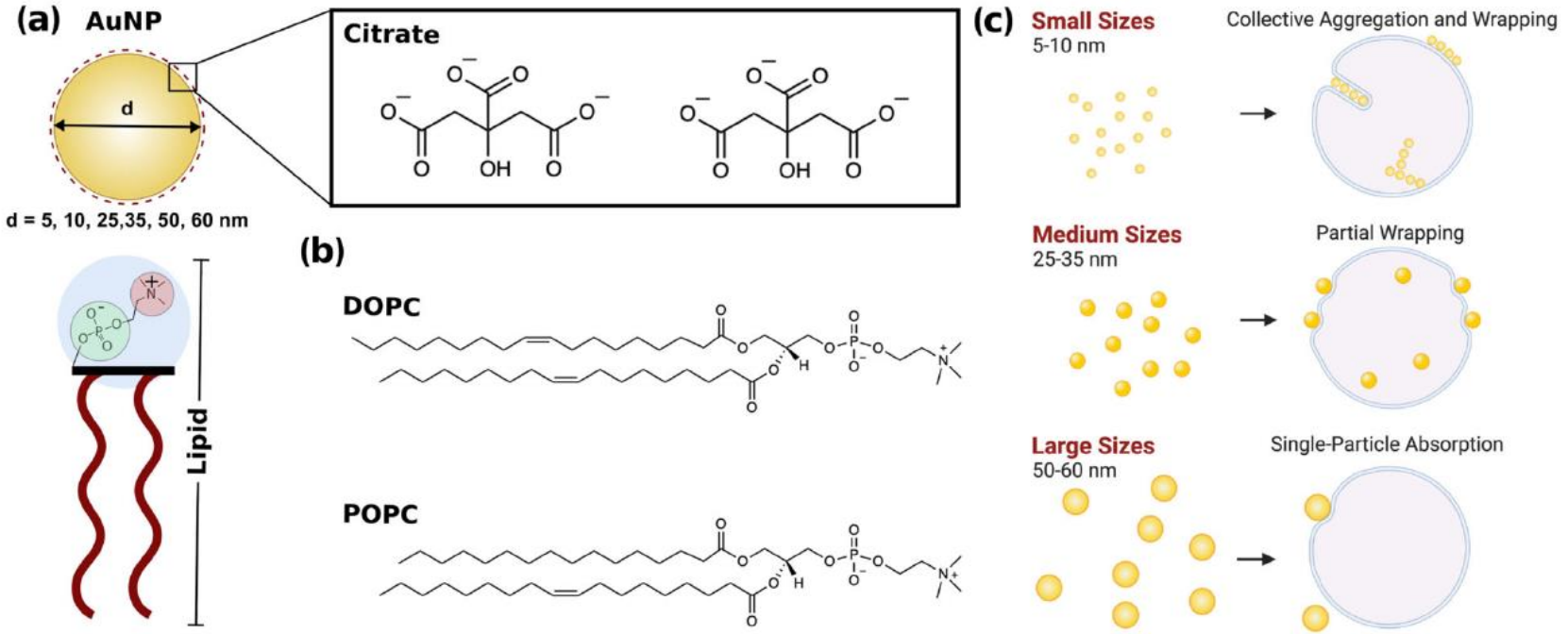
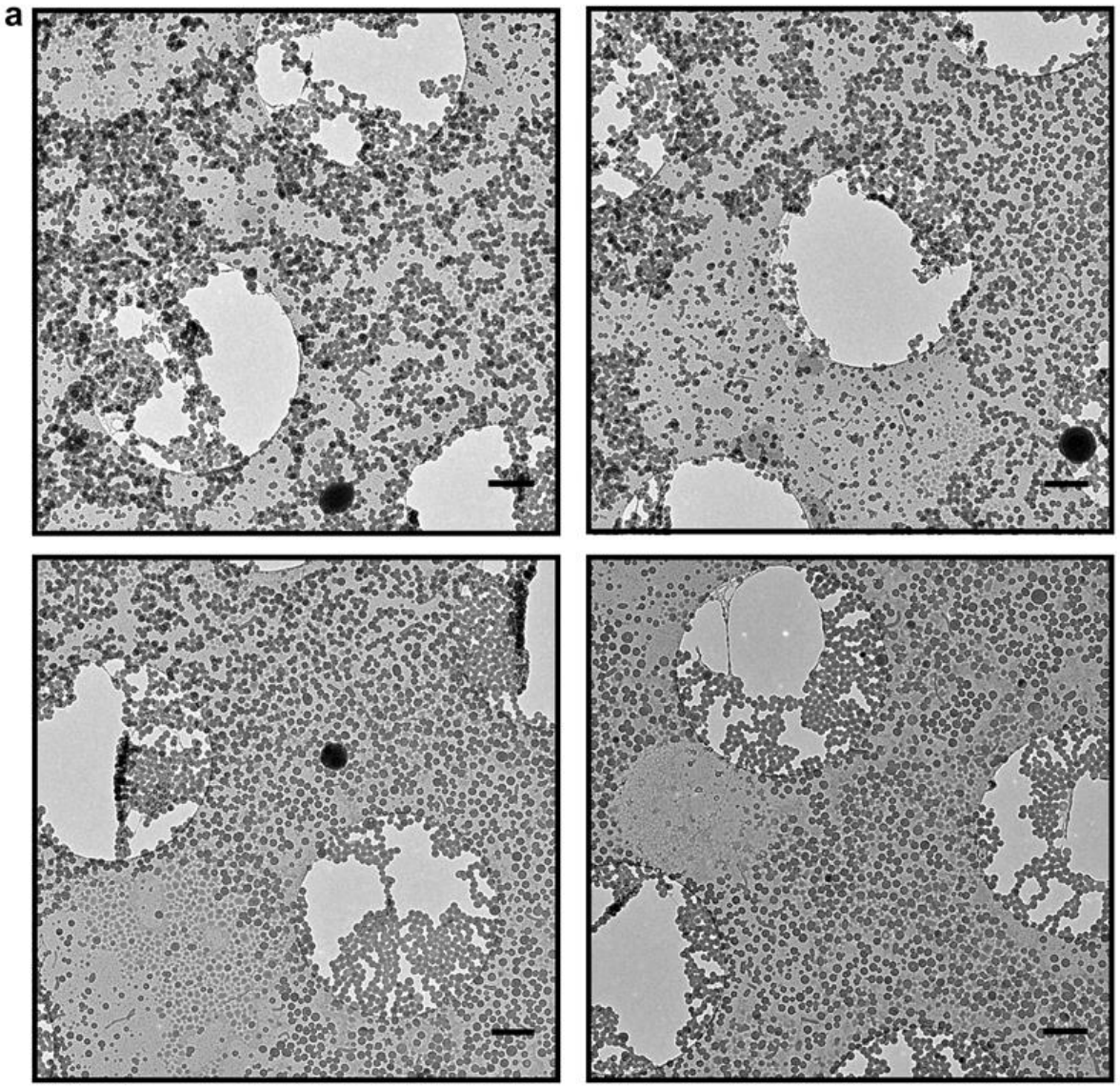
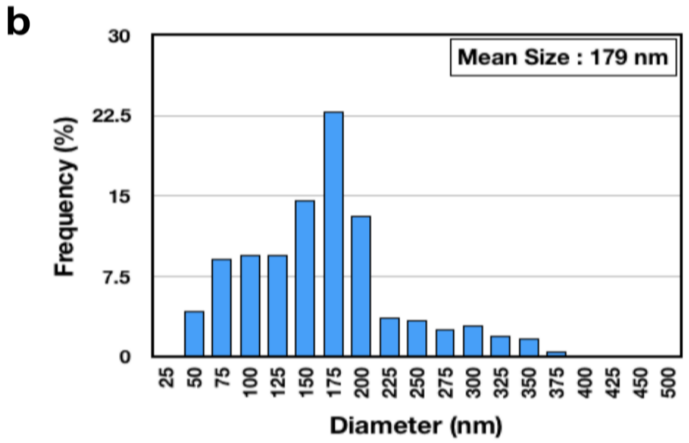


Fig. 1 Schematic representation of the AuNP and lipid interactants and diverse outcomes arising from AuNPs–lipid membrane interactions at different size ranges. a Schematic of the citrate-stabilised AuNP and PC lipid interaction due to a combination of electrostatic and van der Waals interactions. Chemical structure of **b** DOPC and POPC phospholipids. **c** Summarising representation of the diverse AuNP–lipids interaction outcomes at different nanoparticles size range.

POPC (1-palmitoyl-2-oleoyl-glycero-3-phosphocholine)
DOPC (1,2-dileoyl-*sn*-glycero-3-phosphocholine)

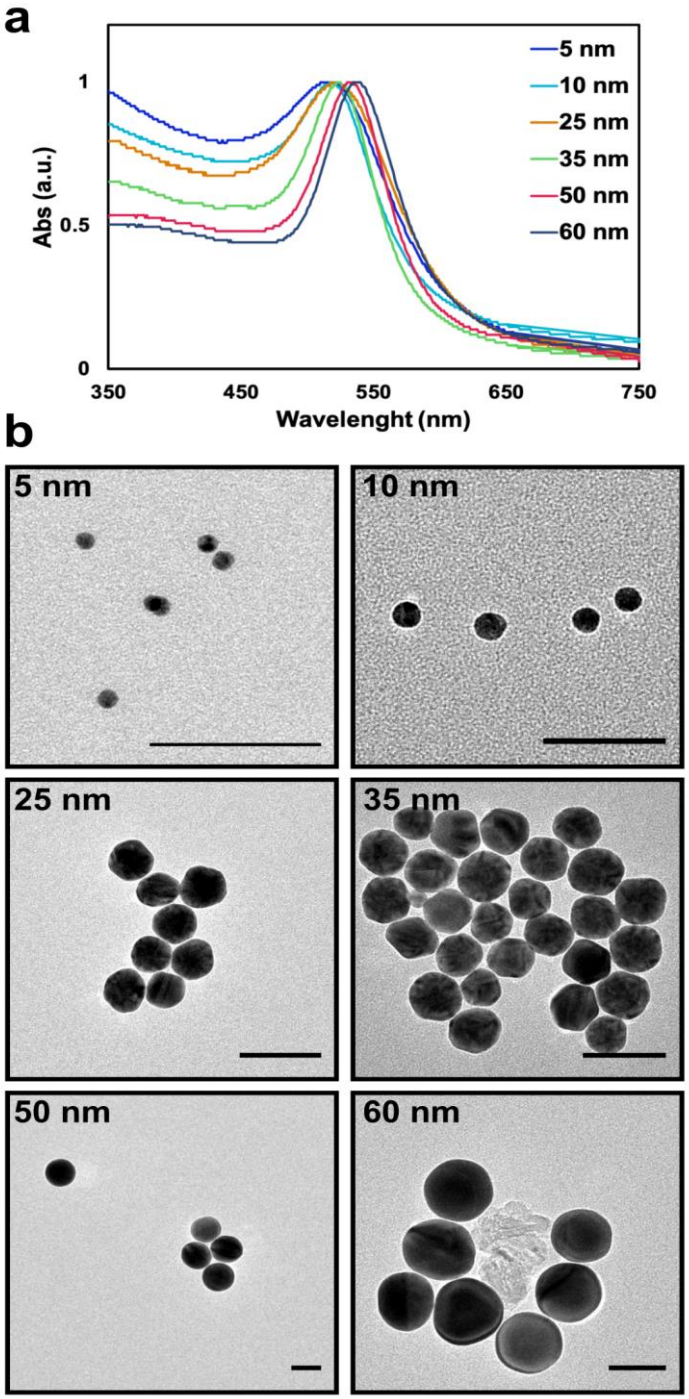
Size distribution characterisation of lipid vesicles.



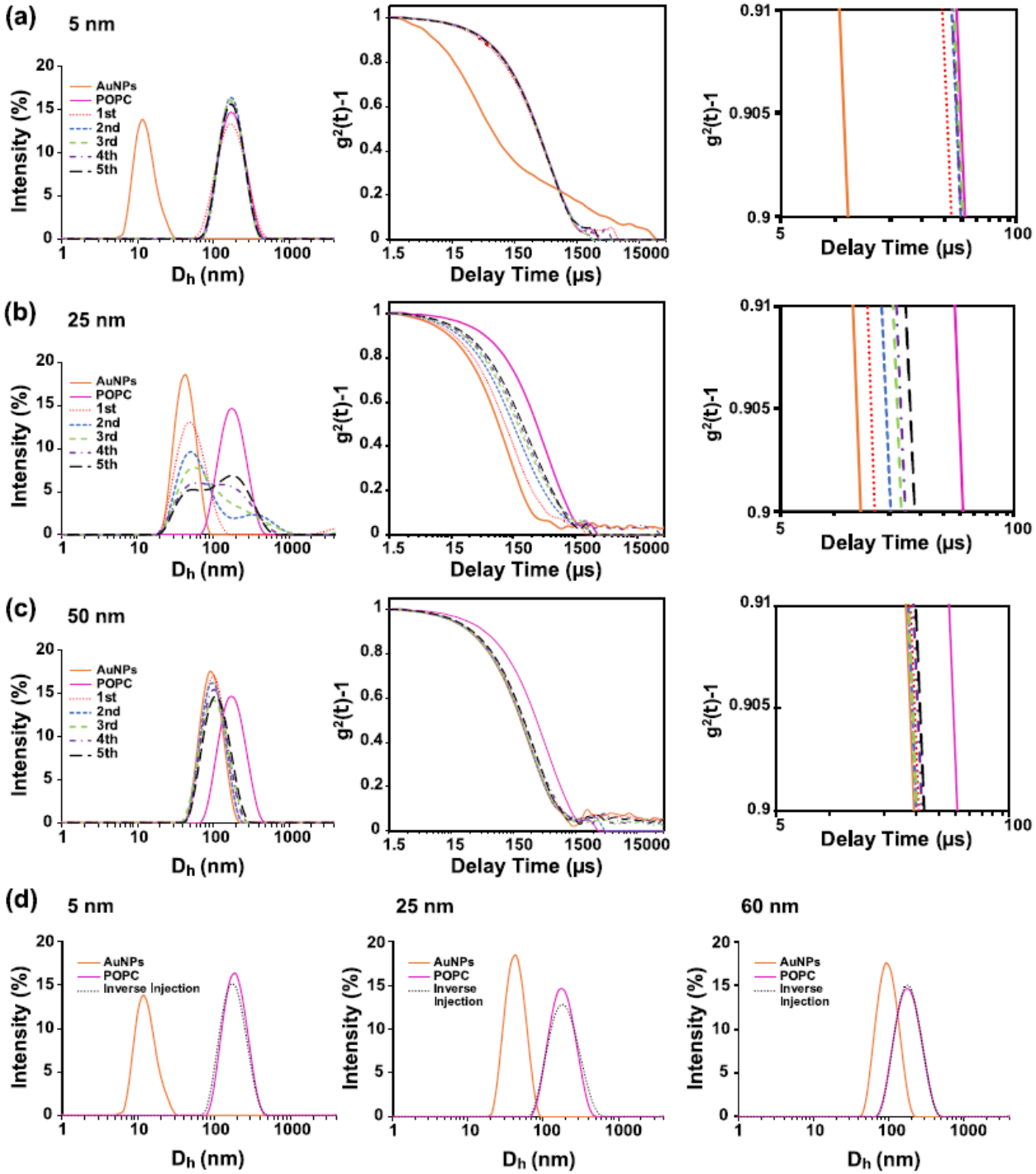


(a) Cryo-EM characterisation of DOPC and POPC vesicles. Scale bars = 1 µm. (b) Size distribution profiles of ~ 500 lipid vesicles from the cryo-EM micrographs analysed using ImageJ software

AuNPs characterisation

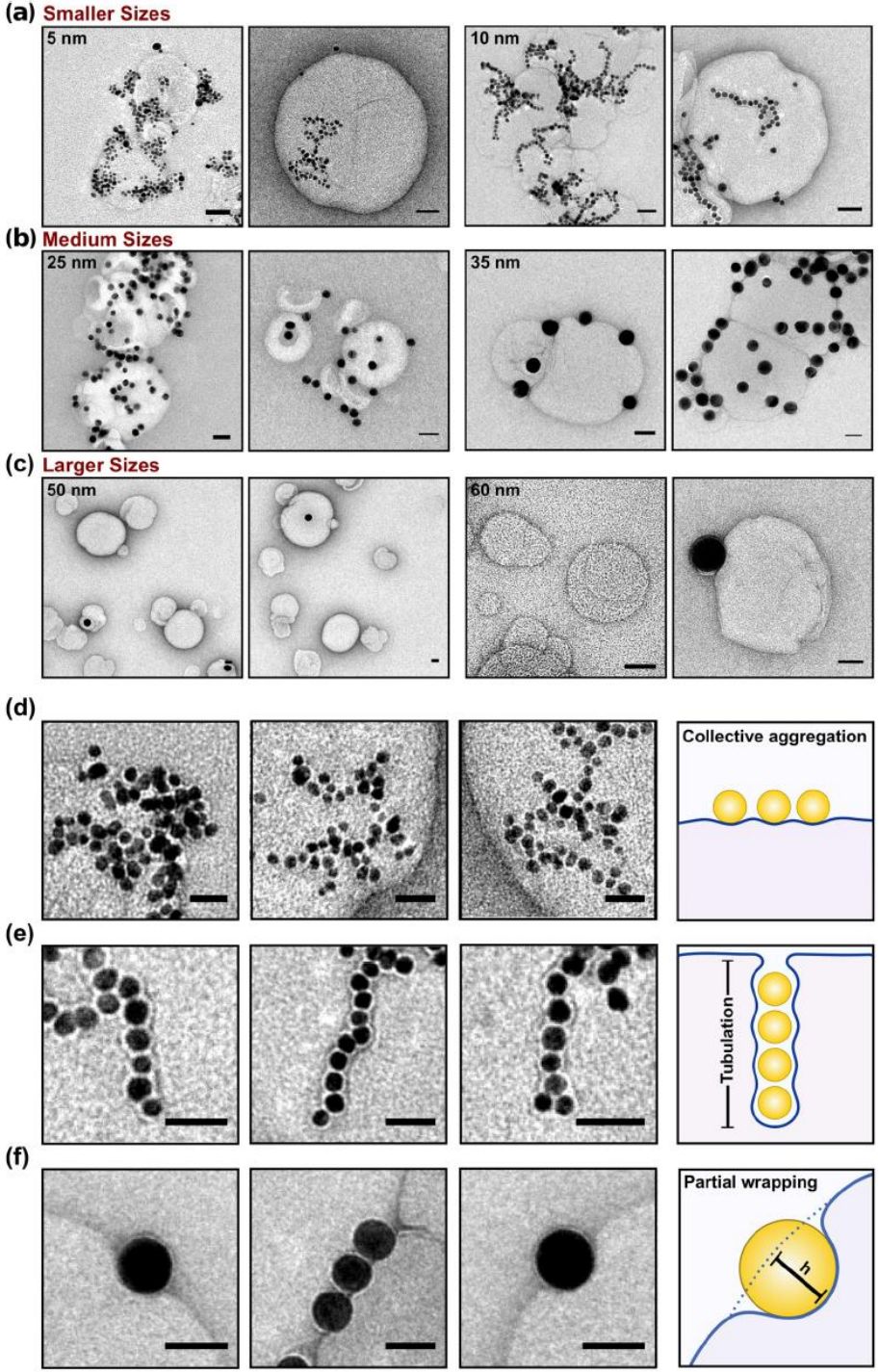


(a) UV-vis absorption¬ spectra of the characteristic and progressive plasmon band red shift as the diameter of AuNPs increases with no reduction in UV extinction or unusual peak broadening or shifting, which confirms the absence of AuNPs aggregation. (b) TEM micrographs of the employed AuNPs. Scale bar is 50 nm.



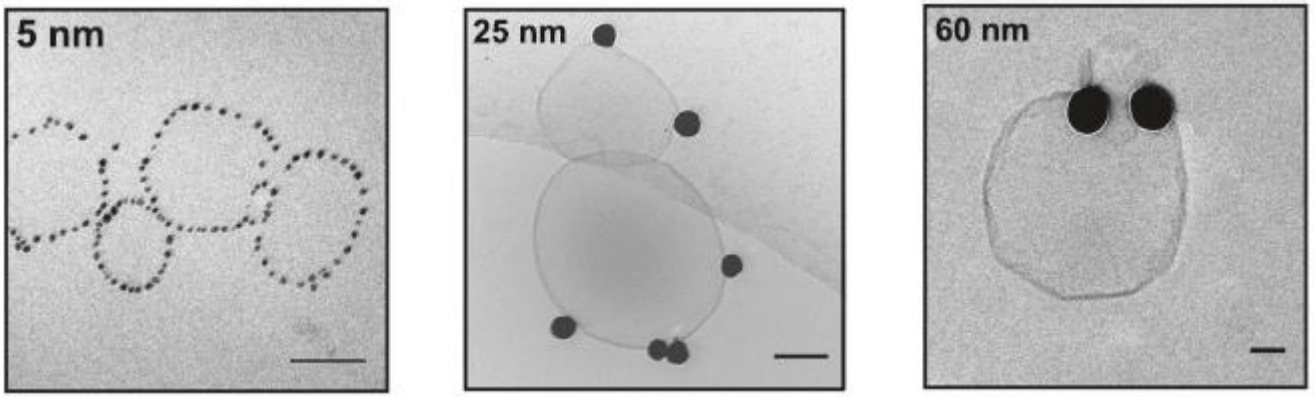
DLS characterization

Size distribution and autocorrelation profiles of **a** 5 nm, **b** 25 nm and **c** 60 nm by injecting LUVs into the AuNPs dispersion. Magnification of the autocorrelation profiles between 5 and 100 µs of delay times is shown on the right end side of the figure. **d** Size distribution profiles of inverse injection: smaller (10 nm), medium (25 nm) and larger (60 nm) size AuNPs into the LUVs dispersion. Control samples were obtained by measuring the AuNP (orange) and LUVs (magenta) dispersions.



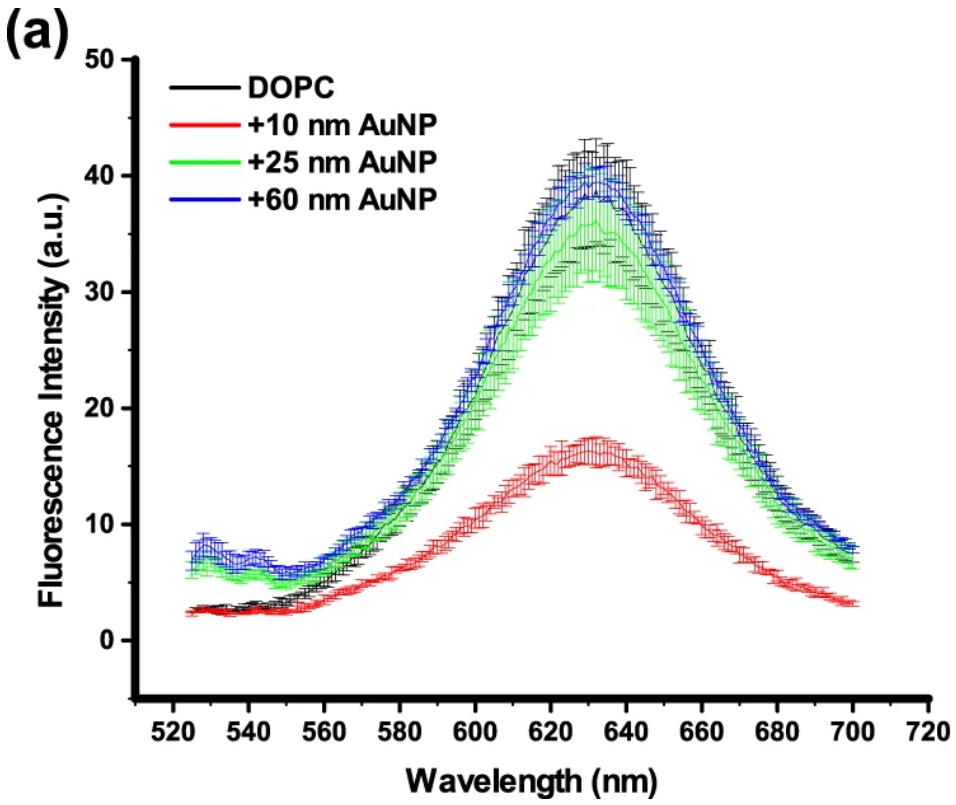
TEM micrographs of **a** small (5–10 nm), **b** medium (25–35 nm) and **c** large AuNP (50–60 nm) interactions with membrane. Scale bar 50 nm. Depending on the A_v/A_{NP} ratio, we observe the presence of a linear cooperative aggregation **d** longitudinal and **e** perpendicular to the bilayer and absorption plane (tubulation) or (for 10 nm) **f** absorption (partial wrapping) characterised by a measurable penetration depth (for medium sized NP).

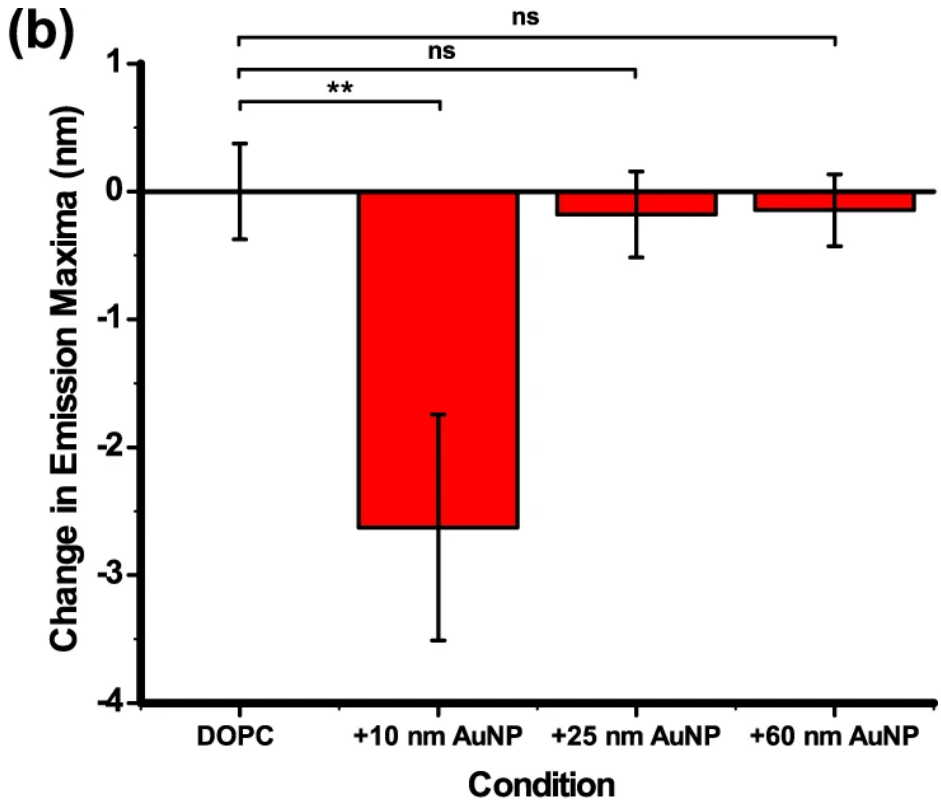
Cryo-EM analysis



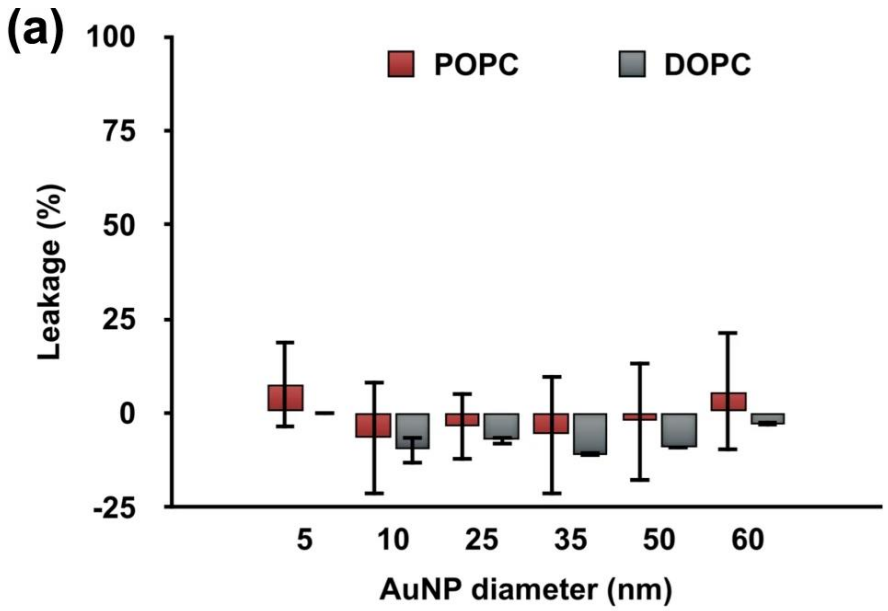
The AuNPs–LUVs mixture of 5, 25 and 60 AuNP interacting with LUVs, has been concentrated by gentle centrifugation and imaged by Cryo-EM. TEM micrographs of

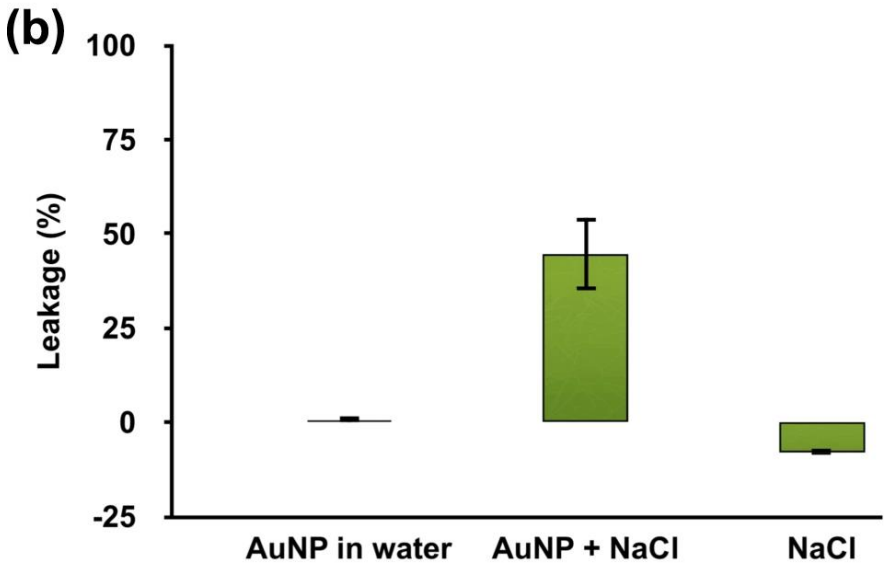
Nile Red fluorescence quenching





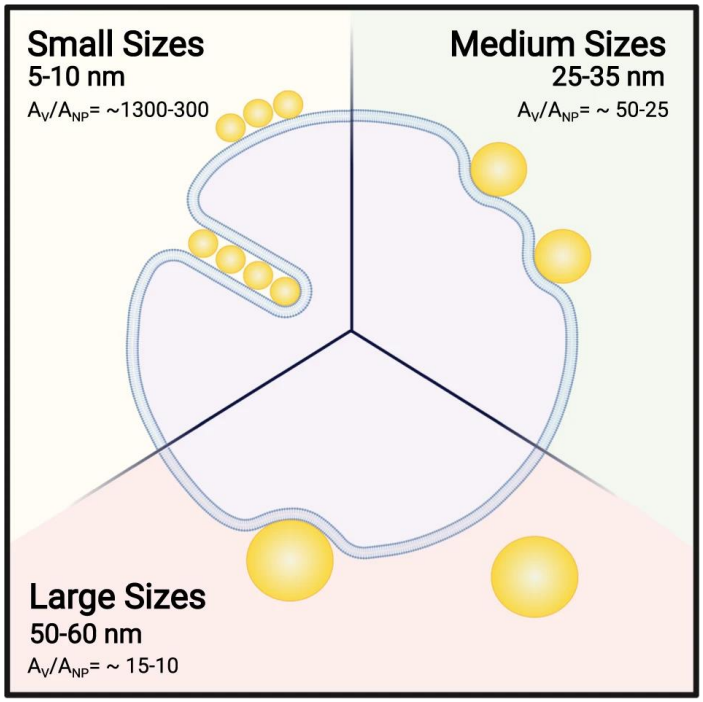
a A reduction in Nile Red fluorescence intensity is only observed upon addition of 10 nm AuNP. **b** A change in the emission maxima of the solvatochromic dye Nile Red shows a size-dependent interaction of gold nanoparticles with lipid membranes.





a The membrane leakage assay has been performed at the same conditions as all the data in order to detect any membrane disruption consequent to the interaction with AuNPs. **b** Summary of the LUVs leakage assay under different conditions: in the presence of 10 nm AuNPs in water and NaCl, and in the presence of salt and absence of AuNPs. The error bars represent the standard error calculated across the range of samples.

Conclusion



Changing the AuNP size from 5 to 60 nm, we observed three different types of outcomes: Small AuNP (5–10 nm) undergoes cooperative aggregation and wrapping characterised by the formation of a membrane tube; Medium AuNPs (25–35 nm) absorb on the membrane's outer surface with a measurable penetration depth; Large AuNP (50–60 nm) interaction is characterised by a few absorption events.

Investigating the physicochemical mechanisms of interaction between NPs and liposomes as a model membrane system is important for the understanding of key initiating events of nanotoxicity at the membrane interface.