

Nanostructured Materials interacting with Synthetic and Natural Lipid Membranes

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The tendency of inorganic or polymeric nanoparticles (NPs) to structurally modify and/or permeate biomembranes requires full elucidation to optimize their biomedical applications and/or minimize health risks in consumer products.

We addressed these interactions in a prototypical case study, using different model membrane systems, (giant unilamellar vesicles (GUVs), supported lipid bilayers (SLB) and liposomes) challenged with Au NPs, of different size, shape and surface coating.

Each of these structural platforms, even starting from the same lipid composition, has distinct physico-chemical properties and lends itself to investigation with complementary experimental techniques, from bulk to surface to single-object level. Therefore, the combination of experimental observations can provide a detailed picture of the relative contributions to the overall interaction scenario.

After an electrostatic and/or surface-energy driven adsorption, the NPs stiffen the region of contact and "freeze" the lipids in raft-like nanoscale domains. [1] Molecular simulations, performed with the Martini model confirmed the experimental observations. [2] Microfluidic-assisted experiments on single GUVs provide further evidence of this membrane stiffening effect [3].

Additionally, a membrane-driven aggregation of nanoparticles was observed, whose extent heavily depends on membrane rigidity and NP surface coatings, which can have important and unforeseen applications for bioanalytical purposes [4]. Given the aggregation-dependent plasmonic properties of the particles, this effect can be exploited in the detection of protein contaminants, as we demonstrated in a case study, involving extracellular vesicle isolation.

In vitro experiments performed on and rat macrophages challenged with the same NPs, indicate a close analogy with the observations in synthetic models, providing validation of our experimental approach and indicating a possible roadmap to fully address biomembrane activity of nanoparticles.

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[2] T. Pfeiffer et al., manuscript under preparation.

[3] C. Montis et al, manuscript under preparation.

[4] D. Maiolo et al., *Analytical Chemistry*, 2015, **87**, 4168.