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Gold nanoparticles and lipid vesicles: a gateway to advanced nanoplasmonic and SERS probes for biomedical applications

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Understanding the interactions at the nano-bio interface is crucial for developing innovative materials and technologies for biomedical applications.¹ In this context, recent studies showed that citrate-capped gold nanoparticles (AuNPs) spontaneously associate on the membrane of lipid vesicles, according to a membrane-templated process that combines the biocompatibility of lipids and the functional properties of AuNPs.¹⁻³ This contribution explores AuNPs-lipid membrane interactions aiming at: (i) probing ensemble-averaged properties of lipid membranes, by exploiting AuNP nanoplasmonics; (ii) designing novel and simple synthetic approaches for Surface Enhanced Raman Spectroscopy (SERS) tags.

First, AuNP nanoplasmonics was applied to characterize lipid vesicles, providing insights on the effect of membrane stiffness and concentration. By combining experimental techniques and numerical simulations, we introduce plasmonic isosbestic points as distinctive markers for the average interparticle spacing in plasmonic assemblies, allowing us to develop a colorimetric assay for quantifying membrane rigidity in biological samples with unknown concentration, such as extracellular vesicles (EVs).

Second, leveraging the spontaneous clustering of AuNPs on lipid bilayers, a simple hybrid platform ("LipoGold tags") was developed, using the lipid membrane as a scaffold to encapsulate hydrophobic Raman-active molecules (Raman Reporters, RRs) and induce AuNPs clustering, enhancing the electromagnetic field for SERS detection. LipoGold tags exhibited high colloidal stability, reproducibility, and adaptability across various RRs. Their functionalization with cellular probes enabled intracellular sensing, successfully detecting GM1 gangliosidosis alterations as a proof of concept. Overall, these findings highlight the potential of AuNP-lipid hybrid systems for biomedical applications, shedding light on the unexplored valence of isosbestic points in nanoplasmonics and introducing an accessible route to design efficient and versatile SERS probes.

[1] J. Cardellini et al., *J. Phys. Chem. C*, **2022**, 126, 4483-4494.

[2] L. Caselli et al., *Nanoscale Horiz.*, **2021**, 6, 543-550.

[3] J. Cardellini et al., *Nature Comm.*, **2024**, 15, 7975.