HYBRID NANOSYSTEMS: ENGINEERING FUNCTIONAL INTERFACES FOR BIOMEDICAL APPLICATIONS

Lucrezia Caselli[1], Jacopo Cardellini[1], Costanza Montis[1], Debora Berti[1,2]
[1]Department of Chemistry, University of Florence, via della Lastruccia 3, Florence, 50019, Italy, lucrezia.caselli@gmail.com
[2]Center for Colloid and Surface Science (CSGI), Department of Chemistry, University of Florence, via della Lastruccia 3, Florence, 50019, Italy

Abstract: Hybrid nanosystems represent cutting-edge materials in nanomedicine, offering significant potential across a range of biomedical applications, including drug delivery, diagnostic imaging, and therapies. By exploiting interactions at the interface between inorganic nanoparticles and both synthetic and natural biomolecules, these systems can be engineered to exhibit highly controlled and unique properties. These features arise from the synergy of their components, enabling unprecedented functionality in biological environments[1].
In particular, leveraging non-specific interactions at nano–bio interfaces—such as those between NPs and lipid scaffolds—offers a straightforward and effective strategy to design biocompatible, functional hybrid materials. Through spontaneous self-assembly, these materials achieve finely tunable structural properties and environmental responsiveness.
This lecture will explore several classes of hybrid systems in which functional NPs (magnetic, plasmonic, or catalytic) spontaneously associate with lipid structures or peptide assemblies. By harnessing interfacial mechanisms such as ligand exchange and hydrophobic interactions, it becomes possible to precisely tailor the structural, morphological, colloidal, and functional features of the resulting hybrids. Examples include: (i) **non-lamellar lipid scaffolds incorporating hydrophobic superparamagnetic iron oxide NPs (SPIONs) for controlled drug delivery**[2]; (ii) **lipid vesicles decorated with gold NP clusters exhibiting enhanced plasmonic properties for biosensing and Raman imaging**[3-5]; (iii) **antimicrobial peptide-coated catalytic NPs capable of light-activated antimicrobial activity**[6,7].
The lecture will also highlight recent advances toward increasingly complex hybrid architectures—from systems combining inorganic NPs with synthetic organic molecules to ***biogenic* soft hybrids integrating natural components** such as Extracellular Vesicle lipids. These emerging **hybrid lipid nanoparticles, which blend synthetic and natural molecules, represent versatile and programmable platforms with great translational potential**. A particular focus will be devoted to the current challenges and future directions in this field, focusing on the design of hybrid nanomaterials responsive to external and endogenous stimuli—systems poised to drive the next generation of personalized and precision medicine.

Key words: *hybrid nanosystems, lipid self-assembly, extracellular vesicles, antimicrobial peptides, plasmonic nanoparticles*

REFERENCES

(1) L. Caselli et al., "The gold nanoparticle–lipid membrane synergy for nanomedical applications," Nanoscale Horizons, 10, 1863-1881, 2025.
(2) M. Mendozza et al. “On the thermotropic and magnetotropic phase behavior of lipid liquid crystals containing magnetic nanoparticles”, Nanoscale, 10, 7, 3480-3488, 2018.
(3) J. Cardellini et al., “Nanoplasmonic Isosbestics Uncover Mesoscale Assembly of Gold Nanoparticles on Soft Templates”, Journal of the American Chemical Society, 147, 23, 20008–20022, 2025.
(4) J. Cardellini et al., “Hybrid lipid-AuNP clusters as highly efficient SERS substrates for biomedical applications”, Nature Communications, 15, 7975, 2024.
(5) L. Caselli et al., “A plasmon-based nanoruler to probe the mechanical properties of synthetic and biogenic nanosized lipid vesicles”, Nanoscale Horizons, 6, 7, 543-550, 2021.
(6) L. Caselli et al., “Antimicrobial Peptide Coating of TiO_2 Nanoparticles for Boosted Antimicrobial Effects”, Advanced Functional Materials, 34, 39, 2405047, 2024.
(7) L. Caselli et al., “Boosting membrane interactions and antimicrobial effects of photocatalytic titanium dioxide nanoparticles by peptide coating”, Small, 20, 30, 2309496, 2024.