Luis M. Liz-Marzán

Self-assembly of gold nanoparticles into optically active nanostructures

Gold nanoparticles have consistently occupied a central spot in nanoscience and nanotechnology because of their unique size- and shape-dependent optical properties [1]. Such properties rely on so-called surface plasmon resonances, which are collective oscillations of conduction electrons in resonance with the oscillating electric field of an electromagnetic radiation. Morphological and environmental details of the nanoparticles determine the resonant frequency, which in turn results in a specific optical response. Although the morphology and dimensions of individual gold nanoparticles allow a wide flexibility in tailoring their (plasmonic) optical response, enhanced and even new effects can be achieved when nanoparticles are located close to each other [2]. Concepts such as plasmon coupling or plasmonic hybridization have been used to describe such effects, and phenomena such as hot spots (areas where local electric field amplification is particularly high) are frequently used to explain surface-enhanced Raman scattering and other surface-enhanced spectroscopies [3]. On the other hand, when plasmonic nanoparticles are arranged into a non-mirror symmetric configuration, chiral nanostructures are obtained, often displaying (plasmonic) optical activity, which is orders-of-magnitude higher than typical values in molecular systems [4].

Among the various nanofabrication tools that have been employed to engineer plasmonic nanostructures, self-assembly of nanoparticles stands out behind the spontaneous organization of nanoscale building blocks into complex structures [5]. An example (illustrated in Fig. 1a) includes the use of hydrophobic interactions to induce self-assembly. These are non-specific interactions that emerge when water molecules rearrange as two hydrophobic species come close to each other. Through controlled water addition, reversible self-assembly of hydrophobic gold nanoparticles can be induced into 3D clusters with controlled dimensions, which has been demonstrated for both isotropic (Fig. 1b) [6] and anisotropic (Fig. 1c) [7] gold nanoparticles as building blocks. Manipulation of such reversible assemblies can be further improved upon the growth of a thin mesoporous silica shell, which allows addition and removal of water without changing the number of nanoparticles in each cluster, as illustrated in **Fig. 1d** [8].

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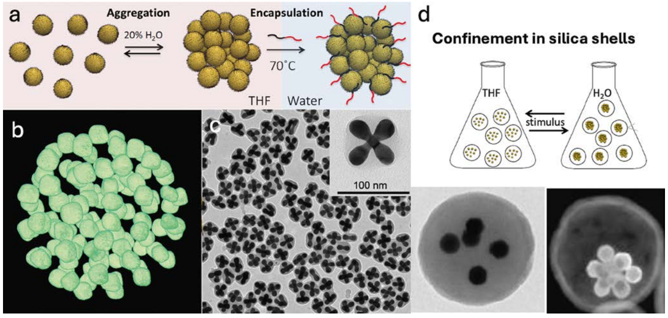

Fig. 1: a) Schematic view of the formation of nanoparticle assemblies by hydrophobic interactions, b,c) Examples of assemblies formed by assembly of spherical (b) and anisotropic (c) gold nanoparticles. d) Scheme and electron microscopy images of hydrophobic gold spheres confined in a silica shell, in organic and aqueous environments.

Chirality in self-assembled nanoparticles

One of the intriguing features of assemblies formed by anisotropic nanoparticles is the possibility of inducing chirality. Indeed, by simply assembling one nanorod (or nanodumbbell, as in Figure 1c) misaligned on top of another, a chiral morphology can be obtained [7]. Although such chiral nanostructures have been shown to display plasmonic optical activity at the single-particle level, this is lost at the ensemble level because the (random) assembly mechanism (through hydrophobic forces) does not impose a preferential handedness and therefore an equal proportion of right-handed and left-handed structures are formed, yielding a racemic mixture [9].

Various strategies have been followed to achieve plasmonic chirality from assemblies of metal (typically gold or silver) nanoparticles. One of the most widely used techniques is the assembly on helical templates. Although DNA origami has arguably been the first successful choice for such templates, it was soon demonstrated that high collective optical activity can be obtained when gold nanorods are assembled on polymer fibers carrying chiral functional groups [4]. In an analogy to molecular systems, the experimentally recorded optical activity was in agreement with theoretical modelling based on a coupled dipole model, showing that efficient coupling between misaligned nanoellipsoids leads to optical activity [6]. When many nanorod pairs with the same handedness are present in a colloidal dispersion, the overall optical activity carries collective information from the entire sample.

This simple concept has been proposed as an accurate and selective biodetection methodology, in situations as relevant as the early diagnosis of neurodegenerative diseases. Most commonly, these disorders are associated to the aggregation of misfolded amyloid proteins into protofibrils, which then evolve into micron-sized fibers, often adopting a (chiral) helical morphology, which accumulate in certain areas of the brain (e.g. substantia nigra). Although still controversial, theories propose that the onset of the disease may be related to the presence of small fibrils, which are difficult to identify by standard methods. A proof-of-concept study [10] demonstrated that, when gold nanorods are added to growing amyloid fibers, they readily assemble via electrostatic interactions on the fiber template. In the case of α-synuclein (associated to Parkinson's disease), the fibers adopt a double-helix structure, which is readily followed by the nanoparticles, resulting in well-defined chiral nanorod assemblies (see Fig. 2). These hybrid nanostructures display strong optical activity (circular dichroism) at near-IR wavelengths, i.e., far away from the spectral region where biomolecules can also display (albeit much weaker) intrinsic optical activity. This concept was further applied to identify the presence of amyloid fibers in the brain of diseased persons who had suffered from Parkinson's disease.

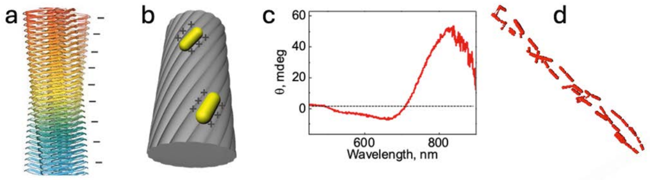

Fig. 2: a) Structure of an α-synuclein amyloid fiber with double-helix structure. b) Schematic view of positively charged gold nanorods adsorbed on a negatively charged fiber. c) Experimental circular dichroism spectrum from an assembly of gold nanorods on α-synuclein amyloid fibers. d) Cryo-electron tomography reconstruction of gold nanorods adsorbed on an α-synuclein amyloid fiber.

Optical activity in assemblies of chiral gold nanoparticles

The field of inorganic chirality has recently experienced a rapid development, mainly due to the successful design of synthesis methods that result in the asymmetric growth of nanoparticles with well-defined chiral features and largely enhanced circular dichroism. Among a variety of recently reported chiral morphologies, chiral gold nanorods are particularly appealing because they exhibit a combination of anisotropy and asymmetry [11]. Interestingly, it has been observed that gold nanorods with twisted lateral facets can recognize each other in colloidal dispersion and in the presence of oppositely charged molecules, forming compact assemblies with further enhanced optical activity. The organization of such twisted nanorods leads to nanostructures with overall reversed handedness, compared to the constituting building blocks, i.e. circular dichroism with inverse sign. These self-assembly properties have been applied for the detection of the biorelevant molecule adenosine triphosphate [12].

The optical response of self-assembled chiral nanoparticles becomes more complex when they are deposited on a solid substrate, rather than in the constant translational and rotational Brownian diffusion when in colloidal dispersion. When a supporting substrate is present and the nanoparticles align into a preferential direction, additional optical effects may arise such as linear dichroism or birefringence. Therefore, more sophisticated optical spectroscopy methods must be implemented, in which the inclination angle between the substrate and the illumination beam can be controlled. An example of these systems and associated effects is provided in Fig. 3. In this example, so-called wrinkled gold nanorods (Fig. 3a) [11] were organized on patterned substrates, so that they formed aligned arrays with periodicity in 2D (Fig. 3b). Colloidal wrinkled NRs show intrinsic plasmonic CD, as shown in Fig. 3c, with mirror-image CD bands for particles grown in the presence of the different enantiomers of the chiral inducer (1,1'-binaphthyl-2,2'-diamine, or binamine). However, when deposited as periodic linear arrays, a new feature arises in the CD spectrum around 600 nm, which is a consequence of so-caled surface lattice plasmon resonance effects, thus not related to chirality but to the overall structure of the assembly and dependent on the illumination angle. Other effects such as angle-dependent linear dichroism were identified in this system [13], revealing so-called extrinsic chiral optical effects that may be exploited for photonics applications.

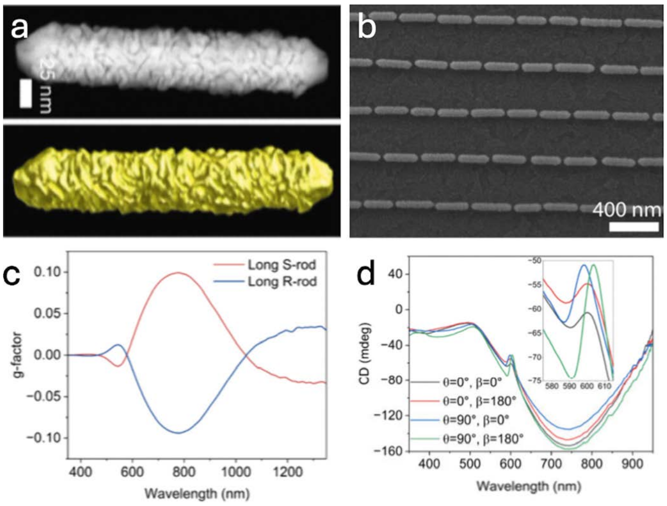

Fig. 3: a) Scanning transmission electron microscopy image (top) and electron tomography reconstruction (bottom) images of a long chiral pentatwinned gold nanorod (PT–Au NR) with a wrinkled morphology achieved through seeded growth in the presence of *S*-binamine. b) Scanning electron microscopy image of a bidimensional array of wrinkled gold nanorods, obtained using a patterned polydimethylsiloxane template. C) g-factor spectra of long chiral PT–Au NRs in aqueous colloidal dispersion. Spectra are shown for PT-Au NRs grown in the presence of both *S*- and *R*-binamine enantiomers. d) CD spectra measured with different orientations (θ = 0°, β = 0°; θ = 90°, β = 0; θ = 0°, β = 180°; and θ = 90°, β = 180°, where θ represents azimuthal (in-plane) rotation, and β denotes vertical-axis rotation, i.e. sample flipping of 1D linear arrays made of long *R*-rods, with lattice spacing Λ = 400 nm. The inset in (c) presents a magnified view of the 575–615 nm wavelength region.

Conclusions

The extensive body of information that has been accumulated over several decades on the preparation, properties, and manipulation of colloidal gold offers countless opportunities to continue devising experimental strategies for the discovery of new materials and properties that may lead to applications in various fields. Synthetic methods allow us to obtain monodisperse nanoparticles in a wide variety of sizes and shapes, currently including also those with well-defined chiral features. This morphological richness additionally provides a powerful

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tool to tailor the optical properties, both at the single particle level and within controlled assemblies. Optical activity for plasmonic nanoparticles can be obtained through directed assembly into chiral nanostructures with collective optical effects, either in dispersion or deposited on solid substrates.

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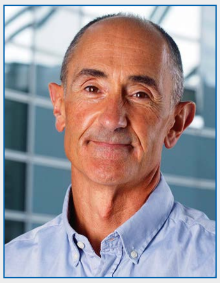

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Luis Liz-Marzán studied chemistry at the University of Santiago de Compostela (Spain), where he also obtained a PhD for work on the use of microemulsions for the synthesis of "magnetic ultrafine particles". After a two-year postdoc at Utrecht University, Luis moved to the recently created University of Vigo, where he established a research program on nanoplasmonic colloids. In 2012, he moved to San Sebastian as Scientific Director and Ikerbasque Research Professor at CIC biomaGUNE, where he leads research on the biomedical applications of plasmonic nanomaterials. He currently leads an ERC Synergy Grant (CHIRAL-PRO) related to chiral plasmonic nanoparticles and their interactions with biomolecules.