SERS-plasmonic biosensors based on Au@Ag@ZIF-8 nanocrystals for multiplex detection.

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Surface Enhanced Raman Spectroscopy (SERS) is a powerful technique that is gaining increase attention in last years in biomedical fields due to its very high sensitivity with almost no need of sample preparation. In this context, the development of efficient SERS substrates capable of achieve very low limits of detection with high selectivity appears as a challenge nowadays. SERS technique is based on the localized electric field that arises on the surface of plasmonic nanoparticles when they interact with the electromagnetic radiation. If a molecule is attached or placed very close to this surface, a significant increase in its Raman scattering is observed.

In this study we prepared a hybrid nanoparticle formed by a plasmonic core (Au@Ag core-shell nanorod) and a ZIF-8 (Zn[2-methylimizadole]$_2$) shell encoded with Raman active molecules. The strategy used consisted in the encapsulation of metallic nanoparticles within MOFs nanocrystals in the presence of a dye mediated by a quaternary ammonium surfactant (CTAB), as previously reported (see Figure 1A).[1] The three dyes used had kinetic diameters larger than pore aperture of ZIF-8 framework, in such way that after the encapsulation they were confined between metallic surface and ZIF-8, so they could not be leached out from the particle. After mixing the enconded particles in appropriate proportions and acquire SERS spectra, we were able to detect at least one characteristic signal of each dye at the mixture spectrum (see Figure 1B). Additionally, the aqueous stability of the ZIF-8 shell could be improved after a shell-ligand-exchange-reaction (SLER) taking advantage of the hydrophobicity (water-repellent) effect and the steric hindrance effect of benzimidazole. After SLER treatment, the modified ZIF-8 retains the structural characteristics of ZIF-8 with improved water stability.

Furthermore, the surface passivated ZIF-8 nanocrystals could be used as platform for the rapid and highly specific immobilization of histidine-tagged proteins through the interaction of unsaturated Zn^{2+} and imidazole moiety of histidines present in His-tagged proteins. The robust immobilization of the proteins on the ZIF-8 surface allowed the direct bioconjugation of the core-shell nanoparticles, making these hybrid systems suitable as SERS tags for multiplex detection in bio-related applications.

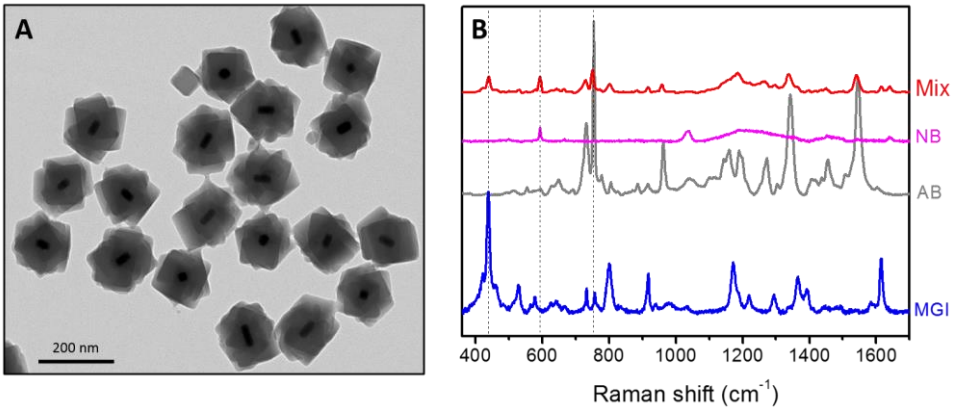

Fig. 1 (A) Representative TEM image of Au@Ag@Dye@ZIF-8 particles and (B) SERS spectra of Au@Ag@ZIF-8 nanoparticles encoded with malachite green isothiocyanate (blue), astra blue (grey), nile blue (pink) and of a mixture (red) of these three enconded particles, where at least one peak of each dye can be identified.

1) Zheng, G., *et. al.*, *Small*, **2016**, *12,* 3935.