Gas-phase fabrication of biomedical nanomaterials for theranostics

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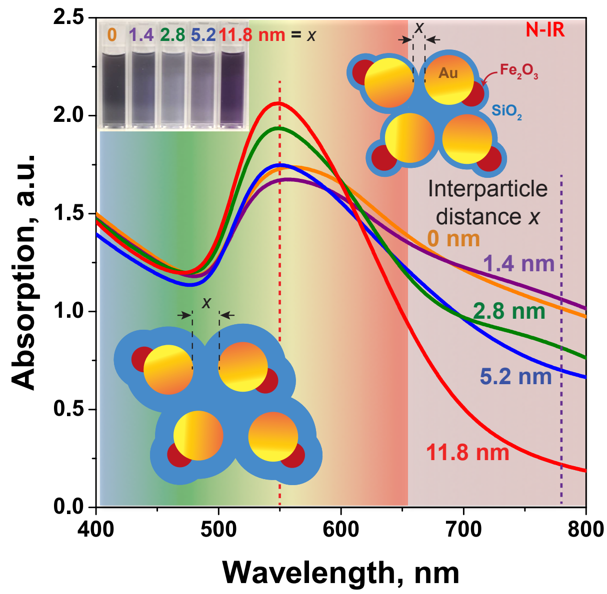
Nanoscale materials show great potential in the biomedical field as they can serve as superior bioimaging contrast agents, diagnostic and therapeutic tools. The small size of nanoparticles allows for: (i) their facile interaction with similarly-sized biological entities such as proteins and viruses or larger ones such as cells, and (ii) their integration in multi-scale systems (Teleki et al., 2016) for the efficient diagnosis (biosensors) and therapeutic intervention of diseases. A *key* element for the successful implementation of nanoscale materials in clinical applications is multi-functionality (Sotiriou, 2013). Here, I will showcase a few examples of how nanoscale materials made by high-temperature gas-phase aerosol processes may be employed to tackle specific medical problems spanning from diagnosis (as biosensors) to potential therapeutic interventions. A specific focus will be placed on the potential of surface functionalization (Sotiriou et al., 2016) with biomolecules (e.g. proteins, antibodies) of such nanomaterials in order to target specific sites/organs *in vivo*.

For example, plasmonic (e.g. Ag, Au) nanoparticles may be combined with a magnetic material (Fe_2O_3) and *in-situ* coated with a nanothin layer of amorphous SiO_2 forming, therefore, hybrid nanoparticles (Sotiriou et al., 2011). Such hybrid nanoparticles can also be detected by magnetic resonance imaging (MRI), with which small magnetic nanoparticles can be used as contrast agents. Furthermore, the hermetic SiO_2 coating on the surface of such nanoparticles facilitates their aqueous dispersion and surface bio-functionalization (Sotiriou et al., 2010) and further prevents their magnetic particle-particle interaction and flocculation (Sotiriou et al., 2011). Furthermore, by finely tuning the plasmonic interparticle distance using the SiO_2 film thickness (or content) the plasmonic coupling can be finely controlled bringing their optical absorption to the near-IR that is most important for human tissue transmittance (Sotiriou et al., 2014). Their effectiveness as photo-thermal agents is demonstrated by killing human breast cancer cells with a short, four minute near-IR laser irradiation (785 nm) at low flux (4.9 W cm^{-2}).

Figure 1 shows the optical absorption spectra of SiO_2-coated Au/Fe_2O_3 nano-aggregates for various average interparticle distances *x* (twice the SiO_2 shell thickness). An interparticle plasmonic coupling occurs that broadens the spectra, which becomes stronger as *x* decreases. The spectra at 550 nm demonstrate that for thicker coatings, the Au nanoaggregates behave like single, non- interacting Au nanospheres. The spectra at 785 nm indicate that thinly coated Au nanoparticles in a highly aggregated state are most attractive for the photothermal treatment of cancer cells.

Furthermore, the small size of nanoparticles gives them ultra-high surface-to-volume ratios, that is often important for biosensing specific biomolecules (e.g. proteins). We show also here how we can engineer the nanoparticle size during their flame synthesis in order to maximize their biosensing performance.



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