# Use of Gold Nanoparticles to Tune the Heating Capacity (ILP) of Iron Oxide Nanoparticles

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# Abstract

Small changes in the synthetic conditions of the coprecipitation of iron oxide-gold nanocomposites have an effect on morphology and magnetic properties of iron oxide (Fe<sub>3</sub>O<sub>4</sub>) nanoparticles resulting in tunable heating through magnetic hyperthermia. Characterisation was achieved through spectroscopic, optical and magnetometry analysis allowing us to show the development and growth of the gold nanoparticles. The nanocomposites were analysed for heat generation through magnetic hyperthermia and addition of hydrogen tetrachloroaurate trihydrate (HAuCl<sub>4</sub>) gives control over the tuning of heat generation giving a maximum intrinsic loss power (ILP) of 2.1 nHm<sup>2</sup>kg<sup>-1</sup>

# 1. Introduction

Iron oxide is of significant interest due to the accessibility to superparamagnetic properties when at a nanoscale range. Utilisation of this superparamagnetism is currently pushing the research of iron oxide nanoparticles for novel biomedical devices and treatments<sup>1–3</sup>, such as within: drug delivery, magnetic separation, MRI contrast agents and magnetic hyperthermia.

Gold coated iron oxide nanoparticles are of significant interest as they have the potential to open up facile synthesis of covalently bonded ligands. And will provide a basis for optical spectroscopy, including surface plasmon resonance (SPR), surface enhanced Raman spectroscopy (SERS) and photoacoustic spectroscopy leading to the possibility of multi modal biomedical probes.

These particles are utilised for magnetic alternating current hyperthermia (MACH) as the primary focus of this study. Within an alternating magnetic field the magnetic vectors flip which provides energy to the particles *via* hysteresis. This energy is then dissipated as heat, causing localised heating, of which temperatures of 41 -  $56^{\circ}$ C lead to damage and ultimately necrotic malignant cells at long exposure times<sup>4</sup>.

# 2. General Instructions

Experimental

Citrate coated iron oxide nanoparticles were synthesised via the co-precipitation of ferrous and ferric chloride salts. A solution of a 2:1 ratio of FeCl<sub>3</sub>:FeCl<sub>2</sub> was heated to  $70^{\circ}$ C under inert atmosphere. NH<sub>4</sub>OH was added as a reducing agent precipitating out the Fe<sub>3</sub>O<sub>4</sub> nanoparticles. Citric acid was added as a stabilising ligand producing a black ferrofluid

The pre-synthesised iron oxide was then added to a boiling solution of hydrogen tetrachloroaurate,  $HAuCl_4$  to form the nanocomposites. Varying concentrations of  $HAuCl_4$ , between 0.1 - 5.0 mM, were added and upon heating formed a deep red/brown ferrofluid.

## Characterisation

Fig 1 shows IO-Au micrographed via TEM to show the morphological changes gold addition makes. It shows that the particles are of a spherical shape with polydispersity,  $\sigma = 2.2$ . Moreover, gold nanospheres have formed, which have aggregated the smaller iron oxide particles. The average calculated particles size, negating the large gold nanospheres, is 8.6 nm.

The higher the gold concentration added results in the formation of larger gold nanoparticles. At 5 mM concentrations, a median diameter of 188 and  $\sigma = 41$  was recorded. In comparison, at 0.25 mM concentrations, the diameter was given as 25 nm and  $\sigma = 5$ .

The predominant peaks from the XRD diffraction pattern of the iron oxide – gold nanocomposites still clearly depict the peaks of unfunctionalised iron oxide. There is however a lower signal to noise ratio present compared to the as-synthesised iron oxide detailing that the gold particles are coarser in morphology. XRD also showed no shift in diffraction angles meaning there has been no structural changes upon formation of the iron oxide – gold nanocomposite.

Mössbauer spectroscopy has also been used to determine

the oxidation state of the iron species present. The mean isomer shift of the spectra relative to  $\alpha$ -Fe was 0.37 mm/s, which lies between those of pure maghemite (delta = 0.32 mm/s) and pure magnetite (delta = 0.53 mm/s). This value indicates a magnetite content of approximately 23% - implying that the samples were either non-stoichiometric magnetites, or magnetite/maghemite composites, or some combination of the two. Upon the formation of gold nanoparticles it can be seen from the Mossbauer analysis that the iron oxide particles underwent a change in their spatial arrangement. Thus resulting in variations in magnetic susceptibility, due to a change in the amount of larger magnetically blocked particles.

The generation of heat for hyperthermia treatment is the fundamental application of this study. The heating was seen to varying degrees for different Au concentrations. Fig. 2 shows that we can use this variation in intrinsic loss power (ILP) to tune the generation of heat from the iron oxide nanoparticles. We discovered that a gold concentration of 0.75 mM has given rise to the most efficient heaters with an IPL of 2.1 nHm<sup>2</sup>kg<sup>-1</sup> compared to 0.8 nHm<sup>2</sup>kg<sup>-1</sup> for the as-synthesised iron oxide with no gold.



Fig. 1 TEM image and size distribution histograms of (a) IO-Au $_{0.25}$ , (b) IO-Au $_{0.75}$  showing the iron oxide-gold nanocomposites and the aggregation of iron oxide around gold nanospheres.



Fig 2 ILP heating values against the synthetic gold concentration used in formation of iron oxide – gold nanoparticles showing the peak performance at  $0.75 \text{ mM HAuCl}_4$ .



Fig. 3 (a) Mössbauer spectra measured at room temperature for increasing amount of gold in the IO-Au colloid nanostructures and (b) corresponding difference profile between the initial, uncoated sample (IO-C) and those with increasing gold concentrations. (c) Room temperature Mössbauer spectrum of IO-C sample folded relative to  $\alpha$ Fe foil. (d) Best fit to the measured spectra of IO-Au<sub>0.75</sub>. The subcomponents of the initial IO-C are shown in grey, with additional subcomponents highlighted in orange (sextet) and pink (doublet).

#### 3. Conclusions

It can be seen that a simple co-precipitation synthesis of iron salts can produce highly tunable superparamagnetic iron oxide nanoparticles. It is also possible to further improve the magnetic hyperthermia characteristics of citrate coated iron oxide nanoparticles by the addition of hydrogen tetrachloroaurate. The addition of the gold has altered the structure and morphology of the iron oxide and hence increased the magnetic behaviour and hyperthermia possibilities. The synthesis has resulted in the aggregation of small iron oxide nanoparticles around large gold nanoparticles, forming clusters of a mixture of particles. Using magnetometry we have then concluded that the greater proportion of small clusters that are present, the greater the ILP rises.

This is a highly positive outcome for these particles showing that gold has a positive effect on hyperthermia, with a high degree of potential future applications, such as cancer therapy and imaging modalities.

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### References

- Q. A. Pankhurst, J. Connolly, S. K. Jones, & J. Dobson, J. Phys. D: Appl. Phys., 2003, 167, R167.
- [2] Q. A. Pankhurst, N. Thanh, S. K. Jones, & J. Dobson, J. Phys. D: Appl. Phys., 2009, 42, 224001.
- [3] L. A. Thomas, L. Dekker, M. Kallumadil, P. Southern, M. Wilson, S. P. Nair, Q. A. Pankhurst & I. P. Parkin. J. Mater.
- [4] A. P. Khandhar, R. M. Ferguson, H. Arami and K. M. Krishnan., Biomaterials, 2013, 34, 3837.