

Synthesis and Characterization of Paramagnetic Iron Nanoparticles with Minimal Gold Coating for Optimal Drug Delivery

David Banner¹, Emre Firlar^{1,2}, Hasti Asayesh-Ardakani^{2,3}, Reza Shahbazian-Yassar² and Tolou Shokuhfar¹.

¹ Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, USA.

² Department of Mechanical and Industrial Engineering, University of Illinois at Chicago, Chicago, Illinois, USA.

³ Department of Mechanical Engineering, Michigan Technical University, Houghton, Michigan, USA.

Gold-coated iron nanoparticles (AuFeNPs) have been previously used as contrast agents in medical imaging, such as in MRIs, and have more recently been employed as a drug delivery medium [1, 2]. Here, a previously described AuFeNP synthesis method was refined to decrease the thickness of the gold coating, which would lower the AuFeNP size without changing the paramagnetic iron volume [1, 2]. The smaller spherical nanoparticles would increase the number of nanoparticles (NPs) that could be packed into confined space, resulting in a net increase in the surface area of the NPs to which the bioactive agents bind. This would increase the amount of the bioactive agent that could be loaded within an implant or other confined systems.

Iron nanoparticles (FeNPs) below approximately 20nm exhibit a paramagnetic response, at which the magnetic moment can orient freely, rendering the NPs unresponsive to conventional magnetism [1,2]. This paramagnetism is important because it prevents the unintended influence of magnetic fields. However, a strong magnetic field aligns the iron magnetic moment, which allows a magnetic gradient to manipulate the NPs. Below 2nm, NPs are toxic because the NPs diffuse into cells [3]. At small particle sizes iron is quickly oxidized, which prevents the FeNP from being paramagnetic. One commonly used approach for solving this problem is coating the NP with gold, which not only prevents oxidation but also provides easily functionalized thiol groups to which a wide range of bioactive agents can be bound. In controlled drug delivery applications AuFeNPs should be optimized to allow maximal control of the paramagnetic properties of AuFeNPs while delivering as much of the bioactive substance as possible. To achieve this, this study attempted to optimize a previously described procedure by minimizing the gold coating thickness, while retaining a 10nm to 20nm paramagnetic iron core to provide greater surface area for bioactive drug binding [1,2].

Reverse emulsion is a method commonly used to create highly uniform AuFeNPs. In one mixture, an aqueous phase containing a chemical reagent is mixed into a larger hydrophobic phase, while in a secondary mixture an aqueous chemical reactant is mixed into a larger hydrophobic phase. This creates micelles in each solution when stirred. The two solutions are then combined, and the micelle size is used to control the diameter of the resulting product. In this study, as in previously described procedures, octane was employed as the hydrophobic phase along with centrimonium bromide (CTAB) and n-butanol surfactants [1, 2]. One mixture contained aqueous iron sulfate, while the secondary solution contained aqueous sodium borohydride. These solutions were mixed at 800rpm and then combined to form the FeNP core. After that, gold chloride, sodium borohydride, CTAB, and n-butonal were mixed into the solution. In previous studies, the micelles were expanded to allow the addition of the gold coating, and then bulk gold chloride and additional sodium borohydride were added [1, 2]. In contrast to the method reported by Lin *et al.*, a smaller amount of gold chloride was simply added manually to the

FeNP being stirred, followed by immediate addition of additional sodium borohydride with less micelle size expansion.

In previously described studies, magnets were used to separate larger magnetic NPs from the paramagnetic AuFeNPs [1, 2]. In this study uncoated iron NP controls larger than 20nm synthesized by altering the micelle size exhibited an initial magnetic response, but after overnight oxidation, they did not exhibit a visible response to conventional magnets. The experimental AuFeNPs synthesized in this study, however, did not show any visible magnetic response and did not require separation. In previous studies, Transmission electron microscopy (TEM) examination showed a visible lighter gold halo surrounding a darker iron core [1,2]. TEM results did not show any surrounding gold halo showed that the diameters of the spherical NPs were between 7nm to 20nm. EDS results showed that the NPs contain both gold and iron, suggesting that the NPs have a larger iron core with a very thin gold coating. After three months, the AuFeNP solution remained black, and repeated EDS and TEM show the presence of gold and iron as well as minimal aggregation.

The stable AuFeNPs synthesized in this study can be rehydrated in water or isopropyl alcohol without damage, and have an extended lifetime. This stability as well as the increased surface area of the AuFeNPs are ideal for further research in implant drug delivery applications. Further AuFeNP synthesis studies will focus on quantifying the AuFeNP paramagnetic properties, optimizing the NP diameter precision, minimizing particle aggregation, and continued monitoring of the AuFeNP lifetime. [4]

References:

- [1] J Lin. *Journal of Solid State Chemistry* **159**, (2001) p. 26-31
- [2] W Zhou, E Carpenter, J Lin, A Kumbhar, J Sims, C O'Conner. *The European Physical Journal D*. **16**, (2001) p. 289-292
- [3] Y Pan, S Neuss, A Leifert, M Fischler, F Wen, U Simon, G Schmid, W Brandau, W Jehnen. *Small* **3** (2007) p. 1941-1949
- [4] This work made use of instruments in the Electron Microscopy Service (RRC, UIC). This project was partially supported by NSF, Award No. 1350734

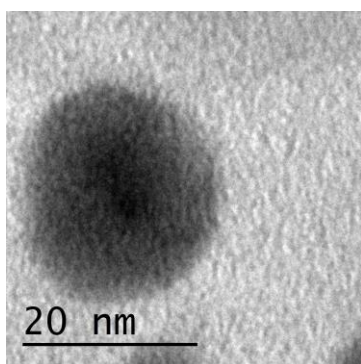


Figure 1. Bright field TEM image of AuFeNP. Collected via a JEOL 3010 at 300 kV.

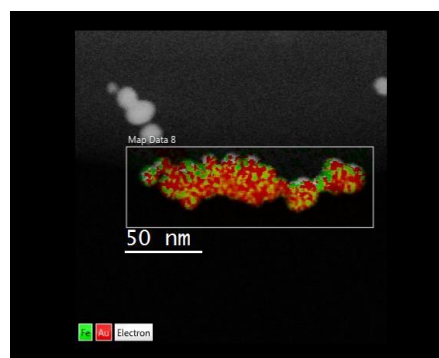


Figure 2. EDS element map, which shows the gold (green, light) and iron (red, dark) distribution. Imaged via a JEM-ARM200CF.