

MS2/MS3

Bench-top Magnetic Susceptibility Analysis of Magnetic Nanoparticles

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In our chemistry lab we make magnetic nanoparticles (MNPs) through classic wet chemistry precipitation methods. We mainly synthesise magnetite, but also work with the platinum alloys FePt and CoPt (Figure 1a). The simplest method of producing MNPs is by oxidising/precipitating iron ion out of solution by increasing pH under N_2 to form magnetite, or by reducing/precipitating iron or cobalt and platinum salts out of solution with $LiEt_3BH$ to form FePt or CoPt respectively. These methods are quick, cheap and produce high yields. However, the level of control over the size and shape of these MNPs is not ideal without modification to this process (Figure 1a). We are interested in biomineralisation and the fact that magnetic bacteria produce mono-dispersed populations of magnetite MNPs within their cells (called magnetosomes) under very tight genetic control (Figure 1b)¹. We are interested in using these magnetosomes, as well as understanding how the bacterial proteins within the cell control the process. We have studied a few of these proteins namely Mms6^{2,3} and MmsF⁴, and have added these proteins to the simple wet chemical precipitation of MNPs to control the composition, size and shape of the resultant MNPs (Figure 1c and d)^{2,4}. The magnetosomes and the more precise MNPs produced are valuable materials for a range of applications from nanotechnology to biomedical application in diagnostics and drug delivery. For all our research, analysing and understanding the magnetic characteristics of the MNPs we produce is fundamental to our work.

The standard analytical instruments that magnetic materials chemists like us tend to use and show data from in our publications are SQUID and VSM magnetometers. These are very sensitive, temperature variable instruments (they use liquid helium to reduce down to temperatures of 5K or lower) and as such are very expensive (in the £100k's price range) high-end instruments which are thus typically in short supply (there may be 1 or fewer instruments per University). Further

compounding this availability problem is that each sample takes some time to set up and run and there is an expense associated with running and analysing each sample.

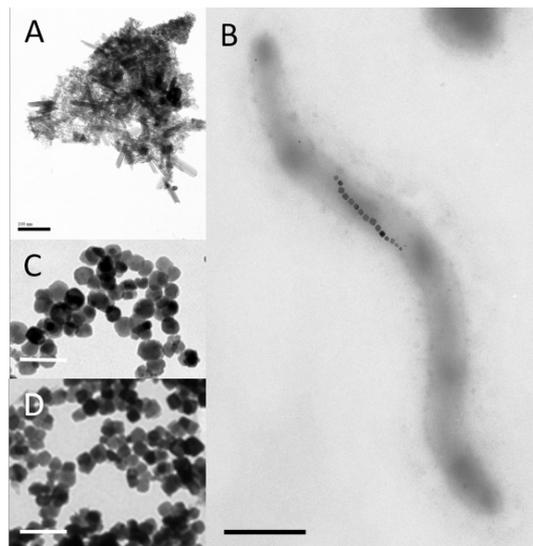


Figure 1. Magnetite magnetic nanoparticles (MNPs) synthesised by different methods: A. Room temperature co-precipitation of ferric and ferrous ions. B. Magnetite biomineralised in magnetosomes within magnetic bacteria¹. C and D. Room temperature co-precipitation of ferric and ferrous ions with the addition of the proteins Mms6² and MmsF⁴ respectively. Scale bars are 100 nm for A, C and D and 1 µm for B

For much of our work, this type of analysis is overkill, and inefficient in time and resources. We spend a lot of time optimising conditions, which means running many synthesis reactions over a large parameter landscape, yielding many samples that simply cannot all be assessed by SQUID or VSM. What we really needed was a benchtop, simple instrument to quickly assess the magnetism of a large number of samples in a high-throughput manner, to assess the quality and/or the quantity of the MNPs we produce.

The MS2/MS3 is ideal for this. The small instrument is inexpensive and uses a very small amount of lab bench space (Figure 2).

CS 0021 16/08

After calibration the samples are simply placed in the sample holder at room temperature, the reading is taken, then the sample is removed.

There is no time-consuming sample preparation, and this means the sample is completely recoverable (the samples often remain in the solute solution) (Figure 2). Two examples demonstrate this below.

Quality/Composition of the MNPs

We assess the iron oxides produced when the conditions for making magnetite are varied. If the ratio of ferrous and ferric ions varies then the iron oxides produced vary, in most cases giving a mixture of magnetite (magnetic) ferrous hydroxide and green rust (non-magnetic).

The MS2/MS3 can be used to quickly assess how much magnetic material is present in our reaction mixture (all calibrated to be the same amount of product). Further to this we add the protein Mms6 and see that it preferentially nucleates the formation of magnetite over the other iron oxides at more ferrous-rich conditions, showing Mms6’s function in vitro and suggesting a similar function in vivo.



Figure 2. A demonstration of the MS2/MS3 system in use in our lab.

This important work has been published³ and while a huge amount of analysis was used to support this finding, the MS2/MS3 shows a clear magnetic correlation to the rest of the analysis (i.e. more magnetic material in the Mms6 high ferrous ratio than in the control) and is included in the supplementary data of this publication.

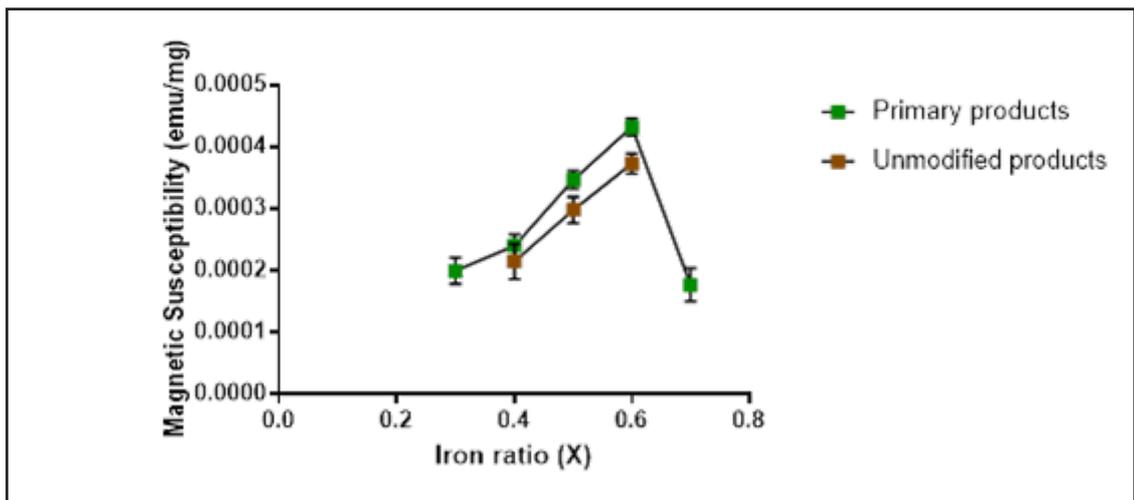


Figure 3. Comparison of magnetic nanoparticles prepared at different ferric to ferrous ratios.

We have gone on to do a more in-depth study varying the iron ion ratios, and as this is an optimisation study over a large parameter set, we have relied more heavily on the MS2/MS3 assay which has given clear relationships supported by our other data (Figure 3). This is currently being written up with a hope to be published by the end of this year or early next year.

Quantity analysis for biomedical assays

We are working with medics to develop nanomedicines using our MNP as drug-delivery vehicles, as well as for diagnostics and therapeutics. When we give a sample of our nanomaterials to the medics to perform cancer uptake experiments it is essential that they know exactly how much MNP material is present so that the cancer assays can be calibrated. We can calculate roughly how much should be there from our starting materials used, but chemical synthesis rarely has a 100% yield, especially if we have modified the particles through several steps. Thus again we need a quick and simple method to measure the amount of magnetite MNP in our 1 ml solution. Again the MS2/MS3 is ideal, as we simply insert our sample into the instrument to get our reading (Figure 2). We know magnetite has a magnetic saturation of 91 emu g^{-1} , but we have also calibrated against a known sample of our magnetite MNPs so that we have a simple conversion factor to obtain the mass of magnetite MNP quickly, simply, cheaply and reliably.

References

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- 2 Amemiya, Y., Arakaki, A., Staniland, S. S., Tanaka, T. & Matsunaga, T. Controlled formation of magnetite crystal by partial oxidation of ferrous hydroxide in the presence of recombinant magnetotactic bacterial protein Mms6. *Biomaterials FIELD Full Journal Title: Biomaterials* **28**, 5381-5389 (2007).
- 3 Rawlings, A. E. *et al.* Ferrous iron key to Mms6 magnetite biomineralisation: A mechanistic study to understand magnetite formation using pH titration and NMR. *Chemistry A European Journal* **22**, 7885-7894 (2016).
- 4 Rawlings, A. E. *et al.* Self-assembled MmsF proteinosomes control magnetite nanoparticle formation in vitro. *Proceedings of the National Academy of Sciences* **111**, 16094-16099, doi:10.1073/pnas.1409256111 (2014).