

# Experimental synthesis of safer nanomaterials through computational modelling and design

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## 1. Introduction

Iron-oxide magnetic nanoparticles (NP) have extensive applications in many different fields such as biomedicine and biochemistry, high density data storage, magnetic resonance (MR) contrast enhancement and immunoassay analysers to name a few [1,2]. These NPs have been approved by the food and drug administration for clinical applications as MRI contrast enhancers and are a biocompatible material. However, the study of the toxicity of these NPs mainly focusses on particles with tens to hundreds of nanometres while little is known about the toxicity of ultrasmall magnetic NPs [3]. The safe application of magnetic NPs to these various fields is therefore highly dependent on the ability to control the particle's physicochemical properties.

Two common phases of iron-oxide NPs which are magnetite ( $\text{Fe}_3\text{O}_4$ ) and goethite ( $\alpha\text{-FeOOH}$ ). Whereas magnetite is commonly used as a contrast agent in MR-imaging [4], goethite (iron-hydroxide) has wide application in material science, manufacturing and environmental pollution remediation [5].

One of the easy and cheap approaches to fabricate  $\text{Fe}_3\text{O}_4$  NPs, is coprecipitation, where surfactants are always used to control the particle size and shape. Nonetheless, to obtain single-phase, monodisperse, lowly-aggregated NPs with a specific morphology remains a challenge.

Since it is known that ultrasmall  $\text{Fe}_3\text{O}_4$  (<10 nm) NPs display a high toxicity *in vivo* due to the distinctive capability in inducing the generation of hydroxyls in multiple organs [3], and that this toxicity is related to both the iron element and size of the NP, the need of comprehensive evaluation of their physicochemical properties under different conditions of size, shape, phase and coating, cannot be over emphasised.

Thus, in this investigation we report on how computational modelling and complementary experimental work, can lead to the design and synthesis of safer nanomaterials. We show how computational modelling and simulations can lead to a fundamental understanding of how to control the particle size and shape and the phase that ultimately control the NP's physicochemical properties and consequently its cytotoxicity.

## 2. Computational modelling and simulations.

For this work, a combination of molecular dynamics (MD) and Monte-Carlo-based simulated annealing adsorption was performed on small and ultrasmall magnetite

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( $\text{Fe}_3\text{O}_4$ ) NPs and various surfactants. This was done for sizes ranging from 1.0 to 7.0 nm. Shapes were also varied from spherical to cuboidal to observe the changes in binding energy (BE) and to qualitatively determine the change in pH of a solution. Furthermore, density functional theory (DFT) was used to analyse the different surfactants and draw conclusions on their reactivity with these NPs. The resulting simulated predictions were then used to synthesize (experimentally) the various NPs and to investigate their physicochemical properties.

### 3. Experimental setup

Co-precipitation and thermal decomposition were used to synthesize  $\text{Fe}_3\text{O}_4$  NPs according to the predictions and schemas gained from the computational modelling and simulations. These NPs were further characterized with high-resolution transmission electron microscopy (HR-TEM), powder x-ray diffraction (PXRD), Fourier transform infrared spectroscopy (FTIR) and vibrating sample magnetometer (VSM).

### 4. Results and discussion

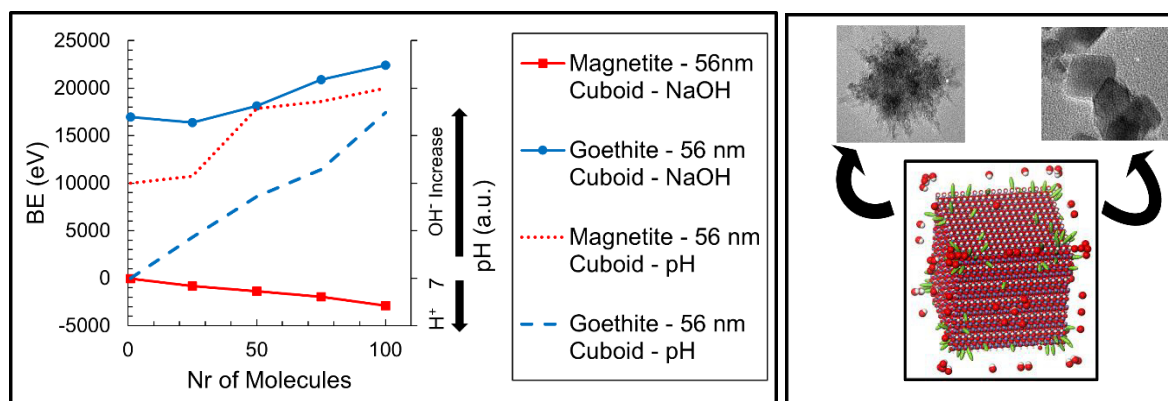


Figure 1: (Left) Calculated Binding Energy (BE) for magnetite and goethite NPs after simulated structures (bottom right) were obtained. Experimental HRTEM images (top right) were obtained to validate the simulated results.

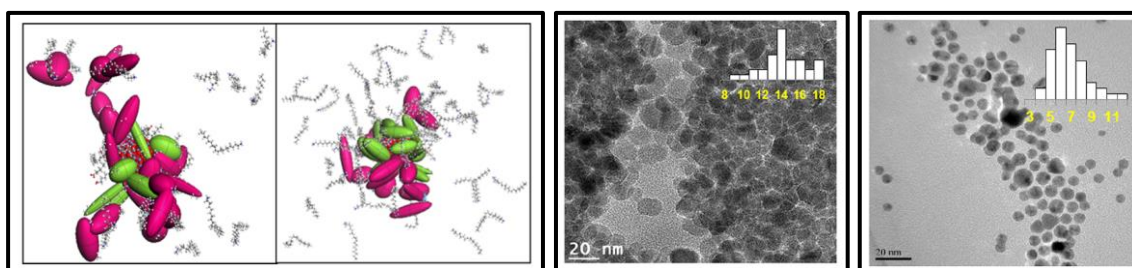


Figure 2: (Left) Simulated geometries of  $\text{Fe}_3\text{O}_4$  NPs with different ratios of OA and OLA adsorbed leading to NPs with different hydrodynamic sizes. Insights gained from these computational simulations allowed us to synthesise these small NPs with a mixture of cuboidal and spherical shapes that were highly agglomerated (figure 2 middle) versus the ultrasmall spherically shaped NPs with a very low polydispersity index (figure 2, right).

Figure 1 shows the calculated BE for the simulated magnetite and goethite NPs after the adsorption of different amounts of surfactants. This was done to gain a qualitative understanding of the role that a change in the pH may play in the stability of these various nanostructures. This allowed us to fine-tune the pH during a real-world experiment (figure 1, right) wherein we successfully synthesised both magnetite and

goethite by only varying the pH and observing the exact point where the phase changed occurred.

Furthermore, we simulated the optimized geometries and calculated the resulting BEs of spherical and cuboidal magnetite NPs with different surfactants (oleic acid (OA), oleylamine (OLA), NaOH, NH<sub>4</sub>OH) and observed the effect that the change in size and shape has on the BE (figure 2, left). This descriptor was used as a predictor of the stability of these NPs and, consequently, we used these simulation results to successfully synthesize ultrasmall NPs with controlled size, shape and polydispersity index (figure 2, middle and right).

The correlation between NP stability and the number of dispersion medium acid–base complex pairs and free proton concentration was investigated and it was concluded that (as advocated) combinations of OA and OLA play an important role when synthesizing magnetic iron oxide NPs. OLA molecules act as proton acceptors and help to regulate the electrostatic pressure, responsible for OA desorption, caused by an excess of free protons. Too much OLA may also lead to the desorption of the stabilizing OA molecule from the NP surface to form acid-base complex pairs; therefore, an ideal ratio of OA/OLA is to be used that allows for a perfect fit between the NP surface charge, free proton concentration in the dispersion medium, and zeta potential. The fluctuating dynamic kinetic conditions allow for the engineering of specific shapes and sizes of magnetic nanoparticles.

## 5. Conclusions

MD simulations have revealed that the binding energy of OA to the NP is maximized at an acid/amine ratio of 3. As a result, a better control of the reaction and growth of the NP was obtained, theoretically. We then successfully (in a real-world experiment) demonstrated that at an optimized OA/OLA ratio of 3, the NPs show the lowest monodispersity without a need for any post synthesis size-selective precipitation.

Furthermore, MD were used to predict the more favourable phase when NaOH is used to control the pH, to grow magnetite and goethite NPs. The role of pH was investigated qualitatively by noting the ratio of desorbed/excess hydroxyls to free protons (hydrogen ions) in the solution. BE was used as an indicator of the stability of the cuboid magnetite versus goethite systems. It was predicted that neutral to low pH values (i.e., neutral to acidic solutions) will lead to the formation of cuboid goethite NPs that are stable. Conversely, a more basic solution will lead to the formation of stable, cuboid magnetite. This was used to employ the co-precipitation method in a real-world experiment to successfully synthesize more stable and therefore safer nanomaterials through modelling and design.

## 6. References

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