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Magnetic Nanoparticles Based on Iron: Synthesis, Characterization, Design, and Application

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Magnetic Nanoparticles Based on Iron: Synthesis, Characterization, Design, and Application

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

by

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B. S., James Madison University, 2003

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April, 2008
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Abstract

MAGNETIC NANOPARTICLES BASED ON IRON: SYNTHESIS, CHARACTERIZATION, DESIGN, AND APPLICATION

By Michael D. Shultz, Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Virginia Commonwealth University, 2008

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Magnetic nanoparticles are of great interest for a wide range of applications. This work has focused on three primary forms of iron based nanoparticles and combinations thereof: α-iron, iron oxide, and iron carbide or cementite. The synthesis of several core-shell particles including cementite-iron oxide, α-iron-cementite, and α-iron-iron oxide was accomplished through reverse micelle routes and high temperature decomposition of iron pentacarbonyl in various media. Structural analysis to confirm the structures was performed using extended x-ray absorption fine structure (EXAFS) techniques. A rapid characterization technique was developed utilizing a correlation between Fourier transform infrared spectroscopy and EXAFS to determine the full metal cation distribution between the octahedral and tetrahedral sites in manganese zinc ferrite (MZFO). This method was then used to show that the initial Fe$^{3+}$ to Fe$^{2+}$ ratio in MZFO
synthesis could be used to design a desired cation distribution and affected the zinc incorporation levels into the resultant ferrite.

Functionalization of nanoparticles for aqueous dispersions and ferrofluids has varying degrees of importance, depending on the application. In applications such as magnetic resonance imaging (MRI) where the targets are biological systems, it was important to produce solutions that will not aggregate in the high magnetic field of the MRI. It was also vital to characterize decomposition mechanisms and products that would be presented to the body after use as a contrast agent. This work has provided insight into both the preparation of magnetic samples for MRI applications and implications of the biocompatibility of reactive and decomposition products. Three successful methods of forming dispersions that would not aggregate in the high magnetic field of the MRI were comprised of cysteine/polyethylene glycol (PEG), PEG based ferrofluids, and dopamine/PEG. The dopamine functionalization however showed reactivity with the iron/iron oxide nanoparticles and led to the formation of the cytotoxic dopamine quinone and resulted in the destruction of the nanoparticles. Using all three types of dispersions to compare the iron based nanomaterials, the MRI measurements concluded with the iron oxide ferrofluid yielding the highest R2 enhancement.
Chapter 1: Introduction

Inspiring Thoughts #1

“When the going gets tough, the Tough get going!”
1.1 General Overview

Magnetic nanoparticles are surging in interest for a wide range of applications. This is partially due to the fact that nanoparticles are on a size dimension that yields a high surface area to volume ratio, thereby typically giving very high surface reactivity. More importantly however is that the magnetic properties and other characteristics exhibited by nanoparticles are completely different from those seen in the bulk or larger scale materials.\(^1\) An example of this would be the emergence of superparamagnetism on the nanoscale. The applications in which magnetic nanoparticles are thriving are from a wide range of disciplines. In biological and biochemical research, magnetic nanoparticles are being functionalized in order to perform protein separation and cell sorting.\(^2,3\) Medical advances are being driven by these nanomaterials in areas like targeted drug delivery, tumor treatment, and magnetic resonance imaging contrast enhancement.\(^4-8\) Other fields that benefit from the small size and various electronic and magnetic properties of these nanoparticles include radio and other communication devices, transformers, transducers, and data storage.\(^9,10\)

Although various methods of synthesis exist, there are many questions pertaining to nanoparticle growth and nucleation for which the answers remain elusive. Some of the difficulty in gaining this knowledge lies with the characterization methods required for investigations on the nanoscale. Some of these required techniques are high cost and unavailable to many research groups. Therefore, the development and implementation of new characterization techniques and unique combinations of techniques is in some ways as vital in nanoparticle studies as the actual novel synthesis of a new material.
Many of the magnetic materials that are focused on in research are primarily iron based. The three main categories of iron to be presented in this work are metallic iron, iron oxide, and iron carbide. Metallic iron has the highest saturation magnetization of any elementally pure material and is biocompatible. Both the metallic iron and iron oxide have structural variations that can be investigated for various application studies, though some have not yet been seen stable in ambient conditions. The iron carbide offers a variation that puts the iron atoms in similar structures to those not thermodynamically stable at room temperature and atmospheric pressure while maintaining the zero-valent state being in the form of an iron-carbon alloy. Iron oxide properties are frequently altered by doping with different amounts of other transitions metals, which as long as these mixed metal oxides maintain a majority component of iron they are termed ferrites.

Along with the drive for new materials and the understanding thereof, much of research is application driven. Specifically, magnetic resonance imaging (MRI) contrast enhancement has been achieved by various different materials and methods,\textsuperscript{11-23} of which iron and iron oxides have gained interest due to their biocompatibility. Materials with a higher saturation magnetization is what much of recent literature has been focused on for contrast agents since it should increase the local magnetic field or magnetic field penetration into the specimen, thereby shortening relaxation times and improving imaging contrast. Some work has focused on the oxidation protection of metallic iron by oxidative resistant materials such as gold and investigating their contrast enhancement.\textsuperscript{17,19} One interesting feature from much of this work is that iron oxide, while having a saturation magnetization of only 50\% of the value for metallic iron, yields
a transverse relaxation rate enhancement (R2) that is 10 fold higher than that of metallic iron.\textsuperscript{17} This then implies that although some magnetic contribution may be necessary, the saturation magnetization may not be a main factor for improving contrast enhancement. Therefore metallic iron may not be the best suitable structure of iron or iron based materials for MRI applications.

1.2 Research Focus

The main purpose of this research is to tailor novel magnetic nanomaterials and through collaboration and development of new characterization techniques, fully characterize their structure and gain further insight into their synthesis. This work also will also investigate the magnetic resonance imaging (MRI) contrast enhancing capabilities for some different iron based materials with different structures, and the specific functionalization of such materials for proper application. The specific application of MRI contrast enhancement has been especially troubled by experimentation under a diversity of magnetic fields and other conditions that are not usable for clinical MRI application. This has setback the understanding of how nanoparticles function as contrast agents and possibly misguided the direction to pursue for optimization.
1.3 Research Approach

The success of many research endeavors is reliant on the approach or method of attack. Therefore, this work will address some of the predominant issues within nanoparticle research by the following:

➤ developing rapid and available characterization techniques in conjunction with costly high resolution techniques,

➤ working with such methods to uncover synthesis parameters that can allow for specific tailoring of nanoparticle properties,

➤ gaining further insight into factors that affect the resultant structure of nanocrystalline materials through novel synthesis and characterization,

➤ controlling synthesis parameters to synthesize specific crystal structures,

➤ functionalizing such materials and investigating their magnetic resonance imaging (MRI) contrasting capabilities.

Before progressing further into the research, the next several chapters will first discuss some background information about crystal structures of iron, ferrites, magnetism in materials, and synthetic and characterization techniques that is necessary for better understanding and interpretation of the results presented.
Chapter 2: Crystal Structures of Iron

Inspiring Thoughts #2

“Lead or get out of the way!”
2.1 Introduction

For all of the vast and different materials that exist, there are only fourteen basic crystal structures. These crystal structures are known as the Bravais lattices. Though materials primarily follow one of these basic structures, there are still variations in atom arrangements within the same structures that yield many different properties. A good example of this is how magnetic properties vary with the various structures of iron, which will be discussed in more detail in later chapters. Since such properties vary between crystal structures, it is important to understand some basics behind atomic packing in some crystal structures. This chapter will cover some simple crystal structure concepts while focusing on the structures of iron dealt with in this research.

2.2 Metallic Iron

In general, metallic iron crystallizes in either a body centered cubic structure or a face centered cubic crystal structure. The body centered cubic (BCC) structure of iron is the thermodynamically stable form in ambient conditions and is denoted as $\alpha$-Fe. The BCC structure can be seen in Fig. 2.1. The unit cell of this structure can be built by placing one iron atom in each of the eight corners of the cube and one atom in the center. The corner atoms count as $\frac{1}{8}$ and the center counts as 1 for a total of 2 iron atoms per unit cell. The face centered cubic structure (FCC) seen in Fig. 2.2 is built in a similar beginning fashion by placing an atom in each corner of the unit cell. The difference is that instead of an atom occupying the center of the unit cell, atoms are placed on the six faces of the cube. As before the corners add to 1 atom and with the faces counting for $\frac{1}{2}$,
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Fig. 2.1. Illustration of the packing known as body centered cubic which is the thermodynamically stable state of metallic iron known as $\alpha$-Fe.
Fig. 2.2. Illustration of the packing known as face centered cubic which is the crystal structure of $\gamma$-Fe. In comparing to Fig. X, it is evident why FCC is considered a close packed cubic structure while BCC is not.

As was stated, the BCC structure of iron is the most common and sought after form due to its strong magnetic properties. The difficulty in obtaining this form in nanoparticles is due to the ease by which metallic iron is oxidized. Upon oxidation, the magnetic properties are greatly altered due to the structural changes that occur. For this reason much effort is put forth to passivate the surface of nanoparticles and prevent the loss of
magnetic properties. Later chapters of this research will address some methods of passivating metallic iron that have been successful.

2.3 Iron Carbide

Fig. 2.3. This illustrates the atomic arrangement present in the cementite structure of iron, Fe₃C. The red spheres represent iron with the two different sites labeled 1 and 2, while the black spheres represent carbon.
The iron-carbon alloy of zero valent iron is known as cementite and typically possesses the chemical formula Fe$_3$C. This structure falls into the orthorhombic crystal structure category and forms in bulk synthesis as γ-Fe is cooled while dissolved carbon is allowed to fall out of solution and into the alloy. It is the primary component of carbon steel and thus is also very resistant to oxidation and other forms of corrosion. This iron based material can also be ferromagnetic with quite high saturation magnetization. For description purposes, the cementite structure can be thought of as a distorted close packed structure and is illustrated in Fig. 2.3. There are two different iron environments which are in a specific 2:1 ratio, or in other terms one iron site is 66.67% while the other accounts for 33.33% of the iron. Although there are favorable magnetic properties which will be discussed later, this material is hard and brittle which are not as favorable mechanical properties in comparison to the α-Fe, thus making α-Fe the typically more sought after metallic phase.

2.4 Ferrites

The term ferrite most commonly refers to metal oxides that have a primary component of iron. In some cases, one can think of a ferrite as an iron oxide that is doped with other metals to gain variation in the magnetic and electronic properties. The type of ferrite that will be introduced here is that which possess the spinel structure. The spinel structure was named for the mineral MgAl$_2$O$_4$, in which the oxygen atoms for a face center cubic (FCC) crystal structure with the metal cations occupying interstitial sites. These interstitial sites are of two types: metal cations coordinated to 4 oxygen
atoms and metal cations coordinated to 6 oxygen atoms. These sites are known as tetrahedral and octahedral respectively. For visual assistance, Fig. 2.4 depicts the basic spinel structure showing the two different interstitial sites and some oxygen arrangement.

![Diagram of the spinel structure](image)

**Fig. 2.4.** Drawing of the spinel structure illustrating the octahedral and tetrahedral sites and their relative position to the oxygen atoms in the structure. To the right is an extended portion of the structure better illustrating the 4 coordinate tetrahedral site and the 6 coordinate octahedral site.

The simplest unit of the spinel crystal structure of iron oxide has eight molecules of $\text{MFe}_2\text{O}_4$ where M stands for some dopant metal cation. The 32 oxygen atoms
assembled in a face centered cubic fashion produces a total of 64 tetrahedral sites and 32 octahedral sites, of which only 8 tetrahedral and 16 octahedral sites are occupied by a metal cation. The primary reason for only 24 of the interstitial sites being occupied is for charge balance. In the case of the mineral spinel, the trivalent aluminum cations occupy the 16 octahedral sites and the 8 tetrahedral sites are occupied by the divalent magnesium cations for a total charge of +64, which balances the -64 charge from the 32 oxygen atoms. This arrangement of atoms where the octahedral sites are solely occupied by trivalent atoms and the tetrahedral sites are occupied by the divalent atoms is known as the normal spinel. In the case of ferrites, the same charge balance is required but the arrangement of cations is different. In some ferrites, the divalent atoms actually prefer to occupy half of the octahedral sites, with the remaining octahedral and all of the tetrahedral sites being filled with the trivalent cations. This state may seem more logical since divalent cations are typically larger than trivalent cations, thus occupying the larger octahedral site as opposed to the smaller tetrahedral site would seem favorable. The extreme case where all divalent cations are in the octahedral sites is known as the inverse spinel. Many ferrites are still simply referred to as having the spinel structure because the actual distribution of cations is somewhere between the normal and inverse spinel form due to other electronic considerations where an atom may prefer to be tetrahedrally coordinated as opposed to octahedrally coordinated. A good example of this would be zinc cations, which are divalent yet in order follow the eighteen electron rule will only occupy tetrahedral sites to become coordinatively saturated.
2.5 Mixed Metal Ferrites

Mixed metal ferrites often have the mixed distribution between the normal spinel and the inverse spinel. This concept is very clearly seen in the case of nickel zinc ferrite, \( \text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4 \). \( \text{NiFe}_2\text{O}_4 \) is typically found to exist in the inverse state where \( \text{ZnFe}_2\text{O}_4 \) is always in the normal state. It then makes perfect sense for the combination to be somewhere in the middle. Since the site that each dopant metal would occupy is fairly straight forward, altering the electronic and magnetic properties can be achieved by simply altering the ratios of nickel and zinc doped into the iron oxide. Manganese zinc ferrite however offers a different challenge for successfully achieving altered magnetic properties. For the same reason that manganese can be harmful to the body due to its ability to occupy sites in a biological process that requires iron, manganese can also interchange between the octahedral and tetrahedral sites along with iron. This makes it less reliable to predict the distribution of cations in the ferrite and thus requires further characterization to fully determine the cation occupancies. Before discussing how the doping in of other metals alters the magnetic properties, we will first discuss the concepts of ferromagnetism, ferrimagnetism, and superparamagnetism in order to better understand the reasoning behind magnetism in ferrites and how some properties can be tunable with synthetic techniques.
Chapter 3: Concepts of Magnetism in Materials

Inspiring Thoughts #3

“Pain can be a great thing. It lets you know that you are still alive.”
3.1 Introduction

Magnetism in a general sense arises from unpaired electron spins in outer shell, or valence electrons of an individual atom. Arranging these atomic spins into crystal structures greatly complicates magnetic theory, but also introduces a wide variety of properties for materials that can be used in many different applications. Various materials attraction to a magnetic field, ability to become magnetized thus affecting their surrounding environment, and ability to maintain magnetization is what drives research and allows for such applications as targeted drug delivery, magnetic resonance imaging, and computer data storage. Now we will discuss some basic concepts of magnetism in materials and how atomic arrangement can affect these properties between materials.

3.2 Diamagnetism and Paramagnetism

As we all know, everything that exists anywhere in the universe is magnetic. Magnetism of a material or atom is based on how it reacts to the presence of a magnetic field. Basic science tells us that for any applied action, there is some type of reaction to counteract or interact with a given force. The most common form of magnetism for a material is known as diamagnetism which directly opposes the change induced by an applied field. Then the direct antonym of diamagnetic is paramagnetic, which takes on an alignment with the direction of the applied magnetic field. Another key feature to note is that where there is no permanent dipole present in diamagnetism, paramagnetic materials already contain magnetic moments from unpaired electron orbits or spins. The presence of magnetic moments in a material is a commonality between paramagnetism
and all of the other basic forms of magnetism: ferromagnetism, ferrimagnetism, antiferromagnetism, and superparamagnetism. The key behind the transition from paramagnetism to the other forms is the ability of these individual spins to couple and the mode by how they interact.

3.3 Exchange Coupling

There are three categories of exchange coupling by which atomic spins in a material can interact. These are direct exchange, indirect exchange, and superexchange. Direct exchange occurs directly between neighboring atoms. The root of this exchange is quantum mechanical coupling between electrons of adjacent atoms. A simple example would involve two atoms, each with one electron. If the interatomic distance is relatively small, the electrons will spend most of their time between the nuclei to minimize Coulomb interactions. Pauli’s exclusion principle tells us that electrons in the same space and time must possess opposite spins, thus giving rise to antiferromagnetic arrangement illustrated in Fig. 3.1.

![Fig. 3.1. The small interatomic distance shown here between the adjacent atoms leads to an antiparallel alignment of the electrons. This is due to Pauli’s exclusion principle when the electrons are located in the same space and time.](image-url)
A ferromagnetic arrangement then arises when interatomic distances are larger. The electrons then spend more time away from each other, thus minimizing electron-electron repulsion. This results in the parallel alignment seen in ferromagnetism and illustrated in Fig. 3.2 below.

Fig. 3.2. The larger interatomic distance shown here between the adjacent atoms leads to a parallel alignment to minimize electron-electron repulsion. This leads to ferromagnetic coupling in materials.

Indirect exchange is then an interaction that occurs at greater distances, or between non-adjacent atoms. This interaction is primarily seen in metals and occurs when a magnetic atom induces a spin polarization in the conduction band electrons. This then is carried on and couples to other atoms in the material. With this in mind one can understand that different metals will have a different distance to which indirect exchange can act due to conductivity and atomic spacing variations. This in turn affects the critical diameter of a crystallite that causes a transition from multidomain to single domain, and then to superparamagnetic.
Fig. 3.3. Graphical depiction of the superparamagnetic to single domain to multidomain transitions. The critical diameter can be linked to the size of a typical domain.

In looking at Fig. 3.3 and starting at larger particle sizes which are multidomain, we see that the coercivity levels off at some bulk value (green region). As you shift to smaller particle size but stay as multidomain, the coercive field increases. This can be due shape anisotropy or just stresses or constraints in the crystal structure due to size confinement. The critical diameter then is the point at which the indirect exchange coupling reaches throughout the entire particle, thus forming a single domain. This will have the highest remnant magnetization and coercivity due to sufficient spin-spin alignment (blue region). Then the superparamagnetic region is active once the size of the
domain has too few spins to couple together and overcome thermal energy in the system, dropping the coercive field to zero (red region).

Superexchange is the method by which the metal cations in the ferrite structure and other oxides interact. This means that superexchange occurs between two atoms that are connected by some other “nonmagnetic” atom, such as oxygen. Fig. 3.4 shows a simple representation of superexchange between two spins connected by a common atom.

![Fig. 3.4](image)

Fig. 3.4. This picture illustrates superexchange between two magnetic atoms through a “nonmagnetic” atom. This coupling mechanism is the primary method by which magnetization is exhibited in ferrites and other oxides.

The distance and orientation or bond angles of the exchange will affect whether the coupled electrons align parallel or anti-parallel. For example, the tetrahedral sites in the spinel ferrite structure align anti-parallel to the octahedral sites via this superexchange mechanism. The fact that there are more octahedral than tetrahedral sites leaves an incomplete cancellation of moment and thus the presence of ferromagnetism. Then in the case of a non-spinel iron oxide, such as hematite, all of the iron atoms are in a similar
coordination and local environment which results in antiferromagnetic character. Before progressing to further detailed descriptions of these forms of magnetism that arise in materials, we will now discuss some temperature affects on these coupling interactions.

3.4 Curie Point, Néel Point, and Blocking Temperature

The first temperature transition I will describe is the Curie temperature or Curie point for a material. This temperature in simplest terms is a transition point temperature at which a material will spontaneously change from ferromagnetic to paramagnetic. The driving force that causes this transition is thermal energy. When the thermal energy and vibrations of the system are too great, the spins break alignment from each other and take on a more random alignment relative to each other. Spontaneous magnetization is lost and typical paramagnetic behavior is exhibited. The second temperature transition applies more to antiferromagnetism and is called the Néel temperature. Similar to the Curie point for ferromagnetic materials, the Néel transition is the temperature at which an antiferromagnetic material displays paramagnetic behavior. Both the Curie point and Néel point are phenomenon that can be classified as secondary transitions and both occur when thermal energy in the system is equal to the exchange coupling energy.

The blocking temperature, denoted $T_B$, is another critical temperature typically measured in the analysis of magnetic materials. This temperature is also a critical temperature at which thermal energy is sufficient to break some magnetic alignment between spins or moments. The difference with the Curie point and Néel point is that where these are higher temperature transitions describing complete loss of exchange
coupling, the blocking temperature is measured at lower temperature, typically between 5 and 300 K. The blocking temperature then is the point at which spins that were aligned by an applied magnetic field at room temperature and then frozen in place (around 5 K) gain enough thermal energy to become more unaligned. This is not a total loss of magnetization and coupling, but rather a loss of interaction typically between domains formed in a material.

3.5 Ferromagnetism

The best way to comprehend magnetism in iron and iron containing compounds, which is typically ferromagnetism, is to focus on the differences when comparing to paramagnetism. In a ferromagnetic material, neighboring magnetic moments are somewhat in alignment with each other. Just as people tend to subdivide into “neighborhoods” out to a certain distance, these spins tend to align out to given distances in the absence of a magnetic field. The small regions that a material divides into are known as Weiss domains, named for Pierre Weiss who theorized their presence in 1907. These domains though aligned internally, will take on random orientation relative to each other which is why a basic piece of iron is not a “magnet.” When a magnetic field is applied however, these regions now take on the preferred alignment as a group, thus resulting in an overall magnetic moment. Typically with ferromagnetic materials, very little field strength is required to saturate, or reach the maximum magnetic moment. Paramagnetic materials do not saturate in this same manner because the individual moments, due to distance or energy, tend to maintain a predominately random orientation.
and though they gain some alignment to the magnetic field, do not align or have coupling interactions with each other. A simple representation of paramagnetic spin orientation is seen in Fig. 3.5 and a representation of ferromagnetism is seen in Fig. 3.6.

![Diagram of paramagnetic spin orientation](image1)

**Fig. 3.5.** This graphic presents the typical random spin orientation that occurs between atoms in a paramagnetic material. This random orientation leads to a zero net moment and a weak magnetization with the presence of an applied magnetic field.

![Diagram of ferromagnetic spin orientation](image2)

**Fig. 3.6.** This depicts the typical parallel alignment of spins between adjacent atoms in a ferromagnetic material. These coupled spins result in a much higher magnetization in the presence of an applied magnetic field, and can also result in a non-zero moment in the absence of an applied field.
Another interesting feature of ferromagnetic materials is an event known as hysteresis. This occurs when applying a saturating field to a material, and then measuring the moment while scanning through zero to a negative field. A fictitious data set is shown in Fig. 3.7 to better illustrate and visualize the measurement and appearance of hysteresis. As the field reaches zero there is tendency for the material to maintain some alignment gained from being present in the saturating magnetic field and from the internal alignment of spins. Therefore, the value of the magnetic moment at zero field is known as the remnant magnetization.

Fig. 3.7. Fictitious data set scanning the applied field from 0.7 T to -0.7 T while measuring the magnetic moment.
This characteristic can be affected by temperature and structure. We will talk more about the temperature effect later in a description of superparamagnetism. For now though, the structural effect is present when defects or just proximity of neighboring spins in the material require some amount of force or energy to make them flip alignment and become parallel with the negative field. The magnetic field strength required to reach zero moment in the material (the x-intercept in Fig. 3.7) is termed coercivity. Though not directly dependant on the same properties of a material, the presence of remnant magnetization and coercivity is what defines a material as undergoing hysteresis and adds to the definition of ferromagnetism.

3.6 Superparamagnetism

Superparamagnetic materials saturate similar to ferromagnetic materials yet do not undergo hysteresis. Another way to briefly describe this is that even at temperatures below the Curie temperature there is no remnant magnetization and the thermal energy in the system is enough to overcome any internal magnetization or spin alignment. Thus below the Curie point (or Néel point in the case of antiferromagnetic material), there is enough thermal energy to cause paramagnetic behavior in the absence of an applied magnetic field. When a high magnetic field is applied however, the spins align with each other resulting in saturation of the magnetic moment (similar to ferromagnetism). This phenomenon primarily occurs with nanoparticles or nanocrystalline materials that possess a crystallite size between 1-10 nm as described in section 3.3. The crystallite is too small for Weiss domains to form and thus there is no remnant magnetization or coercivity ($H_C$)
for superparamagnetic materials. These materials can also be termed as being single domain. The differences in magnetization versus applied field plots for diamagnetism, paramagnetism, ferromagnetism, and superparamagnetism can be seen in Fig. 3.8.

![Graph showing magnetization versus applied field for different magnetic materials.](image)

**Fig. 3.8.** This plot illustrates expected data when measuring magnetization while scanning the applied field through a loop from negative to positive for ferromagnetic, superparamagnetic, paramagnetic, and diamagnetic materials.
3.7 Ferrimagnetism

Ferrimagnetism is very similar to ferromagnetism except there are differing magnetic spins involved in the structure. A good example of ferrimagnetism is in the case of a mixed metal ferrite system. If we take nickel ferrite as an example with the formula NiFe$_2$O$_4$, both the nickel and iron are paramagnetic atoms. Assuming a perfect normal spinel arrangement, the Ni$^{2+}$ occupies solely the eight tetrahedral sites of the unit cell and the Fe$^{3+}$ occupies the sixteen octahedral sites. In the case of the spinel structure, the tetrahedral sites and octahedral sites align in an antiparallel fashion. Some of the resulting magnetic moment present in nickel ferrite is due to the fact that there are more octahedral sites present than tetrahedral sites. The ferrimagnet definition comes from the differing spin moments between Ni$^{2+}$ and Fe$^{3+}$. Since Fe$^{3+}$ has a higher spin moment than Ni$^{2+}$, not all of the spin contribution is cancelled out from the antiparallel arrangement. A representation of this arrangement is shown in Fig. 3.9. The presence of a moment resulting from incomplete cancellation of spins is what makes a material ferromagnetic instead of ferromagnetic or antiferromagnetic.

3.8 Antiferromagnetism

Antiferromagnetism occurs then when spins align exclusively opposite to one another. This opposing alignment causes a direct cancellation of the magnetic moment. This is the origin for why antiferromagnetic materials have similar magnetic properties to that of diamagnetic materials which oppose an applied field, except when crossing the
Néel point as discussed earlier. A depiction of antiferromagnetic spin alignment can be seen in Fig. 3.10.

Fig. 3.9. This illustrates the antiparallel alignment of two differing atomic spins between adjacent atoms. The weaker spin is not capable of fully cancelling the larger spin, thus resulting in an overall magnetic moment.

Fig. 3.10. This is an illustration of antiparallel alignment for atoms of similar spins in adjacent locations. The complete cancellation of spins in this antiferromagnetic orientation yields similar properties to that of a diamagnetic material.
Once again as with paramagnetism and ferromagnetism, the difference between
diamagnetism and antiferromagnetism is the presence of exchange coupling between
atomic spins which is present in the latter. One other characteristic of
antiferromagnetism occurs at low temperatures (such as 10 K, depending on the
material.) At such temperatures the spins are in slow relaxation which can result in a
canting alignment illustrated in Fig. 3.11.

Fig. 3.11. This demonstrates the net direction that an antiparallel alignment can achieve
at low temperatures or in slow relaxation. This arrangement is known as a canted
antiferromagnet and has similar properties to a ferromagnetic material.

This canting then takes on a particular alignment with the magnetic field, resulting in
properties similar to a weak ferromagnet. This feature becomes more prevalent with
nanoparticles due to unique surface arrangements around differing cores which will be
mentioned in the research later.
3.9 Conclusion

These concepts of magnetism are the basics behind much of magnetism in materials. There are other principles pertaining to permanent magnetism and many other different magnetic characteristics not mentioned herein because they are not necessary in understanding this research. This work is primarily focused on superparamagnetic nanoparticles and relatively soft magnetic materials which offer low coercivity and remnant magnetization.
Chapter 4: Characterization Methodology

Inspiring Thoughts #4

“It really is mind over matter. If you don’t mind, it doesn’t matter!”
4.1 Introduction

In any type of synthetic research, understanding the chemical composition, structures, and physical properties of a material is of vital importance. When it comes to characterization, materials synthesis is particularly interesting for a couple of reasons. First, many materials may possess similar crystal structures and sizes, yet exhibit drastically different magnetic or electronic characteristics due to cation or atomic arrangement as discussed in the previous chapter. This then requires more advanced and time consuming characterization methods to fully understand the underlying synthesis parameters or material characteristics that yield the desired functional properties. The fact that many of the characterization methods required are advanced, expensive, and time consuming has at times inhibited understanding and pushed to large scale batch processing. This shifts the focus to obtaining the desired property, rather than understanding and tuning the synthesis to achieve the properties based on deeper understanding of how the material is made.

Another issue with characterization with materials synthesis is the fact that size and morphology of the solid material can greatly affect the ability to characterize it using conventional and standard methods. Many magnetic properties are affected by shape and size thus resulting in further synthetic control. The primary challenge with nano-sized materials is that some characterization methods require longer ranged order, which is obviously not present on the nanoscale. Therefore with nanomaterials as opposed to some bulk materials, it is necessary to specifically use many characterization methods in
conjunction with each other to fully determine what has been made from a given synthesis. This chapter will briefly describe the characterization methods used in this work, and how many of the methods are employed together to corroborate the each others’ result and obtain the full picture of the nanomaterials.

4.2 X-ray Absorption Spectroscopy

4.2.1 Introduction

X-ray absorption spectroscopy in the basic sense involves the absorption of high energy x-rays by core electrons of an absorbing atom. These high energy x-ray experiments are typically done with synchrotron radiation, from beamlines such as the National Synchrotron Light Source at Brookhaven National Lab, since it is a good source of broad spectrum, high intensity x-rays. A box diagram of a typical beamline setup is shown in Fig 4.1. The broad spectrum x-ray beam is passed through a computer control monochromater in order to deliver the x-ray with the desired energy to the sample. Slits can be put in between the monochromater and detectors, and between the sample and transmitted x-ray detector to minimize beam resolution loss.
Fig. 4.1. Box diagram of a typical beamline experimental setup. Shown is the synchrotron light source, the x-ray beam, monochrometer, and 3 detectors for the initial x-ray intensity $I_0$, transmitted x-ray intensity $I$, and fluorescent signal $I_f$.

The first detector is placed just before the sample holder to measure the intensity of the x-ray beam as it hits the sample. When the incoming x-ray has sufficient energy to raise a core electron above the Fermi level, an absorption edge is noted in the spectra through a decreased intensity measured by the detector opposite the sample. This would be operating in transmission mode. Another effect from this absorption is seen when the core hole formed is re-filled, thus a fluorescent x-ray is emitted corresponding to the energy between the Fermi level and the core hole. This signal can also be used for analysis and is detected adjacent to the sample position. This is denoted as operating in fluorescent mode.

Coinciding with the absorption event, there are four main spectral features investigated which include pre-edge, edge, near-edge or x-ray absorption near-edge
structure (XANES), and extended x-ray absorption fine structure (EXAFS). The location and typical appearance of these four regions is shown in Fig. 4.2.

Fig. 4.2. Sample of normalized data collected from a beamline of metallic iron foil illustrating the 4 regions typically used for analysis.
4.2.2 Background

The data obtained at beamlines is typically a measure of intensity, I, of the x-ray as it passes through a material of a given thickness. This intensity signal is exponentially related to the thickness of the material, t, and a term called the absorption coefficient, µ, as given by:

\[ I = I_0 e^{-\mu t} \]  

(4.1)

In this equation, \( I_0 \) is the intensity of the x-ray hitting the sample, t is the thickness of the sample, \( \mu \) is the absorption coefficient, and I is the received intensity that makes it through the sample. A pictorial representation of Eq. 4.1 is seen in Fig. 4.3.

![Fig. 4.3. Pictorial representation of the x-ray intensities before entering and after exiting a sample of thickness t, from which the absorption coefficient can be calculated.](image)
The absorption coefficient also varies between materials due to strong dependences on factors such as x-ray energy $E$, atomic number $Z$, atomic mass $A$, and the density $\rho$ as per the following relationship:

$$\mu \approx \frac{\rho Z^4}{AE^3}$$  \hspace{1cm} (4.2)

Plotting the absorption coefficient as a function of x-ray energy is a typical way to visualize and begin working with the data. Fig. 4.4 shows the decay of the absorption coefficient with $E$ and the differences between elements due to variations in atomic mass and atomic number. The sharp absorption edges seen in Fig. 4.4 correspond to the energy difference between a core-electron and the Fermi level of the given elements shown.

Fig. 4.4. Plot illustrating how the absorption coefficient decays with x-ray energy $E$ and the differences between some elements.
Now we will introduce XANES and EXAFS and how they can be used to obtain structural information and chemical composition not available by other methods and especially pertaining to the nano-realm.

### 4.2.3 X-ray Absorption Near Edge Structure

XANES, as before mentioned, is an x-ray absorption spectral feature that occurs just beyond (maybe 30 eV) and concurrent with the absorption event. Though some shorter range order can affect the XANES spectra, one can typically think of XANES as giving information about the absorbing atom itself. Since the energy distance to the Fermi level is different for all elements, there exists a unique energy for every atom of interest thereby fingerprinting the vast different elements. In some sense, you can use information in the XANES region as a form of elemental analysis, though you would have to be scanning in the proper region to detect the element of interest. Typically with these high energy x-ray techniques, one will set up the experiment due to known elements of interest that are thought to be possible in the material. Then the first, most basic information acquired by the edge jump is the presence of a certain element in the sample.

Another piece of information that can be obtained from XANES is the oxidation state of the absorbing atom. The differing oxidation state will cause a shift in the edge and some shape differences due to local geometry and bond length changes between the
absorbing and scattering atoms. This shift is also due to changes in binding energy of the core electron due to changes in the charge density and valence state. In some core shell work though, it is easier to perform linear combination fits or principle component analysis on the XANES edge with already obtained standard scans of the possible phases that would exist in a sample. For example, a sample that is 50% iron oxide and 50% metallic iron would have a XANES edge that is an equally weighted linear combination of a metallic standard edge and an iron oxide edge. Examples of this type of analysis will be presented in later chapters.

4.2.4 Extended X-ray Absorption Fine Structure

EXAFS analysis deals with the absorption data that extends beyond the XANES data region as shown in Fig. 4.2. The data in this region is basically a modulation of the x-ray absorption coefficient or oscillations caused by interference between the ejected photoelectron wave function and components that are back scattered from nearby atoms in the structure. A schematic of this process is shown in Fig. 4.5. The x-ray of a particular energy for the specific atom of interest, E, is absorbed and the photoelectron is ejected with energy (E-E₀). During the lifetime of this photoelectron, it will encounter other atoms thereby scattering off and returning to the absorber, thus causing oscillations in the absorption signal µ(E).
Fig. 4.5. Schematic showing the method by which the outgoing photoelectron ejected from the absorbing atom crosses paths and interacts with the scattered photoelectron returning to the point of origin.

For use in later equations used for modeling, it is simpler to use the absorption signal as a function of the photoelectron wavenumber $k$ defined as:

$$k = \sqrt{\frac{2m(E-E_0)}{\hbar^2}}$$  \hspace{1cm} (4.3)$$

The EXAFS signal $\chi(k)$, for which $k$ is the wavenumber of the photoelectron, is obtained then by subtracting a smooth varying background with normalization by:
\[ \chi(k) = \frac{\mu(k) - \mu_0(k)}{\Delta \mu_0(0)} \]  

(4.4)

For this equation, \( \mu(k) \) is the total absorption, \( \mu_0(k) \) is the background or supposed signal of a bare atom, and \( \Delta \mu_0(k) \) is the normalizing factor that is equal to the height of the edge jump. This normalization is done to account for variations in the concentration of the absorbing element in the sample.

Once the EXAFS \( \chi(k) \) data has been normalized and an appropriate bare atom background subtracted, it is necessary to utilize an equation in a form that accounts for all of the necessary parameters. The basic EXAFS equation is given by:

\[ \chi(k) = \sum_j \frac{F_j(k,r)}{k} \int \sin(2kr + \delta_j(k,r)) \frac{P_j(r)}{r^2} \, dr \]  

(4.5)

In this equation, \( F(k,r) \) is the scattering amplitude, \( k \) is the photoelectron wavenumber, \( r \) is the distance between the absorbing and scattering atoms, \( \delta(k,r) \) is the phase shift, and \( P(r) \) is the probability density function of the absorber-scatter pair. The summation over \( j \) is necessary to include many different scattering atoms and the possibility of multiple scattering events. There are four main types of scattering events including single scattering between two atoms, triangle paths involving three atoms, and focused multiple scattering paths either between two atoms or involving three atoms by passing back through the absorber. An illustration of all four types is seen in Fig. 4.6.
In working with the basic EXAFS equation 4.5, it is necessary to further define some of the parameters within the equation and take other factors into account, thereby obtaining a form of the equation that is more suitable for modeling the data. Firstly, the probability density function, \( P_j \), can further be defined as a thermal attenuation of the atomic positions. With the assumption that the thermal motion is Gaussian, we can write the probability density function as follows:
\[ P_j = \frac{1}{\sqrt{2\pi \sigma_j^2}} e^{-\frac{\left| r_j - \bar{r}_j \right|^2}{2\sigma_j^2}} \quad (4.6) \]

The effect of this distribution is a modulation of the EXAFS signal by a factor defined as follows:

\[ e^{-2k^2 \sigma_j^2} \quad (4.7) \]

In this factor, \( \sigma_j \) is the root mean square deviation in the bond length, \( r \). The next addition to the EXAFS equation will be to account for the finite lifetime of the core-hole and photoelectron and for the possibility of inelastic scattering which will inherently result in the photoelectron not returning to the absorbing atom. These situations are handled by introducing a damping factor and a variable denoted as the photoelectron mean free path, \( \lambda(k) \), defined as follows:

\[ e^{-2r/\lambda(k)} \quad (4.8) \]

The last adjustment to the EXAFS equation is due to multi-electron interactions of the incident photon. An example of this would be when the incident photon gives energy to both the core electron and a valence electron. This will shift the EXAFS signal by a continuous variable amount and is typically denoted as \( S_0^2(k) \) and called the passive electron reduction factor. This factor can be thought of as part of the background but cannot be treated as such due to the involvement of valence electrons and thus is not the
same between compounds. It also can be described as a many-body contribution due to the relaxation of the remaining electrons in the absorbing atom after the creation of the core hole. The $S_0^2(k)$ factor is directly correlated with the coordination number $N_j$, the number of equivalent atoms at a distance $r_j$, and thus a factor of $N_j$ is also used in the EXAFS equation. Therefore, the addition of $N_j$, $S_0^2$, Eq. 4.8, and Eq. 4.7 to Eq. 4.5 yields the EXAFS equation in a form used for modeling purposes:

$$
\chi(k) = \sum_j \frac{N_j S_0^2 F_j(k,r)}{k r_j^2} \sin(2k r + \delta_j(k,r)) e^{-2k^2 \sigma_j^2} e^{-2r_j/\lambda(k)} \tag{4.9}
$$

Determining structures of materials from EXAFS data is performed on modeling software that is specifically design for the input and analysis of beamline data. The current method used in modeling EXAFS data, first developed in the 1970’s, is known as the curve-fitting method. This method involves using Eq. 4.5 to calculate the $\chi(k)$ of a model system, with the subsequent adjustment of free parameters to match the model signal to the EXAFS signal obtained from data collection. FEFF, software developed by John Rehr’s group at the University of Washington, can be used to calculate $F_j(k,r)$ and $\delta_j(k,r)$ for all of the different scattering paths in Fig. 4.6 for a given model structure and absorbing atom input; details of algorithms used by the FEFF program are found in the literature. $\lambda(k)$ is taken into account by the FEFF software from core-hole lifetimes that have been measured and tabulated. The remaining parameters in Eq. 4.5 can be varied until either an apparent match or mismatch to the data is deduced. The main setback to EXAFS analysis is that multiple structures and structural combinations could
yield a similar signal. The primary method to combat this is having other information from multiple characterization techniques to at least give partial information about the composition of a sample, thus limiting the number of free parameters and resulting in a more conclusive structural determination.

4.3 Other Spectroscopy Techniques

Fourier-transform infrared (FT-IR), UV-vis, and inductively coupled plasma optical emission spectroscopy (ICP-OES) are well defined and utilized spectroscopy techniques used in chemical research. Since these techniques are well known, a thorough discussion will not be provided. Therefore, this section will outline some of the information obtainable from these techniques that directly applies to nanomaterials research.

4.3.1 Fourier-Transform Infrared Spectroscopy

As well known, FT-IR deals with the absorption of electromagnetic radiation by a sample or material due to vibrational modes between atoms and groups of atoms. When the frequency of the incident light matches to resonant frequencies of the internal atomic vibrations in a material or compound, absorption occurs thereby producing an absorption spectrum when plotted as a function of frequency, or wavenumber in most cases. One typical use of FT-IR is to identify functional groups present in a compound based on the known symmetric and random vibrational modes of different atomic arrangements and
makeup. This can be very helpful in functionalization studies for nanomaterials research. For example, the shifting or disappearance of absorption bands in the spectrum of a given functional ligand can be evidence as to which end or component is coordinated to the nanoparticles surface. Although this technique does not typically give conclusive evidence alone, it can be very powerful if used in conjunction with other data.

FT-IR can be used in some cases to analyze the nanomaterials directly. Research found in the literature illustrates how FT-IR spectra of ferrites can change with varying amounts of doped metal cations. The primary reason behind such changes in resonant frequencies is due simply to mass differences. In the same ways that a C-O stretch differs from a C-H stretch, changing the metal in the same oxide structure will shift the vibrational frequency. Yet again this type of data is difficult to interpret independently, but when coupled to another characterization technique such as EXAFS, it can be a powerful analytical tool. The collaborative use of FT-IR and EXAFS will be presented in great detail in later chapters.

4.3.2 UV-vis

Probably one of the most universal utilized spectroscopy techniques, the absorption of electromagnetic radiation in the range from ultraviolet to visible is still a versatile research tool. Just as in the case of FT-IR, UV-vis can be used to analyze certain compounds used in the functionalization of nanoparticles for dispersions and
applications. Changes in the UV part of the spectrum can commonly be contributed to charge transfer (CT) bands between a surface metal cation and the functional ligand. In this region, although it can be difficult to distinguish between CT bands and typical π to π* transitions, the information obtained can still be helpful in understanding and interpreting other data about the system of interest. Also, specific n to π* transitions and the absence of absorption in the UV-vis range can indicate the presence or change in certain functional groups. This can be helpful in illustrating the difference between a surface adsorption, absorption, and a surface reaction.

Nano-sized materials often present color changes when dispersed in a solvent that are correlated to size of the particle or thickness of the shell in a core-shell particle. Gold for example has various color transitions related to size shell thickness, primarily due to changes in the surface curvature affecting the plasmon resonance. Most of these transitions occur in the visible portion of the spectrum and when used in certain cases, can give information about some nanoparticles size and morphology.

4.3.3 Inductively Coupled Plasma – Optical Emission Spectroscopy

Elemental analysis by inductively coupled plasma optical emission spectroscopy (ICP-OES) is a fairly standard method of determining concentrations of elements in a sample material. Typically, a sample is dissolved in an acid digestion bomb at high temperature and pressure. Standards for different elements of interest are run on the ICP-
OES first in order to form a calibration curve. Although the ICP-OES can reach detection limits in the ppb range, it is important to find a range of concentrations for the standards that is linear, in which you estimate the concentration of the element of question will fall. Knowing the mass of the sample going into the digestion bomb will allow for the calculation of concentration results in terms of mass percentages of the elements relative to each other.

In terms of nanomaterials research, ICP-OES is not necessarily the method of choice, it is the method that I used for much the research presented in later chapters. Elemental analysis can be performed by other methods with equal or better efficiency as the ICP-OES. The important part for materials research that elemental analysis fulfills is to monitor elemental ratios with respect to one another while altering synthesis parameters or attempting to change sizes. For example, the use of NaOH for precipitating iron oxide is water is a standard method of synthesis for ferrite. When this synthesis is altered and performed in aqueous reverse micelles, the proximity and exchange that occurs between aqueous droplets could lead to the formation of a sodium ferrite, instead of just the iron oxide. Powder x-ray diffraction, especially with nano samples, will not be able to distinguish between the sodium ferrite and ferrite, thus elemental analysis is required to verify the results.

Elemental analysis also is a means of correcting magnetic data. In example, there are two primary methods of this. For a manganese zinc ferrite sample one would be to convert the mass ratios to mole ratios. Then knowing the structure from a characterization
like XRD, one can include a mass of the oxygen required to match the structural form. This can be subtracted from the total mass to determine how much surfactant or other material was still present on the surface of the particles during magnetic analysis. The other method would be in the case that you have only one magnetically contributing element. Then the elemental analysis can be directly used to transform magnetic analysis into terms of bohr magneton per atom.

4.4 Magnetic Characterization

4.4.1 Superconducting Quantum Interference Device Magnetometry

A superconducting quantum interference Device, or SQUID, is a powerful combination of superconductors and Josephson junctions that can be used to perform magnetic measurements to $10^{-14}$ kG resolution or better. SQUID’s are so sensitive, they can even be used to detect the nerve currents of some physiological activity. The key behind the sensitivity, well described in the literature, is the Josephson effect and superconductivity. A simplified and basic diagram of a SQUID magnetometer is seen in Fig. 4.7.
Fig. 4.7. Basic diagram of a SQUID magnetometer. To the right of the shield in the diagram is the actual SQUID, with the Josephson junctions shown in red connecting the 2 superconductors (blue). On the left side of the shield is the sampling apparatus or input.

As illustrated, the sample (green oval) is magnetized or reacts to the applied magnetic field ($B_a$) as it is passed through a pickup coil. This causes and induction ($L$) that is transferred to a superconducting coil in the presence of the SQUID, thereby creating a small magnetic flux ($\Phi_a$) oriented orthogonally to the SQUID. The shield is to keep the $B_a$ field from reaching the SQUID and ensure the only magnetic field detected is $\Phi_a$. A measuring current ($I$) is applied to the superconductors which is evenly distributed between the weak Josephson links. With no phase difference between either sides of the
ring, there is a zero potential (V) read across the superconductors. When $\Phi_a$ is applied, a small current ($i$) is induced through the ring thus producing a phase difference between the two Josephson junctions. With the proper measuring current used, this small current would be enough to cross the critical current and produce a measurable potential.

The requirement of superconductivity, and thus liquid He, is on feature that makes SQUID measurements vital for nanomaterials research. This gives the ability to measure at low temperatures, such as 5-10 K, which is necessary in fully determining if a material can be classified as superparamagnetic as discussed earlier. Also, scans can be performed as a function of temperature at constant applied field. This allows for the determination of the blocking temperature, $T_B$, which is related to the thermal energy or temperature required to misalign some spins that were frozen in alignment by cooling in the presence of a magnetic field. Though other factors are involved, there is a direct size correlation with $T_B$ and thus is another tool in analyzing nano-morphology. The extreme sensitivity also yields the ability to extrapolate the slope of a magnetization versus applied field plot, which is necessary to calculate the Weiss domain size. This information can be used in corroboration with TEM images and XRD data to better pinpoint the average size of the nanoparticles.

4.4.2 Vibrating Sample Magnetometry
Vibrating sample magnetometers (VSM) are based on a more simple approach to measuring the magnetization of a sample material. The ability to perform measurements at various temperatures is available for the VSM but they do not possess the resolution and sensitivity of the SQUID, and thus many are only set up to measure at room temperature. The main principle that a VSM works under is Faraday’s Law of Induction. A sample is placed between two pickup coils in the presence of a magnetic field. The sample will become magnetized, thereby creating a magnetic field of its own. If the sample is vibrated at a known frequency, the modulation of the magnetic field produced by the sample will produce an electric field in the pickup coils based on Faraday’s Law of induction. The current induced in the coils is amplified in order to measure but will be proportional to the magnetization of the sample.

The main advantage that the VSM offers to material research is that the measurements can be done much more quickly than using a SQUID, and do not require liquid He. This offers a quicker feedback loop to sample series and thus can be used as a quick check of magnetization or measuring many samples in order to adjust synthetic parameters, such as washes, to achieve the highest magnetic moment.

4.5 Powder X-ray Diffraction

Powder x-ray diffraction is a tool used in solid state chemistry to determine the crystal structure of various materials. There are many types of analysis that can be performed, of which two will primarily be discussed. Firstly, XRD works by bombarding
a sample with x-rays of a known wavelength. These x-rays will scatter and diffract according to Bragg’s law, which says that diffraction will occur for specific values of θ and spacing between the crystal planes as per the following equation:

$$2d \sin \theta = n\lambda$$  \hspace{1cm} (4.11)

In this equation θ is the angle of the incident x-ray, n is an integer for the order of reflection, λ is the known wavelength of the x-ray, and d is the spacing between crystal planes in the sample. This phenomenon creates diffraction patterns as you scan the incident angles, which are typically reported and graphed as 2θ. These diffraction patterns have been calculated and experimentally tabulated into data bases for easier matching and sample crystal structure determination. Thus one of the major uses of XRD is to identify the crystal structure of a sample material. This also quickly checks for phase purity and uniformity which is more difficult and time consuming to perform via XANES/EXAFS and HRTEM.

The other primary use of XRD to discuss is in the determination of crystallite size or diameter. As can be seen from Eq. 4.11, Bragg’s law can give the interplanar spacing. The order of reflection, n, will affect the amplitude of the signal received which is affected by the amount of constructive interference. The more crystalline a material is, a higher amount of constructive interference will occur, thereby producing a sharply rising peak. In smaller crystallites, such as in nanomaterials, there are edges, mild distortions, and finite crystalline planes that will cause a broadening affect in the diffraction pattern.
which relates to a small range of incident angle when the constructive interference occurs. In simplest terms, taking the derivative of Eq. 4.11 in both $d$ and $\theta$ yields the basic Scherrer equation as shown:

$$\Delta d = \frac{\lambda}{2\Delta \theta_x \cos \theta_x}$$  \hspace{1cm} (4.12)

For this equation, $\lambda$ is of course in wavelength of the incident x-ray and $\theta_x$ is the angle of the incident x-ray obtained from the center of the diffraction peak with the x denoting that it is one individual peak of interest. Then $2\Delta \theta_x$ needs to be a good measure of the average change or range of $\theta_x$ from baseline to apex for the peak of interest. What is used for this value is the width of the peak at half the amplitude, also known as the full with at half max (FWHM). This leaves $\Delta d$ to be interpreted as the thickness of the crystal planes in question since it can be thought of as the change in or range of $d$ as we did for $\theta_x$. The thickness value solved for by the Scherrer’s equation (Eq. 4.12) is what is also known as the crystallite size or crystallite diameter.

Literature has shown that the crystallite size as calculated by the previously described method typically skews toward the larger crystallites in the system. In other words, it doesn’t take much of a large impurity in a sample to overwhelm the diffraction pattern and give a size value much larger than would be representative of the majority of the sample in question. This is one reason that other sizing methods such as TEM are required for nanomaterials research. Another reason for other sizing methods is that only crystalline materials are apparent in the XRD diffraction pattern. This means that
amorphous regions, say on the surface of nanoparticles would not be included in the sizes determined by XRD. Also band broadening becomes a major factor in nanoparticles research. Even for crystalline materials, once below 5-10 nm the diffraction pattern peaks appear more as broad humps than spikes. As the peaks broaden it becomes more difficult to separate background, sample, and impurities.

4.6 Thermogravimetric Analysis

Thermogravimetric analysis (TGA) is in a basic sense in just monitoring the change in mass of a sample as a function of time and temperature. As pertaining to nanomaterials research, TGA can be useful several ways. First, a TGA can be used to burn off organic ligands on the surface of a metal or oxide nanoparticle. This gives two pieces of information simultaneously: the mass correction value to be used in conjunction with magnetic analysis and the mass percentage of the organic ligand in the sample. The latter information can give indication of how well a surface is coated with a functional ligand, and in some way give insight to the surface area to volume ratio of the sample.

Another use of a TGA is in monitoring the mass loss of a sample during an annealing process. This use may not be as common, but has the advantage of working with smaller amounts of materials than a traditional heating furnace, such as a tube furnace, while obtaining useful data to mass correct in other analysis during the process. The last use I will mention is in determination of the Curie point of some ferromagnetic material. Some TGA’s come equipped with a magnetic coil that when engaged will show
as a mass gain. Once the Curie point is reached, the mass will decrease by the same percentage that was gained initially due to the transition from ferromagnetic to paramagnetic.

4.7 Transmission Electron and Scanning Electron Microscopy

Microscopy of nanoparticles requires electron beam techniques due to the small size. Both transmission electron microscopy (TEM) and scanning electron microscopy (SEM) utilize electron beams to detect the size and morphology of materials. Briefly, a TEM produces an image by passing an electron beam through a sample placed on a grid. The electron density of the solid nanomaterial scatters some of the electrons, with the remaining electrons passing by to produce a silhouette of the material on a screen for imaging. The main pieces of information obtainable are morphological in nature such as size, shape, size distribution, and uniformity. Sometimes if the outer surface of a nanoparticle is another material from that of the core with a different enough electron density, a core-shell type image can be seen. High resolution TEM can see lattice fringes and can be used for electron diffraction which will give insight into the crystal structure similar to XRD.

SEM does not quite have the resolution of a TEM but does offer some more information. Where a TEM image is produced by electrons passing through the sample, an SEM image is produce from electrons detected after scattering off the surface of the sample. This gives the ability to look at the surface morphology and gives a more three
dimensional analysis, as opposed to strictly two dimensions from the TEM. Both of these techniques however are vital in nanoresearch. Although a magnetic domain size can be determined by a SQUID, which with nanomaterials that are superparamagnetic happens to be most of the particle, and a crystallite size can be determined by XRD, the SEM and TEM offer the only full measure of particle size. Both XRD and SQUID are unable to detect amorphous portions which are very prevalent, especially in spherical nanoparticles. The SEM for nanoparticles cannot stand alone either. Since typical SEM procedures involve a Au coating, this coating will cover the surface of the larger shapes in the sample. Much nanosynthesis involves capping agents and sometimes polymers which upon washing may form polymer/nanoparticles composites. Thus an SEM would only show the larger polymer composite size and not the nanoparticles within. If the polymer or capping agents causing particle aggregates are in low enough concentration, a TEM would pass the electrons through the entire composite and show the drastic difference in electron density between the polymer/organic and the inorganic material. This would reveal the nanoparticles within and allow for proper size analysis.

4.8 Conclusion

This chapter has outlined many characterization methods used in nanomaterials research today. Of the methods discussed, most cannot stand alone as a proper analysis of nanoparticles and must be used in corroboration with each other. The best example is the XRD and TEM. The Scherrer analysis of XRD data typically skews to the largest
size in the sample.\textsuperscript{27} That being said, a TEM analysis may at times miss larger particles which would constitute as an impurity in the sample. In this case, the XRD is able to detect an impurity sometimes missed by the TEM and thus both analysis techniques are necessary in evaluating a synthesis. This is just one example of how the characterization of nanoparticles must thorough, and although not all methods are required all of the time, a proper combination of characterization techniques is critical.
Chapter 5: Synthesis Procedures and Techniques

Inspiring Thoughts #5

“If your heart is still beating and your covered with blood, sweat, and tears, then what are you waiting for! Keep going!”
5.1 Introduction

There are many different methods and synthesis techniques used to produce nanoparticles of various size and composition. The following is a list of just some of the more common methods used currently: laser pyrolysis, thermal decomposition, coprecipitation, reverse micelle, and polyol or other reduction methods. All of these listed methods have much variation within the same category of synthesis which is done in attempts to control properties such as size, shape, and size distribution. This chapter will outline four synthetic techniques used in the research in following chapters and describe the benefits and shortcomings of each method.

5.2 Reverse Micelles

Reverse micelles form when mixing an oil phase, aqueous phase, and surfactant in the proper proportions or region of phase space. The surfactant is required to have an affinity to both the aqueous and oil phases, which acts to provide the barrier between the primarily immiscible phases. Two types of systems can be achieved: the micelle which is oil droplets suspended in aqueous phase, and the reverse micelle which is aqueous droplets in oil phase. Both of these situations are depicted in Fig. 5.1. The droplets that are formed act as little reaction vessels in which to carry out nanoparticles synthesis. Reverse micelles have been shown to be uniform in size and part of the control gained by using micelles is that the size of the micelle or reverse micelle can be regulated and
adjusted as shown in the literature. Using these systems allows for both aqueous and oil phase reactions, though the rest of this discussion will focus on the latter.

![Diagram of a water in oil reverse micelle (left) and an oil in water micelle (right).](image)

**Fig. 5.1.** Depiction of a water in oil reverse micelle (left) and an oil in water micelle (right).

One major reason behind the use of reverse micelles is the vast chemistry and reactions that can be carried out in aqueous conditions. Oxidation–reduction chemistry, precipitation, and substitution reactions are only to name a few. There are several types of surfactants that can be used to form reverse micelles which all fall into one of four categories: cationic, anionic, zwitterionic, and nonionic. There are advantages and disadvantages to each type which can be found in the literature. In any case, the reverse micelle is formed when the critical micelle concentration is reached and the polar region of the surfactant molecules align around aqueous droplets with the hydrophilic tails pointing outward, thus isolating the aqueous phase from the oil phase. There is some
exchange between surfactant in the reverse micelle and surfactant in the bulk solution which occurs on the microsecond time scale. Surfactant type can play a role in such micelle dynamics and may also affect the stability of the system. The fact that reverse micelle systems are dynamic leads to some exchange of material between micelles and thus allows for sequential synthesis techniques. An illustration this exchange can be seen in Fig. 5.2.

Fig. 5.2. Illustration of exchange of media between reverse micelles.

Reverse micelle systems can be formed with two separate reacting species. These solutions can be purged under nitrogen or treated as needed for the synthesis. Upon mixing the contents will exchange on a fairly uniform time scale, thus greatly aiding in size distribution control. A third reverse micelle system could be added to the mixture of
the first two solutions, in order to form core-shell type morphologies. Another advantage of reverse micelle work is that the size distribution can be improved even in room temperature reactions. Typically, size distribution is better for higher temperature reactions due to fast nucleation events followed by a slower growth. If the reaction temperature is too low, the nucleation and growth events compete greatly expanding the range of acquired nanoparticle sizes. The reverse micelles isolate reactants from one another, thereby better regulating the nucleation and growth at lower temperatures. This will be addressed further in later chapters.

5.3 Thermal Decomposition

Thermal decomposition reactions are typically used to control the size distribution of nanoparticles and produce some of the smaller sizes obtainable. These reactions are only advantageous if the material of interest can be obtained from the spontaneous decomposition of another compound and the decomposition temperature is reasonable. A good example of this type of situation is iron pentacarbonyl, Fe(CO)₅. With this compound, the decomposition temperature is around 200 °C at which zero valent iron atoms are obtained. The injection of such a compound into a 200 °C solution with a capping agent included will result in a spontaneous decomposition and nucleation event that is impressively uniform. Size distributions obtained from these types of reactions can be so narrow that self assembled structure form and are visible on TEM. If
performed in the absence of oxygen, some of the zero valent Fe is retained and metallic nanoparticles are formed.

Capping agents can be used in such systems to adjust the size of the resulting nanoparticles. They act similar to surfactants mentioned in reverse micelle formation, but instead of separating liquid phases, they separate the forming particles from one another. This prevents aggregation and will often result in the formation of spherical nanoparticles. The ratio of capping agent to reactant will affect the size of the nanoparticles due to the surface area to volume ratio. If a reaction that yields a given size of nanoparticle is modified with the addition of more reactant relative to capping agent, a lower surface area to volume can be coated to maintain isolated particles, and thus the size must increase. This method will be discussed further and utilized in chapter 9.

5.4 Coprecipitation

Coprecipitation routes are based on one of the oldest synthetic methods of precipitation. First, metal salts are dissolved in a solvent to which a precipitating agent is added to form the insoluble solid, which in some cases could be the nanoparticles of interest. For example, iron oxide can be precipitated at high pH based on the Pourbeix diagram shown in Fig. 5.3. Coprecipitation comes into play especially when trying to make a mixed metal ferrite based on this iron oxide precipitation.
In attempting to make a ferrite doped with nickel and zinc, NiZnFe$_2$O$_4$, all three metal salts would be combined together and precipitated simultaneously. This either traps some of the desired Ni$^{2+}$ and Zn$^{2+}$ cations in the precipitation iron oxide structure, or precipitates the hydroxides together which upon further mild annealing to minimize
aggregation, will form the desired mixed metal ferrite. These types of reactions, along with borohydride reduction reactions, are optimal candidates for the reverse micelle systems and have been performed successfully therein.
Chapter 6: Material Characterization Method Development

Inspiring Thoughts #6

“True courage is the endurance for one moment more.”
6.1 Introduction

In search of the optimal material for many different applications, characterization methods play a major role in the discovery of new materials as well as their chemical makeup and physical properties. The first part of my research was focused on the development of a quick characterization method, which would allow for rapid analysis to aid in the tailoring of synthetic parameters in the preparation of manganese zinc ferrite (MZFO) nanoparticles. Variations in synthesis technique and procedure can change multiple physical and structural properties of ferrites. The property we chose to investigate in this work was the cation occupancy, or the manner in which the manganese, zinc, and iron cations are distributed throughout the octahedral and tetrahedral sites of the oxygen lattice.

One technique that has been successful in determining cation occupancies within bulk and nanoparticle mixed metal ferrites is extended x-ray-absorption fine-structure (EXAFS). However, this method is not practical for daily laboratory analysis to develop synthetic routes due to the necessity of traveling to a synchrotron radiation source. It has been demonstrated through theory and experimentation that in ferrite systems, Fourier transform infrared spectroscopy (FT-IR) data can be correlated to cation occupancy in tetrahedral and octahedral sites. This led us to investigate the use of FT-IR for determining cation occupancy in manganese zinc ferrite (MZFO).
6.2 Materials and Methods Employed

In this work, elemental analysis by inductively coupled plasma-optical emission spectroscopy (ICP) is used to determine the cation concentrations and ratios between the components in the system. Cation distributions within the ferrite lattice, as determined by EXAFS, were then used to establish a correlation with measured FT-IR absorption bands. These bands were assigned to different cation-oxygen vibrational frequencies based on the quality of the data fit and trends observed.

To establish the versatility of this method the MZFO data was collected using both nanoparticulate MZFO (sample labels A2, A3, B1, B2) as well ceramic bulk samples (sample labels - S2, S3). Reverse micelle techniques were used to synthesize the nanoparticles as detailed in Calvin et al. EXAFS spectroscopy was performed at beam line X11A of the National Synchrotron Light Source at Brookhaven National Laboratory. Samples were prepared for FT-IR by grinding them with mortar and pestle into a mixture with silver bromide at approximately a 1:10 mass ratio. The mixture was then pressed in a 13mm pellet die at an applied load of 9 tons, to yield approximately 1 mm thick pellets. Silver bromide was chosen for the analysis because it has a wider transparent range in the far-IR than potassium bromide. The spectra were collected on a Nicolet Nexus 670 FT-IR with a polyethylene beam splitter, deuterated triglycine sulfate (DTGS) detector, and a purge cell apparatus to minimize moisture in the measuring environment. A single beam background spectrum was taken to minimize CO₂ and H₂O signals in the measurements. A AgBr spectrum was collected and used for the background subtraction of each sample. Spectra of the samples were collected in the far-
IR region from 600 to 200 cm\(^{-1}\) and normalized to the maximum absorbance value between 450 and 300 cm\(^{-1}\), to account for differences in the thickness and concentration of each pellet.

6.3 Results and Discussion

The FT-IR spectra collected contained two absorption regions between 600 and 200 cm\(^{-1}\). This region was chosen based on a potential energy study by Waldron in 1955 in which he derived that 480 cm\(^{-1}\) was an approximate mean between the cut-off frequencies of the oxygen and metal cation vibrations.\(^{32}\) The presence of two absorption regions was to be expected due to the two different coordination environments of the cations in ferrite, along with differences in bond lengths. The first absorbance region \((\nu_1)\) did not resolve into separate peaks, while the second region revealed the presence of 3 bands \((\nu_2, \nu_3, \nu_4)\) as seen in Fig. 6.1. The maximum value of \(\nu_1\) shifted within the range of 553 and 571 cm\(^{-1}\) for the various samples of MZFO. The percentage of interstitial sites occupied by a specific metal within the spinel structure can be calculated from ICP and EXAFS data. This allows a direct comparison of the shifts in the absorbance peaks with the percentage of either interstitial site occupied by a given cation.
Two common assumptions are made when investigating MZFO; one is that the zinc occupies only tetrahedral sites, and the second is that the amount of Mn$^{3+}$ present is insignificant. Based on these assumptions the percentage of available octahedral sites occupied by Mn$^{2+}$ was compared to the changes in the $v_1$ absorbance band. From this comparison, a strong correlation to EXAFS-determined occupancies was found as shown in Fig. 6.2. This plot can also be done with Fe$^{2+/3+}$ octahedral occupancy since the first absorption region is actually a combination of the six coordinated Mn$^{2+}$-O stretch and Fe$^{2+/3+}$-O stretch. Since Mn$^{2+}$, Fe$^{2+}$ and Fe$^{3+}$ have similar masses and similar bond
lengths when octahedrally coordinated, the two stretches appear as one unresolved peak that shifts due to the ratio of concentrations of Mn$^{2+}$ to Fe$^{2+/3+}$.

Fig. 6.2. Plot of the percentage of available octahedral sites occupied by Mn$^{2+}$ versus wavenumber
In the second absorption region, the separate bands do not appear to shift but the relative intensity of each peak changes. This change in intensity of individual bands can be attributed to concentration differences between samples as well as different concentrations of a given metal in a tetrahedral site. The lowest frequency band, ν₄, corresponds to Zn²⁺, which is the heaviest metal in the system. The change in intensity in this band as seen in Fig. 6.1, is due to the amount of Zn²⁺ in the sample. The remaining two absorbance bands therefore correspond to Mn²⁺/Fe²⁺-O and Fe³⁺-O when tetrahedrally coordinated. The Fe³⁺-O stretch should have a higher natural frequency than the Mn²⁺/Fe²⁺-O stretch due to the significantly shorter bond length of the former. Thus ν₂ should correspond to the Fe³⁺-O stretch, while ν₃ corresponds to the Mn²⁺/Fe²⁺-O stretch. This relationship is verified in our results because the intensity of ν₂ increases as the percentage of tetrahedral sites occupied by Fe³⁺ increases, allowing the vibrational difference to become more apparent.

These results can be explained in terms of a classical mechanics model in which the cation-oxygen bonds are defined as springs. In comparing the two types of interstitial sites one can envision two harmonic oscillator systems, each composed of a single mass in the center with one containing four springs and the other containing six springs. Fig. 6.3 below gives a general picture of the two different spring systems.
In either traverse motion or vibration along an axis, the four spring system will have a lower natural frequency than that of a six spring system based on the corresponding equations.

For motion along an axis:

\[ \omega = \sqrt{\frac{k}{m}} \]

and for traverse motion:

\[ \omega = \sqrt{\frac{f}{l_b}} \]

where \( \omega \) is frequency, \( k \) is the total spring constant of the system, \( m \) is mass, \( f \) is related to the driving force, and \( l_b \) is length of the spring which is related to bond length. An atom bound by six bonds will have a higher probability of vibration along an axis which will increase the natural frequency of random vibration. The four bond system having greater
angles between the bonds will increase the probability of traverse contributions and less on axis vibrations. Therefore, a four bond system should have a lower natural frequency than the six bond system given the same central metal.

Qualitative trends in site occupancy can also be seen by looking at magnitude plots of the Fourier transform in EXAFS analysis. For a k weight of 1, predominately octahedral occupancy yields a peak at 2.6 Å and a node at 3.3 Å as seen in Fig. 6.4. High tetrahedral occupancy removes the node and shifts the peak toward 3.1 Å. A similar shifting trend can be seen when looking at the first absorption region of the FT-IR data shown in Fig. 6.5.

![Plot of the magnitude of Fourier transform versus effective radius (k weight of 1) for the Mn edge.](image-url)

Fig. 6.4. Plot of the magnitude of Fourier transform versus effective radius (k weight of 1) for the Mn edge.
A freshly prepared MZFO sample was used as a double-blind validation step in which FT-IR and the correlation curve in Fig. 6.2 were used to predict the site occupancy, which was then compared to independently determined EXAFS results. The two techniques showed impressive agreement, with FT-IR indicating that 15% of the octahedral sites were occupied by manganese, while EXAFS yielded 13 +/- 2% for the same value. This is particularly noteworthy because it represents an extrapolation, rather than an interpolation; all of the samples used to calibrate Fig. 6.2 had a greater fraction of octahedral sites occupied by manganese than was found in this sample.
6.4 Conclusion

These results show a correlation of FT-IR measurements to data derived from EXAFS analysis. The resulting curve, shown in Fig. 6.2, can be used to determine the percentage of available octahedral sites occupied by Mn\(^{2+}\) and Fe\(^{2+/3+}\). Using elemental analysis to determine the total concentration of zinc, manganese, and iron, the percentage of tetrahedral sites occupied by each can be determined.
Chapter 7: Nano-Ferrite Cation Distribution Design

Inspiring Thoughts #7

“You must lead by example. There is no other way.”
7.1 General Introduction

The main form of iron oxide that is used for making ferrites is magnetite, or \( \text{Fe}_3\text{O}_4 \), which is has an inverse spinel structure. It is known that in the inverse spinel crystal structure there exist 8 tetrahedral (A) sites and 16 octahedral (B) sites for every 32 oxygen arranged in a face centered cubic structure. The magnetic moments of the A sites and the B sites display an anti-parallel orientation for \( \text{Fe}_3\text{O}_4 \).\(^{33}\) Since there are twice as many B sites as compared to A sites, there is a resultant magnetic moment. Substitution of weaker or diamagnetic ions like Zn into the A sites of the lattice leads to an increase in saturation magnetization up to a certain point where the coupling is disrupted between B sites and thus a decrease in saturation magnetization takes place. This briefly describes one method by which some of the magnetic and electronic properties are adjusted between ferrites and will be further discussed.

7.2 Introduction to Cation Distribution Design

The next step in the development of such a characterization method as detailed in the previous chapter is to test the method and use it to investigate how a certain synthesis parameter affects a property such as the cation distribution in MZFO. The ability to specifically and consistently tailor MZFO that posses desired electronic and magnetic properties is of great interest. The cation distribution throughout the octahedral and tetrahedral sites in the spinel structure greatly influences these properties,\(^{33,34}\) thus it is important to determine an adjustable synthesis parameter that can be used to control the cation occupancies thereby creating the optimal MZFO for the desired applications. Here
we examined the differences in cation occupancy and zinc incorporation in MZFO nanoparticles synthesized via reverse micelles, and investigated whether or not the initial $\text{Fe}^{3+}/\text{Fe}^{2+}$ ratio would allow for variation of these characteristics.

7.3 Materials and Methods

MZFO nanoparticles were synthesized via reverse micelle techniques utilizing nonylphenoxy poly(ethyleneoxy)ethanols with differing head group repeating units of 7 and 4 as surfactant and co-surfactant (NP7/NP4). The metal hydroxides were precipitated at room temperature while employing Schlenk line techniques under N$_2$. One reverse micelle micro emulsion containing aqueous FeCl$_2$, FeCl$_3$, MnCl$_2$, and ZnCl$_2$ was quickly added to a second micro emulsion containing 4 mL of concentrated NH$_4$OH in order to rapidly raise the pH and precipitate the metal hydroxides. In typical ferrite format, the mole ratios of the metals used were as follows: MnCl$_2$ = 0.5, ZnCl$_2$ = 0.5, FeCl$_X$ = 2 ($X = 2, 3$). The only variable that was varied between samples was the initial Fe$^{3+}$ and Fe$^{2+}$ molar ratio with the sum always equal to 2, relative to the other metals. Samples were then washed in air with methanol, collected by centrifugation, and dried in a vacuum oven at room temperature. The dry material was then annealed in a tube furnace under flowing nitrogen for 5 hours.

7.4 Initial Synthesis Results

Powder x-ray diffraction showed pure crystalline MZFO phase, with a slight phase impurity in the 90/10 sample. Fig. 7.1 shows the diffraction pattern for 80/20,
which is comparable all other samples, and the diffraction pattern for 90/10. The small peak and shouldering pointed to in Fig. 7.1, are indicative of some form of zinc oxide (ZnO). This impurity should have a greater affect on the magnetic characterization than on the actual occupancy analysis for that sample. Scherrer analysis revealed an average crystallite size of 14 nm and TEM images confirmed a nano-morphology consistent with this size.

Fig. 7.1. Powder x-ray diffraction pattern of 80/20 sample (top), which is similar to all other samples, and the diffraction pattern for 90/10 (bottom). The arrows point to shouldering and a small peak at 2θ = 32, that are indicative a ZnO impurity.
7.5 Employing of Characterization Method

In order to elucidate how the initial Fe$^{3+}$/Fe$^{2+}$ ratio effects the cation distribution in nanoscale MZFO, we employed the FT-IR method previously developed that allows for fast determination of the cation occupancies due to a correlation between vibrational modes in the far-IR region and EXAFS determined octahedral manganese occupancy.$^{36}$ Fig. 7.2 shows this correlation that has been adjusted from the previous work by the addition of a data point that had been used as a validation sample.

![Graph showing correlation between Mn occupancy and wave number](image)

Fig. 7.2. Plot of the percentage of the available octahedral sites occupied by Mn versus wave number. This same peak in the far-IR also correlated to the octahedral Fe occupancy and yields the same occupancy results shown in Table 1.
The wavenumber values in Table 7.1 correspond to the maximum in the center of the first absorption region in the far-IR spectra from 600-200 cm\(^{-1}\) for each sample. The fraction of octahedral sites occupied by \(\text{Mn}^{2+/3+}\) were then calculated and are listed in Table 7.1. Assuming that all of the \(\text{Zn}^{2+}\) resides in tetrahedral sites,\(^{33}\) the mass ratio obtained from elemental analysis can be converted to a molar ratio. Then when dividing by the stoichiometric number of tetrahedral sites in the ferrite structure you obtain the percentage of tetrahedral sites occupied by \(\text{Zn}^{2+}\). Also along with this same assumption you can obtain the octahedral sites occupied by \(\text{Fe}^{2+/3+}\) from the simple fact that the remaining fraction of sites not occupied by \(\text{Mn}^{2+}\) should be \(\text{Fe}^{2+/3+}\). The next step is to calculate from elemental analysis the remaining amount of \(\text{Mn}^{2+}\) not in octahedral sites. In order to do this it is necessary to multiply the fraction of octahedral sites occupied by \(\text{Mn}^{2+}\) obtained from the FT-IR analysis by 2, which is the stoichiometric number of octahedral sites in the ferrite structure. Then subtracting this from the molar ratio of \(\text{Mn}^{2+}\) determined from elemental analysis yields the fraction of tetrahedral sites occupied by \(\text{Mn}^{2+}\). Thus the remaining tetrahedral sites are occupied by \(\text{Fe}^{2+/3+}\) and a full cation distribution has now been determined which is listed in Table 7.1.
Table 7.1. Results from FT-IR analysis, relative stoichiometry of metals by ICP-OES listed in conventional ferrite formula \((AB_2O_4)\), calculated cation distribution in fraction of A and B sites occupied, and observed XRD purity.

<table>
<thead>
<tr>
<th>initial Fe(^{3+}/)Fe(^{2+}) ratio</th>
<th>10/90</th>
<th>30/70</th>
<th>50/50</th>
<th>60/40</th>
<th>70/30</th>
<th>80/20</th>
<th>90/10</th>
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<tr>
<td>wavenumber (cm(^{-1}))</td>
<td>566.98</td>
<td>563.12</td>
<td>555.41</td>
<td>553.48</td>
<td>551.55</td>
<td>549.62</td>
<td>549.62</td>
</tr>
<tr>
<td>stoichiometry (ICP):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mn</td>
<td>0.49</td>
<td>0.47</td>
<td>0.49</td>
<td>0.48</td>
<td>0.50</td>
<td>0.54</td>
<td>0.42</td>
</tr>
<tr>
<td>Zn</td>
<td>0.36</td>
<td>0.24</td>
<td>0.19</td>
<td>0.20</td>
<td>0.30</td>
<td>0.25</td>
<td>0.42</td>
</tr>
<tr>
<td>Fe</td>
<td>2.16</td>
<td>2.29</td>
<td>2.32</td>
<td>2.33</td>
<td>2.20</td>
<td>2.21</td>
<td>2.16</td>
</tr>
<tr>
<td>calculated occupancy:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tetrahedral (A) Mn</td>
<td>0.00</td>
<td>0.01</td>
<td>0.15</td>
<td>0.16</td>
<td>0.22</td>
<td>0.30</td>
<td>0.18</td>
</tr>
<tr>
<td>tetrahedral (A) Zn</td>
<td>0.36</td>
<td>0.24</td>
<td>0.19</td>
<td>0.20</td>
<td>0.30</td>
<td>0.25</td>
<td>0.42</td>
</tr>
<tr>
<td>tetrahedral (A) Fe</td>
<td>0.65</td>
<td>0.75</td>
<td>0.66</td>
<td>0.65</td>
<td>0.48</td>
<td>0.45</td>
<td>0.40</td>
</tr>
<tr>
<td>octahedral (B) Mn</td>
<td>0.25</td>
<td>0.23</td>
<td>0.17</td>
<td>0.16</td>
<td>0.14</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>octahedral (B) Fe</td>
<td>0.75</td>
<td>0.77</td>
<td>0.83</td>
<td>0.84</td>
<td>0.86</td>
<td>0.88</td>
<td>0.88</td>
</tr>
<tr>
<td>XRD purity</td>
<td>Good</td>
<td>good</td>
<td>good</td>
<td>Good</td>
<td>good</td>
<td>good</td>
<td>Fair</td>
</tr>
</tbody>
</table>

7.6 Result and Method Validation

Magnetic characterization via vibrating sample magnetometry was then performed to corroborate the calculated cation distributions. It is known that the magnetic moments of the tetrahedral (A) sites and the octahedral (B) sites display an antiparallel orientation for \(Fe_3O_4\). For this inverse spinel structure, there are twice as many B sites than A sites, thus there is a resultant magnetic moment. Since the Mn\(^{2+}\) incorporation is constant across the samples, the relative Zn\(^{2+}\) and the Fe\(^{2+/3+}\) incorporation are changing with the initial Fe\(^{3+}/Fe^{2+}\) ratio. With the substitution of “non-magnetic” ions like Zn\(^{2+}\) into the lattice, this leads to an increase in saturation magnetization. Experimentation has shown that in the case of MZFO, the maximum in saturation magnetization is reached at the stoichiometry of \(Mn_{0.5}Zn_{0.5}Fe_2O_4\).\(^{33}\) Since all
of the samples seen in Table 7.1 have less total Mn$^{2+/3+}$ and Zn$^{2+}$ incorporation than 1.0, the saturation magnetization should be more reliant on the fraction of tetrahedral sites occupied by Fe$^{3+}$. Indeed this is the trend seen in Fig. 7.3, where the saturation magnetization is decreased with increasing tetrahedral Fe$^{3+}$.

Fig. 7.3. Saturation magnetization is plotted versus the fraction of tetrahedral sites occupied by Fe. The inset is an example of the hysteresis plot obtained by VSM. (note: the data from the initial ratio of 90/10 was excluded due to phase impurity seen in the x-ray diffraction pattern)
7.7 Results and Discussion

In the FT-IR calculations, it was observed that as the initial $\text{Fe}^{3+}/\text{Fe}^{2+}$ ratio increased from 10/90 to 90/10, the fraction of octahedral sites occupied by $\text{Mn}^{2+/3+}$ decreased from 0.25 to 0.12 while maintaining a consistent level of incorporation in the ferrite. In contrast, the $\text{Zn}^{2+}$ showed a changing level of incorporation into the ferrite with a minimum value at 50/50 ($\text{Fe}^{3+}/\text{Fe}^{2+}$). A plot of the fraction of tetrahedral sites occupied by $\text{Zn}^{2+}$ versus initial $\text{Fe}^{3+}/\text{Fe}^{2+}$ ratio can be seen in Fig. 7.4.

Fig. 7.4. Plot of stoichiometric fraction of $\text{Zn}^{2+}$ versus the initial percentage of $\text{Fe}^{3+}$, which due to the assumption that all of the $\text{Zn}^{2+}$ is tetrahedral because of a strong electronic preference for these sites, can also be viewed as the fraction of tetrahedral sites occupied by $\text{Zn}^{2+}$. 
The explanation for these two trends can be found when contemplating the differences in the hydroxides precipitated during the synthesis. Starting initially with more \( \text{Fe}^{2+} \) than \( \text{Fe}^{3+} \), the precipitation goes through a green to black color change. Under oxygen deficient conditions, the green color indicates the formation of green rust, and in the presence of \( \text{Cl}^- \) will form chlorine-containing green rust,\(^{37,38} \) in which the \( \text{Fe} \) is in two different types of coordination sites. One of these sites is identical to pure \( \text{Fe(OH)}_2 \) with a coordination to 6 \( \text{OH}^- \), and the other with a coordination to 5 \( \text{OH}^- \) and 1 \( \text{Cl}^- \).\(^{38} \) The solubility of \( \text{ZnCl}_2 \) typically involves the \( \text{Zn}^{2+} \) bridged between \( \text{Cl}^- \) anions.\(^{39} \) This would then allow for the \( \text{Zn}^{2+} \) to be more easily incorporated into this expanded lattice of the precipitated green rust due to \( \text{Cl}^- \) inclusion in the structure. Next during the methanol washing in air, the green rust is converted to an iron oxyhydroxide via oxidation in which the \( \text{Cl} \) is removed and replaced by \( \text{O} \), thus disrupting the lattice and allowing for the \( \text{Zn} \) to migrate into tetrahedral sites. Finally upon annealing under flowing \( \text{N}_2 \), the presence of two \( \text{Fe} \) sites and more \( \text{Zn}^{2+} \) then drives most of the \( \text{Mn}^{2+/3+} \) into octahedral sites. This is noted by the calculated absence of tetrahedral \( \text{Mn}^{2+/3+} \) shown in Table 1. Also during the firing, with the \( \text{Zn}^{2+} \) already in the lattice, the \( \text{Fe}^{2+/3+} \) migrates to octahedral sites leaving the \( \text{Zn}^{2+} \) to fulfill the charge balance.

At the opposite end of the spectrum, when starting with a greater abundance of \( \text{Fe}^{3+} \), the reaction proceeds through an orange to black color transition. The orange color is indicative of a predominantly \( \text{Fe(OH)}_3 \) form of iron hydroxide which is a tetrahedral deficient structure with the \( \text{Fe}^{3+} \) being coordinated to 6 \( \text{OH}^- \). Since \( \text{Fe}^{3+} \) has a greater affinity for \( \text{OH}^- \) than \( \text{Fe}^{2+} \), and has a greater affinity for \( \text{OH}^- \) than for \( \text{Cl}^- \), the \( \text{Cl}^- \) is not
incorporated into this structure. Also, with lack of divalent cations in the system for charge balance in the spinel and the fact that Zn can also coordinate to 4 OH\(^-\) in this type of complex (Zn(OH)&subscript;4\(^{2+}\)),\(^{39}\) the Zn\(^{2+}\) is more easily incorporated into the ferrite upon annealing. The number of octahedral sites occupied by Mn\(^{2+}/3+\) is also lowest at the higher Fe\(^{3+}/Fe\(^{2+}\) ratios due to more Fe\(^{3+}\) initially occupying octahedral sites and the need for more divalent cations to fill the tetrahedral sites. One important feature to keep in mind is that all of the samples were fired for 5 hours under flowing N\(_2\). It is known that there is an interconversion type equilibrium between Mn\(^{2+}/3+\) and Fe\(^{3+}/2+\),\(^{40}\) and thus with extended firing times, it may be possible for more Mn\(^{2+}/3+\) to be incorporated into the octahedral sites. Since the temperature of annealing used in this study is fairly low for ferrites and the time of annealing was held constant and is somewhat short, we were able to discover this trend.

To explain the minimum Zn\(^{2+}\) incorporation at the Fe\(^{3+}/Fe\(^{2+}\) ratio of 50/50, a combination of the two hydroxide forms must exist during the precipitation reaction. This suggests that there would be less tetrahedral and divalent cation deficiencies than in the high Fe\(^{3+}\) case, and less Cl\(^-\) incorporation in the structure to possibly allow for more Zn\(^{2+}\) inclusion than in the high Fe\(^{2+}\) case. During the washing steps there would already be a substantial amount of divalent and trivalent cations present, along with the reduced presence of Cl, resulting in less disruption during the firing process causing slower migration of the Zn\(^{2+}\) into the lattice. This then supports the result that less Zn\(^{2+}\) was found in the 50/50 sample and the parabolic type relationship between initial Fe\(^{3+}/Fe\(^{2+}\) and Zn\(^{2+}\) incorporation.
7.8 Conclusion

With the results found in these studies, it would be possible to better formulate the mechanism behind cation migration and incorporation during the MZFO synthesis. Such a mechanistic understanding would allow for specific tailoring of a desired cation distribution in MZFO, leading to more efficient industrial synthesis and the optimal MZFO.
Chapter 8: Crystal Structure Design of Iron via Synthesis of Novel Nanoparticles

Inspiring Thoughts #8

“It’s not always how much you know. It’s sometimes having the knowledge to tell the difference between what you know, and what you don’t know.”
8.1 Introduction

Theoretical studies involving the stabilities of iron clusters have been presented in the literature showing that size may play an important role in determining the structure of the resultant particle. This leads one to speculate that if a particle can be synthesized small enough while controlling the resultant size, then it is possible to make several different structures of the same metallic material. Some theoretical work calculates that face centered cubic (FCC) iron has four magnetic states. The complexity of the magnetic properties for the FCC iron is primarily linked to different spin states available in the FCC structure that also correspond to slight differences in atomic distances. The high spin version of these magnetic states has a magnetization value of 2.4 $\mu_B$ (or around 220 emu/g), which is comparable to body centered cubic iron (BCC or $\alpha$-Fe) having the same values of magnetization. The BCC structure of is the known stable structure of iron in ambient conditions. The FCC structure, on the other hand, is only known to exist at high temperatures, as small precipitates in supersaturated copper-iron solid solutions, or in the first exposed layers of epitaxial grown iron on an FCC copper surface. The icosahedral ($I_h$) structure is similar to an FCC crystal structure but can be thought of as distorted and less dense. This structure, as with FCC, has only been noted for iron in immiscible copper alloy systems which can aid in locking the iron in this structure. The lower density of the $I_h$ structures leads one to speculate that icosahedral iron would have ferromagnetic properties as seen and theorized for the low-density FCC structure.

Another form of iron that positions the iron atoms in a state similar to a high volume FCC state is the compound cementite, Fe$_3$C. This structure is a primary
component in carbon steel and is very resistant to corrosion and oxidation. Magnetic properties of cementite are similar to one of the low-spin ferromagnetic FCC states with a bulk saturation magnetization of 130 emu/g. Cementite has been reported on the nanoscale, but mainly synthesized via laser pyrolysis and other high temperature methods. On the bulk scale, cementite is formed by first melting metallic iron. As it begins to cool, yet still at a very high temperature, the metallic iron phase that is prevalent is the FCC phase. Cooling at a slow rate will transform the metal to the BCC or thermodynamically stable state of iron. If the cooling conditions are altered properly, the kinetic product of cementite can be formed due to trapping carbon in the structure. At one time the carbons were thought to set interstitial, but upon further investigation, the carbons are covalently bonded to the iron thereby altering the structure from the FCC state and space group Fm3m to the space group of Pnma. This distortion in structure can also be seen as a cubic to orthorhombic type transition. The carbons also distribute to form two different atom environments for the iron, thus altering the individual magnetic moments of the iron. This feature is the primary information that can be used to distinguish the icosahedral structure from the cementite structure.

Synthesis of novel nanostructures is the key to unlocking important details about the formation of different crystal structures and understanding the thermodynamic conditions which can yield both stable and metastable states. The ability to tune the resultant structures involved in a core-shell type nanoparticle by synthesis parameters yields both varieties in magnetic properties and insight into nanoparticle growth and
formation. This chapter focuses on the incorporation of α-Fe and Fe₃C into core-shell nanoparticles and how this was accomplished to give stable magnetic nanomaterials.

8.2 Cementite-Gold Core-Shell Nanoparticles

8.2.1 Introduction

This work describes a cementite, Fe₃C, nanocluster that is air stable at room temperature and ambient pressure. The stability is partially due to the inherent corrosion resistance of cementite itself, and due to using gold oxidizing agent in creating a very thin iron oxide and gold layer around the small cementite cores, which aids in the prevention of further oxidation and allows for easier functionalization to the Au layer. Au was also used since theoretical work has shown the possibility for Au monolayers to enhance magnetic properties through spin-orbit coupling.⁵²

8.2.2 Experimental and Synthesis

Fe₃C nanoparticles were synthesized via a high temperature spontaneous nucleation technique involving the decomposition of iron pentacarbonyl (Fe(CO)₅) in the presence of refluxing trioctylphosphine oxide (TOPO).⁵³,⁵⁴ The particles in TOPO were then placed in the presence of Au³⁺ as per the following example. In a typical synthesis, 5g of TOPO was heated to reflux with an air condenser under a nitrogen atmosphere. Then 0.20 mL of Fe(CO)₅ was injected in the hot TOPO and allowed to age for 30 minutes. During the 30 minutes, a mixture of 30 mL diphenyl ether and 0.20 g of
Au(O_2CCH_3)_3 was heated to 100 °C while vigorously stirring. At the 28 minute mark, 4 mL of 200 MW PEG was added to the Au/ether mixture as a mild reducing agent. Then at the end of the initial 30 minutes the Fe/TOPO solution was transferred into the Au/PEG/ether solution and allowed to age for another 30 minutes.

Fig. 8.1. TEM image of the nanoparticles as prepared on a Cu mesh grid. The TOPO cap was washed by and substituted with pyridine prior to grid preparation. The inset is a histogram of line measurements performed across the nanoparticles on the image.
The solution appeared black/purple in color and the reaction was quenched by bringing the mixture quickly to room temperature by pouring the solution into 200 mL of methanol. The nanoparticles were then treated with subsequent washing in acetone and methanol and magnetically extracted to dry. The diameter of the resulting particles is 2-4 nm as seen by transmission electron microscopy. The TEM image obtained is shown in Fig. 8.1 with a histogram showing a mean diameter of 2.73 nm inset in the figure.

![TEM image of nanoparticles](image)

**Fig. 8.2.** STEM-EDS image and analysis of the same grid as prepared for Fig. 8.1 above. The yellow line corresponds to the Au concentration across the particles; the blue line represents the Fe concentration, while the red line is a baseline. (The particles appear slightly larger due to over or under focus.)
Scanning tunneling electron microscopy – energy dispersive spectrometry analysis (shown in Fig. 8.2) revealed changes in both the Fe and Au concentrations while scanning across the nanoparticles, thus suggesting some amount of Au being present on the surface of the Fe₃C cores. (The particles in Fig. X appear slightly larger than those in Fig. 8.1 due to being slightly out of focus in Fig. 8.2: both images, though on different instruments, were performed on the same sample grid.)

8.2.3 Structural Analysis

Other references reported the synthesis of Fe nanoparticles with similar synthesis, thus it was not apparent at first whether the nanoparticles were Fe₃C or a form of metallic Fe, whether FCC, BCC, or icosahedral (I₃). Therefore, in order to first determine the structure of the Fe cluster, spectra of the x-ray absorption near edge structure (XANES) of the samples were collected and compared to oxide and metal standards, and are shown in Fig. 8.3 (left). Two isosbestic points are evident, at 7127 and 7149 eV, confirming the identification of the samples as a mixture of oxide and metallic or zero valent phases. In addition, two different curves generated by a linear combination of the oxide and metallic standards are shown; one represents a mixture which is 50% oxide and 50% metal, the other 70% oxide and 30% metal.

Fits of the Fourier transforms of the extended x-ray absorption fine structure (EXAFS) spectra were conducted in order to determine the structure of the iron core. Three of these are shown in Fig. 8.3 (right). The “BCC” model shown features a BCC
iron core with an oxide shell on the surface and is clearly ruled out. The “FCC” model allows for an FCC core with an unknown amount of oxide, while the “icosahedral” model includes a 3-shell icosahedral iron core decorated with a monolayer of oxygen. This 3-shell model can also be described as having inner core, outer core, and surface regions or environments. While both of these models result in reasonably good fits to the EXAFS spectra, the icosahedral fit yields a structure remarkably compatible with TEM, XANES, and Mössbauer results: an icosahedral structure of this size has a core diameter of approximately 1.5 nm and a total diameter (including oxygen) of about 2 nm, consistent with TEM; 92 out of the 147 iron atoms (63%) lie on the surface, consistent with the oxidation fraction yielded by XANES.

Fig. 8.3. (left) XANES of samples and standards. The spectra of the two samples shown differ by less than the thickness of the plot line. Two linear combinations of the standards are also shown. (right) Real part of the Fourier transform of the EXAFS data and fits using three different models.
Mössbauer analysis carried out at 4 K revealed a resolved hyperfine (HPF) structure indicating the existence of two sites for the zero valent Fe in the core: One site (inner core) with a HPF field of 219 kOe (39 % relative absorption), and the other (outer core) at 249 kOe (61% relative absorption). These HPF correspond to magnetic moments of 1.46 µB and 1.66 µB respectively. The presence of 249 kOe splitting is indicative of iron which is in the cementite structure, Fe₃C, seen as a distorted FCC since it forms typically from dissolved carbon in and FCC iron melt, or better classified as an orthorhombic structure of space group Pnma. The 219 kOe HPF indicates that, probably in the same structure there are more carbons which reduce by 30 kOe, one by one, the hyperfine field of normal iron in cementite. It is interesting to note from the Mössbauer that the iron oxide layer present is superparamagnetic in nature, and is almost completely in slow relaxation at 4K. The form of the oxide shell was not similar to magnetite or a typical iron oxide thus corroborating the XANES and EXAFS structural results. Instead Mössbauer suggests that the iron oxide is predominately a $3^+$ valence and one sided, which more closely resembles an antiferromagnetic Fe-O structure.

8.2.4 Gold Shell Analysis

Mechanistically, the oxide layer formation occurs through Au$^{3+}$ interacting with the Fe$^0$ and TOPO, resulting in the oxidation of the surface Fe with the TOPO being reduced to the phosphine, thus leaving a completely oxidized surface layer. Some Au is also left on the surface, most likely epitaxially bonding to the Fe due to the strength of
Fe-Au bonding,\textsuperscript{52} with oxygens sitting interstitial. The Au layer presence on the particles was shown in by STEM-EDS in Fig. 8.2. It has been presented in the literature that Au monolayers and thiol capped Au show ferromagnetism.\textsuperscript{55,56} Thus, prior to magnetic analysis it was necessary to determine if Au was present in a phase that might also contribute to the overall magnetization.

Powder x-ray diffraction revealed only sharp Au peaks, which by Scherrer analysis showed a crystallite size of 19 nm. Au EXAFS spectra were indistinguishable from bulk gold, confirming a mean crystallite size greater than 10 nm (also confirmed by TEM). This “large” sized Au present in the sample can be treated as a mass dilution in the magnetic characterization. The Au present on the surface of the Fe\textsubscript{3}C/FeOx/Au particles however could have some type of contribution to the magnetization. From the Mössbauer analysis, the iron oxide formed on the surface acts as an AFM layer. Since the metallic core is ferromagnetic, the FeOx-Au in the shell would take on an alignment with the core similar to a canted antiferromagnet, contributing a small amount to the overall magnetization. The presence of spin-orbit coupling between Fe and Au results in a slightly larger contribution to the overall magnetism than would be expected from a monolayer of typical FeOx alone. Since the amount of Au in the coating is undetermined, it is necessary to investigate the magnetic characteristics in terms of bohr magneton per atom of Fe. Elemental analysis by inductively coupled plasma-optical emission spectroscopy was used to directly determine the amount of Fe present in the sample used for magnetic analysis via super conducting quantum interference device magnetometry.
8.2.5 Further Magnetic Characterization

In the magnetic characterization of the Fe$_3$C/FeOx/Au particles, a zero-field-cooled/field-cooled plot revealed a blocking temperature of 170 K at 1000 Oe. This is much higher than expected and seen for Fe nanospheres of similar size. To analyze the magnetic saturation, some assumptions had to be made first based on the structural information obtained from the XANES, EXAFS, and Mössbauer analysis. First, from the linear combination fits on the XANES edge, we will use 40% for the zero valent Fe and 60% for the oxide. Since Mössbauer indicated all Fe$^{3+}$ for the oxide we will assume 3 moles of oxygen for every 2 moles of iron in the oxide. With this and the 3:1 mole ratio of iron to carbon in cementite, the mass will be corrected utilizing these factors along with ICP-OES determined iron mass in the sample. A hysteresis loop at 10 K (Fig. 8.4) showed a saturation magnetization of 110 emu/g and a coercivity of 1000 Oe. The $M_R/M_S$ of 0.46 and coercivity of 1000 Oe is easily explained by the Stoner-Wohlfarth prediction for non-interacting single domain particles which would be expected to have a $M_R/M_S$ of 0.5. The value of saturation magnetization however should be compared to 130 emu/g for bulk cementite, since the Fe$_3$C core has the largest diameter and thus better magnetic exchange than the oxide shell. This is impressively high especially for such a small nanomaterial and with assuming the highest oxygen content possible for an oxide. This gives possible implications of two modes for enhancement of the core magnetization. First, since the core is ferromagnetic and the shell shows
antiferromagnetic arrangement from Mössbauer, there must be some inherent ordering of the shell that yields a net contribution to the moment.

![Magnetization versus applied field for Fe$_3$C/FeOx/Au nanoparticles](image)

Fig. 8.4. Plot of magnetization versus applied field for Fe$_3$C/FeOx/Au nanoparticles.

This could be possible with the shell taking on a particular direction of opposing alignment, thereby acting more as a canted antiferromagnet as described in chapter 3. Also, with the inclusion of Au in this shell, there is the possibility of spin-orbit coupling to further enhance this contribution and the overall magnetic moment.
8.2.6 Discussion and Conclusions

As before mentioned, the cementite structure of iron is not the thermodynamically stable form and thus there are some factors that may have stabilized the formation of this structure. Two factors that may stabilize this Fe₃C/FeOₓ/Au particle structure is that they are smaller than 5 nm, and that the cementite structure may be a better lattice match to the FeOₓ surface. Likewise, Fe core shell particles that have a BCC core are prone to oxidation over time because of a lattice mismatch between the BCC and FCC structure of the oxygens in the oxide. Since the cementite structure is similar to FCC, the lattice match to the oxide shell is close enough to allow for passivation. Also, the strength of the Fe-Au bond at the surface is possibly a contributing factor. A further factor is simply that cementite itself is not as prone to oxidation as typical BCC iron and thus when synthesized in this magnetic state, it can be more stable for multiple magnetic nanoparticles applications. Passivation against oxidation has been confirmed by comparing the structure and relative amounts of Fe versus Fe-O in samples that were not exposed prior to analysis to other samples that were exposed for more than two weeks prior; all results remained consistent.

8.3 Synthesis of α-Fe-Cementite Core-Shell Particles

8.3.1 Introduction

The results in from section 8.2 show that it is possible to prepare a different structure of zero valent iron, the alloy cementite, on the nanoscale that has comparable
magnetic properties to the low-spin FCC structure, but is stable in ambient conditions. The next stage of nanoparticle development involves the tailoring of a synthesis that with the variation of only one parameter, will allow for core-shell formation using the oxidation resistance of cementite to passivate $\alpha$-Fe. This will produce magnetic nanoparticles that are small, stable, and highly magnetic. It also gives insight into how meta-stable or kinetic products can be achieved as opposed to and in conjunction with the thermodynamic products.

8.3.2 Experimental and Synthetic Reasoning

This synthesis was carried out via the same type of high temperature spontaneous nucleation synthesis using Fe(CO)$_5$, but differs from the synthesis in section 9.2 by the solvent/cap system. Trioctylphosphine (TOP) was used instead of trioctylphosphine oxide (TOPO) to try and reduce the amount of oxide produced at the surface due to the TOPO cap. Hexadecane was then chosen to vary the solvent/cap system since it was miscible with TOP and had a similar boiling point. This would allow for all samples, though being synthesized in different ratios of hexadecane/TOP, to have to almost identical initial injection temperatures to initiate the nucleation event. In a typical synthesis, 10 mL of solvent/cap was placed in a 100 mL round bottom flask while stirring and heated to reflux. The variation between samples was in the solvent/cap ratios which were (in mL/mL) 0/10, 2.5/7.5, 5/5, 7.5/2.5, and 9/1. The 0/10 system can be thought of as using the capping agent as the solvent and is similar to the TOPO system in section
8.2. Once at reflux, 0.2 mL of room temperature Fe(CO)$_5$ was injected into the refluxing solvent/cap and aged at reflux for 30 minutes. (The reaction upon injection is rather violent, but was contained by the reflux condenser.) At the end of 30 minutes the particles were immediately poured into room temperature acetone and then further washed by either magnetic extraction or centrifugation (for 0/10 sample). All of these procedures were carried out under N$_2$ in a glove box.

Now we will discuss some of the synthetic reasoning to clarify why the solvent/cap was chosen to vary over other parameters to produce different structures. If the total volume of the system is maintained and the capping agent to solvent ratio is adjusted, it should be possible to make different sizes of iron nanoparticles and thus different structures. The size difference should come from decreasing the amount of capping agent in the system, which due to the Fe(CO)$_5$ volume being constant, the nanoparticles will have to grow larger in order to decrease the surface area to volume ratio. This method does not only rely on size to change the structure, but another possibility would be solvent templating based on the ligand-solvent exchange rate. In similar synthesis found in the literature of CdSe nanoparticles, it is thought that the capping agent acts as a barrier around the surface of the growing particle, thus slowing down the growth kinetics.$^{53}$ If the solvent and capping ligand are the same, then the ligand-solvent exchange would be at a maximum, thus possibly leading to the kinetic product. Then by diluting the solvent/cap ratio the solvent exchange rate would decrease, thus resulting in the thermodynamic product.
8.3.3 Results and Discussion

For ease of discussion, samples in the order from 0/10, 2.5/7.5, 5/5, 7.5/2.5, and 9/1 will be now denoted as A, B, C, D, and E. Initial investigations into the XANES region of the XAS data shows an apparent transition from sample A to sample E shown in Fig. 8.5.

Fig. 8.5. Zoom in on the XANES region of the XAS data collected: hexadecane/TOP ratios are A = 0/10, B = 2.5/7.5, C = 5/5, D = 7.5/2.5, E = 9/1.

The transition noted gives evidence to work with a principle component analysis (PCA) to investigate how many possible components exist between samples. A quick
description of PCA is that it is a technique based on linear algebra with each spectra
being treated as a vector. It then looks for the number of distinct species or components
required to produce a match to a standard of interest using the spectra series called target
and transform respectively. The first PCA runs with the XANES data were attempted to
match $\alpha$-Fe, $\text{Fe}_3\text{C}$, and $\gamma$-$\text{Fe}_2\text{O}_3$. These were chosen based on the initial work in section
8.2 and collaborative Mössbauer results indicating these types of phases. The PCA in
this region gave clear confirmation of $\alpha$-Fe and $\text{Fe}_3\text{C}$ but was not a clear fit to $\gamma$-$\text{Fe}_2\text{O}_3$.
The rough fit to this form of iron oxide was expected since the Mössbauer indicated that
the oxide is not a standard form. PCA was also conducted on the Fourier transform of the
data (which the Fourier transform is also used in the curve-fitting method described in
chapter 4) and yielded corroborating results and confirming the presence of $\alpha$-Fe, $\text{Fe}_3\text{C}$,
and some form of oxide. The target and transform plots are shown in Fig. 8.6.
Fig. 8.6. PCA results plotting the target and transform for $\alpha$-Fe, Fe$_3$C, and $\gamma$-Fe$_2$O$_3$. 
Next, curve fitting analysis was performed on the EXAFS region of the XAS data (method described in chapter 4) for sample E since it had the largest contribution from each component. The first model using α-Fe, Fe$_3$C, and one path of an Fe-O environment gave an impressive fit to the data and is shown in Fig. 8.7. This clearly indicates that the majority of the scattering paths and signal modulation can be accounted for with α-Fe and Fe$_3$C. The oxide was not a major contributor since only one path was utilized so a further curve-fit was performed utilizing ε-Fe$_2$O$_3$. The result of this fit is seen in Fig. 8.8.
As can be seen, the fit in Fig. 8.8 is very comparable the fit in Fig. 8.7 even though the oxides used to calculate the scattering paths were different. This is not a confirmation of the ε-Fe₂O₃ phase, but illustrates that it could be a possibility, seeing how it contains all Fe³⁺ and can be antiferromagnetic as the Mössbauer indicated. Thus further investigation into the Mössbauer spectra and runs at multiple temperatures could elucidate this structure.
Fig. 8.9. TEM of α-Fe/Fe3C/FeOx particles synthesized with 9/1 hexadecane/TOP ratio. Red circle shows hexagonal packing pattern.

The morphology of these particles is confirmed by the TEM images in Fig. 8.9 for sample E. As can be seen, the particles have a very uniform size distribution illustrated by the affinity to self assemble in a hexagonal close packed type arrangement. This small size distribution is common when utilizing high temperature spontaneous nucleation techniques due to a uniform nucleation event in time. There two things evident from comparisons of the TEM images between samples. First, the size from sample E to A
decreased from around 5 nm to 2 nm. The cause for this is as you decrease the capping ligand relative to moles of Fe(CO)$_5$, the particles must grow to larger sizes to accommodate a lower surface area to volume ratio. In contrast, with more capping ligand available, the particles can maintain a smaller size since there is enough cap to coat a larger surface area to volume ratio.

The second trend seen is that the size distribution increases slightly from E to A. For comparison purposes a TEM of sample A is given in Fig. 8.10. This gives evidence that the ligand to solvent exchange does indeed have an effect on the resultant particles. With a low ligand to solvent ratio, such as with sample E of 1/9, the TOP cap around the particles is more rigid and does not exchange readily with other ligands partially due to a low concentration of free ligand in the solution. In turn, this slows the growth stage which will allow for more uniform growth throughout the system. In the case of samples D to B, the exchange rate increases thereby pushing the growth faster and producing less uniformity in particle size. Therefore, the slight size differences between the particles may aid in giving the different levels of structure incorporation between samples.

Since the ligand exchange rate varies the growth rate post nucleation, this also yields the different structures by pushing for the kinetic versus the thermodynamic products. This feature is more evident in sample A, which along with no apparent presence of α-Fe, it was also not able to be magnetically extracted.
Since Fe$_3$C should be magnetic as well, one explanation for this difference is that the structure formed even faster and packed in a more close packed structure which would be kinetically favored. This would then go along with the metamagnetic phases of the FCC iron, which due to differences in packing density will show antiferromagnetism, and low to high level ferromagnetism. Sample A would have the fastest exchange rate of all synthesis because the solvent and cap were the same compound, TOP, and thus would
exchange at a maximum rate. The TOPO synthesis from section 8.2 also helps explain this since it was synthesized in 100 % TOPO though it was ferromagnetic Fe₃C. This is because the oxide in the TOPO would have a stronger interaction with the Fe than the phosphine alone, thereby slowing the exchange rate and allowing a more thermodynamically stable magnetic arrangement as opposed TOP synthesis.

Then the progression toward more α-Fe incorporation as we go from sample A to E is also logical. As the ligand and solvent exchange slowly, the particle cores post nucleation have more time before other Fe in the system grows on them. This allows for the atoms to arrange in the more thermodynamically stable form and allowing for the atoms to arrange maximizing magnetic coupling. As with the Fe₃C formation in the bulk, the carbon will also have time to diffuse outward, thereby creating the passivating layer around the more so magnetic core. The placement of the oxide phase is not certain, but either on the surface or between the Fe₃C and α-Fe, the Fe₃C still acts to prevent further oxidation.

8.4 Conclusions

The two novel core-shell syntheses discussed in this chapter present several desired properties for magnetic nanoparticles: high saturation magnetization, small size and size distribution, passivation against oxidation and retention of magnet strength, and surfaces available for different types of functionalization. These syntheses have also provided insight into structure and size design of nanoparticles, and shown the importance of corroborating results to properly characterize nanomaterials. With the two
main types of cores produced, \( \alpha \)-Fe and Fe\(_3\)C, we can now use these particles to investigate some structural effects in applications such as magnetic resonance imaging contrast enhancement.
Chapter 9: Material Functionalization

Inspiring Thoughts #9

“If you insist on working on the cutting edge, be prepared to bleed!”
9.1 Introduction

Another important area of research that is needed in conjunction with the development of new materials is the functionalization of such materials for forming well-dispersed colloidal solutions. The ability to disperse the individual nanoparticle is of great importance in many applications, especially those that involve introduction into the human body. Magnetic nanoparticles based on iron oxides or iron oxide shells are especially flourishing in biotechnology and medical applications. These applications include use as magnetic resonance imaging contrast agents, ferrofluid technology for MRI monitoring in hypothermia, cancer tumor detection via SQUID magnetometry, and selective separation and detection of biomolecules. The appeal of these particles is due to their relative inertness, superior magnetic properties, and the apparent simplicity of post synthesis surface functionalization. This chapter will cover three types of functionalization ligands: dopamine for which we also thoroughly investigate biocompatibility, cysteine, and polyethylene glycol.

9.2 Dopamine Studies Introduction

Stability of the bonding between functional molecules and nanoparticles is crucial for most medical applications since the particle is the key to tracking or targeting treatments that the functional molecule is to perform. Early release or uptake of the nanoparticle/molecule system due to other surface reactions could be detrimental to the application or possibly to the patient. While carboxylic acids have been used as stabilizers for ferrofluid applications, they typically are not an ideal functionalization
ligand due to the instability of the chelate bond. It has been reported that dopamine forms a stable, robust anchor on the surface of iron oxide to immobilize functional molecules to the magnetic nanoparticles.\textsuperscript{65} Dopamine has sparked great interest as capping agent due to the stability and strength of the resultant 5-member metallocycle chelate and the ease at which it can be functionalized through amide bonds with other molecules of interest. This work reports on the structure and reactivity of Fe/iron oxide core-shell nanoparticles (Fe-Ox) that have been coated with dopamine. We also confirm the presence of the dopamine quinone which is highly reactive and is suggested to be cytotoxic.\textsuperscript{66}

9.3 Dopamine Studies Initial Results

Attempts to use dopamine as a robust anchor on Fe-Ox were initially successful in dispersing the particles forming a clear, blue/purple aqueous ferrofluid. After remaining in solution for one day however, the particles turned to a dark green precipitate. This precipitate was found to be a combination of both precipitated iron oxide particles (black-magnetite/maghemite) and iron(II)hydroxide (green). Upon further oxidation the green color turned to a red/brown which is typical of iron(III)oxyhydroxide.\textsuperscript{67} The transmission electron micrograph presented in Fig. 9.1 contains functionalized nanoparticles that were immediately dried after sonication. Fig. 9.2 is a micrograph of the precipitate after a solution of Fe-Ox dopamine particles was aged for 1-2 days. The differences seen in the TEM images illustrate that the nano-morphology of the particles is lost, thus implying a
surface reaction between the Fe$^{3+}$ in the iron oxide shell and dopamine instead of the formation of two “robust” Fe-O bonds.$^{65}$

Fig. 9.1. This TEM image is Fe/iron oxide core-shell particles coated with dopamine (Fe-Ox dopamine) and immediately dried on the TEM grid. Inset on the image is a zoomed region for better viewing of the core-shell concentric rings.
Fig. 9.2. This TEM image is of the precipitated particles after 1-2 days in aqueous solution. Note that the particles have changed in size dramatically as compared to Fig. 9.1.

9.4 Dopamine Reactivity Studies

Further evidence of a surface reaction can be seen in the mid-IR in Fig. 9.3. The spectrum of dopamine exhibits a clear and broad OH stretch centered around 3300 cm$^{-1}$. The spectrum of the plain Fe-Ox particles also contains an OH stretch due to surface absorbed water that through intermolecular bonding forms an iron hydroxide hydration
shell. The center of this absorbance is shifted to around 3400 cm\(^{-1}\) due to a higher degree of intermolecular bonding at the surface of the nanoparticles.

Fig. 9.3. Mid-IR spectra from 4000 cm\(^{-1}\) to 2390 cm\(^{-1}\) Fe/iron oxide core-shell particles (Fe-Ox), dried Fe-Ox dopamine particles, and dopamine hydrochloride (dopamine). These samples were prepared in AgBr pellets to minimize water interference in this region since AgBr is less hygroscopic than KBr.

The center of the OH absorbance of Fe-Ox dopamine shifts to even higher energy at 3500 cm\(^{-1}\) which is typical for an alcohol or phenol stretch that is intermolecular bonded.\(^{25}\) This absorbance band also seems to have more than one maximum in the range from 3600-3400 cm\(^{-1}\) which is due to differing proton location, such as being coordinated between the catechol oxygens, between a catechol oxygen and surface oxide, or just an OH of the surface hydroxide. These different proton arrangements can also be described as the intermediate between the dopamine semiquinone complex (compound 2) and the
dopamine quinone complex (compound 3), or possibly to protons coordinated to the oxygen in the initial Fe-Ox dopamine complex (compound 1). The IR spectrum of Fe-Ox dopamine in Fig. 10.4 also contains a peak at 1650 cm\(^{-1}\) that extends through a broad hump to 1590 cm\(^{-1}\) which is indicative of an aromatic ketone and the enol of a diketone.\(^{25}\) This can be attributed to the equilibrium between compounds 2 and 3.

![Mid-IR spectra](image)

**Fig. 9.4.** Mid-IR spectra from 1800 cm\(^{-1}\) to 1000 cm\(^{-1}\) of Fe/iron oxide core-shell particles coated with dopamine (Fe-Ox dopamine) and dopamine hydrochloride prepared in KBr pellets.

El-Ayaan et al. also show that if compound 3 is in an acidic environment there is a ring closure through an internal Michael addition to form leucodopaminochrome (compound 4) and then with more Fe\(^{3+}\) there is conversion to dopaminochrome.\(^{26}\)
To further investigate the steps in the reaction, UV-vis spectra of dopamine and a solution of Fe-Ox dopamine particles were analyzed at three points in time. As expected there is a difference in the absorbance data of dopamine as compared to the Fe-Ox dopamine particles as shown in Fig. 9.5. The absorptions seen for the Fe-Ox dopamine particles between 210 nm and 300 nm are due to the charge transfer (CT) bands of Fe$^{3+/2+}$ complexes.\textsuperscript{27,28} The fact that peaks in this region are present for $\pi \rightarrow \pi^*$ transitions in dopamine, and remain in the supernatant after all of the particles have precipitated out of solution make it hard to draw many conclusions about the reaction taking place.

Fig. 9.5. UV-vis spectra of dopamine, Fe-Ox dopamine, Fe-Ox dopamine after 24 hrs in solution, and the supernate left after 2 days and the particles had precipitated out of solution.
On the other hand, the broad absorbance band around 584 nm is related to the \(d-d\) transitions of Fe\(^{3+/2+}\). The reduction in intensity of this band after 24 hours is clear evidence of less Fe\(^{3+/2+}\) in solution. Once the concentration of Fe\(^{3+/2+}\) is too low, the \(d-d\) bands are no longer visible because they are overwhelmed by the intensity of the CT bands, thus more iron must have precipitated out. This broad absorbance could also be due to simple scattering off the surface of the nanoparticles while suspended in the dispersion. This interpretation of the UV-vis data also indicates that the particles are precipitating out and there is loss of stability of the dispersion.

If the reaction went through the full oxidation process to form dopaminochrome, we would expect to observe a strong absorbance band around 400 nm, which is indicative of a quinone. On the other hand, the absence of this band is expected for leucodopaminochrome (compound 4) since it is UV-transparent. The ring closure of the quinone to form compound 4 is spontaneous with a high reaction rate constant\(^{26}\) and reacts faster when exposed to light, thus making it difficult to ensure that this degradation of the particles is oxidizing the dopamine through the quinone state. To capture this portion of the reaction, dopamine was first functionalized with PEG before reacting with the Fe-Ox particles to prevent the ring closure from occurring. The UV-vis spectrum of the Fe-Ox dopamine/PEG particles in Fig. 9.6 revealed an absorbance around 420 nm, which is typical for the quinone of dopamine\(^{10}\), thus providing evidence for the formation of the quinone in this reaction mechanism.
9.5 Magnetic Studies with Dopamine

Magnetic characterization was carried out on both the initially dried Fe-Ox dopamine particles and the aged precipitant to further investigate changes in the material due to this Fe$^{3+}$-dopamine reaction. As shown in Fig. 9.7, the magnetization versus temperature plot at 1000 Oe demonstrates that the Fe-Ox dopamine particles exhibit superparamagnetic behavior with a paramagnetic tail at low temperatures due to the dopamine. The inset hysteresis shows a saturation magnetization of 80 emu/g, which is fairly high since we included the mass of dopamine in this calculation. The precipitant
material revealed predominately paramagnetic behavior as seen in Fig. 9.8, but also showed slight ferromagnetic behavior in the inset hysteresis plot which could be due to small iron oxide particles surrounded by large amounts of iron oxyhydroxide.

Elemental analysis by ICP-OES revealed that the dark precipitate was 24.2 % Fe thus ensuring the presence of Fe in the material. To determine what form the Fe was in a Curie-Weiss fit was performed on the data suggesting Fe$^{3+}$, most likely in the oxyhydroxide form which would be red/brown in color and often forms when Fe(OH)$_2$ (green) oxidizes in water. The fit revealed deviation from Curie-Weiss law at higher
temperatures, which is most likely due to enhanced coupling between the small amounts of magnetite that remain. A linear fit to the lower temperature portion and using the Lande constant for iron gave a total spin of $\frac{5}{2}$, which would be expected for Fe$^{3+}$.

![Graph showing magnetization versus temperature and hysteresis plot](image)

**Fig. 9.8.** Magnetization versus temperature plot of precipitant material at 1000 Oe with a hysteresis plot at 10 K (inset).

### 9.6 Dopamine Theoretical Studies

Now that our experimental data has put together pieces that support the decomposition of the nanoparticles and dopamine, first principles theoretical studies were performed by a collaborator to look at the modeling of a comparative system to give further insight into the mechanism.$^{68-80}$ The key issue is how the dopamine is absorbed on
an Fe₂O₃ surface and can this lead to a surface reaction which aids in the degradation of the Fe-Ox nanoparticles. The later possibility would exist if the heat of adsorption is sufficient to break a cluster into two fragments. For each cluster XₙYₘ involved in such a process, we first determined the atomization energy, AE, defined by \( AE = n E(X) + m E(Y) - E(XₙYₘ) \). Here \( E(XₙYₘ) \) is the total energy of the cluster while \( E(X) \) and \( E(Y) \) are the total energies of the individual atoms. With such a definition, positive values of AE represent the energy required to break the cluster into isolated atoms. Using the calculated AE, we investigated the energetics of the process involving attachment of semiquinone (C₈H₁₀NO₂) to a Fe₂O₃ cluster and breaking of the complex into various possible products. We first consider the attachment energy according for the reaction:

\[
2\text{Semiquinone} + 3\text{Fe}_2\text{O}_3 \rightarrow 2\text{Fe}_2\text{O}_3\text{-semiquinone} \quad \Delta E = 3.29 \text{ eV} \quad (9.1)
\]

Here, the superscripts represent the ground state spin multiplicity, and the positive sign in \( \Delta E \) indicates that the reaction is exothermic. Then, two possible fragmentation reactions were explored and in the following we provide the energetics for each of the processes:

\[
\begin{align*}
2\text{Fe}_2\text{O}_3\text{-semiquinone} & \rightarrow 4\text{FeO}\text{-semiquinone} + 3\text{FeO}_2 \quad \Delta E = -3.67 \text{ eV} \quad (9.2) \\
2\text{Fe}_2\text{O}_3\text{-semiquinone} & \rightarrow 6\text{Fe}\text{-semiquinone} + 1\text{FeO}_3 \quad \Delta E = -4.99 \text{ eV} \quad (9.3)
\end{align*}
\]

As we notice, reaction (9.2) requires 3.67 eV of energy while reaction (9.3) requires 4.99 eV of energy to proceed. This would seem to imply that the semiquinone can bind to Fe₂O₃ without degradation of the parent cluster.

While this is encouraging, the actual solution contains H⁺ cations and one has to ascertain the stability in the presence of these protons. As a first example, we consider the case when two protons bind to the cluster. Here, we started with a Fe₂O₃-
semiquinone cluster and first investigated where the two protons would prefer to bind. For example, the protons could bind to O sites closer to the semiquinone, or prefer to bind to O sites farther from semiquinone. These possibilities along with the resulting AE are given in Fig. 9.9. Note that the more stable situation corresponds to proton binding to oxygens labeled O₃ and O₄.

![Fig. 9.9. Structural geometries and resulting AE’s for different protonation sites for the Fe₂O₃ and dopamine semiquinone complex.](image)

The preference of the proton to these oxygens can be explained by differences in electronegativity. The oxygens O₁ and O₂ are bridged between an iron and the delocalized negative charge of the benzene ring. This would cause the oxygens bridged between two irons to be more electronegative, thus also making O₃ and O₄ electrostatically favored for proton binding. Also in the case of the protonation O₁ and
O₂, only one O-Fe bond is broken or the two O-Fe bonds are just stretched from 1.99 to 2.03 Angstroms (Fig. 9.9). Having found this, we now investigated the energetics of the process where a Fe₂O₃ with H atoms ligated at the oxygens O₃ and O₄ approaches the semiquinone and whether the heat of formation is enough to drive the cluster to cleavage.

The attachment energy is given by the equation:

\[ ^2\text{Semiquinone} + ^7\text{Fe}_2\text{O}_3\text{H}_2 \rightarrow ^6\text{Fe}_2\text{O}_3\text{H}_2\text{-semiquinone} \quad \Delta E = 3.47 \text{ eV} \quad (9.4) \]

In the following, we outline the results of the fragmentation reaction involving breaking of the complex with two hydrogens attached to O₃ and O₄.

\[ ^6\text{Fe}_2\text{O}_3\text{H}_2\text{-semiquinone} \rightarrow ^6\text{Fe}\text{-semiquinone} + ^5\text{FeO}_3\text{H}_2 \quad \Delta E = -3.28 \text{ eV} \quad (9.5) \]

As seen from Eq. (9.5), the attachment of the semiquinone does lead to a decrease on the fragmentation energy as compared with the intact structure in the absence of H atoms (Eq. (9.3)). We found that (not shown here) addition of 4 H atoms leads to even easier breaking of the Fe₂O₃.

We then calculate the energy required to fragment the bare and hydrogenated Fe₂O₃ cluster in the presence of the semiquinone according with the reactions:

\[ ^2\text{Semiquinone} + ^3\text{Fe}_2\text{O}_3 \rightarrow ^6\text{Fe}\text{-semiquinone} + ^1\text{FeO}_3 \quad \Delta E = -1.70 \text{ eV} \quad (9.6) \]

\[ ^2\text{Semiquinone} + ^7\text{Fe}_2\text{O}_3\text{H}_2 \rightarrow ^6\text{Fe}\text{-semiquinone} + ^5\text{FeO}_3\text{H}_2 \quad \Delta E = 0.19 \text{ eV} \quad (9.7) \]

According with Eq. (9.5) the reaction is exothermic and the hydrogenated Fe₂O₃ cluster will be fragmented.
9.7 Dopamine Reaction Mechanism

The mechanism and reaction rates of the oxidation of catechols by ferric cations has been proposed,\textsuperscript{26,29} but now we outline the mechanism for the decomposition of nanoparticles functionalized by dopamine (Fig. 9.10). Following the initial proposed mechanism, the reaction initially forms an iron(III) complex (compound 1) on the surface of the nanoparticle. Formation of the initial structure with the dopamine coordinated to the surface of the iron oxide nanoparticle is a result of improved orbital overlap of the 5-member ring as well as the reduced steric environment of the iron complex. The stability of iron complex on the surface results from the stable 5-member metallocycle structure. This 5-member ring leads to a far more stable structure than the typical 4-member metallocycle seen with carboxylic acid complexes. Through the transfer of one electron, the dopamine is oxidized to form a semiquinone (compound 2), but the complex is still coordinated to the surface of the nanoparticle. As shown in our calculations the free protons in the solution more favorably coordinate with the inner oxygens connected to the Fe\textsuperscript{2+}. This reduces the overall energy of the system and then allows the dopamine to shift to other Fe\textsuperscript{3+} on the surface and the Fe\textsuperscript{2+} then is free to be released into the solution as a hydroxide, which in air will oxidize to FeOOH. The semiquinone compound reforms on adjacent Fe\textsuperscript{3+} on the surface. Then with one more electron transfer, the semiquinone is converted into an orthoquinone (compound 3). The orthoquinone then spontaneously converts to compound 4 and the resultant functionalized nanoparticle is now less stable.
Fig. 9.10. Proposed mechanism for the decomposition of Fe₂O₃ nanoparticles by dopamine in an aqueous solution. (Top Left) Illustration of the initial complex formed in the coordination of dopamine on the surface of the nanoparticle. (Top Right) Formation of the semiquinone complex through the first electron transfer and iron(II) hydroxide fragmentation. (Bottom Right) Second electron transfer to form the dopamine quinone and second fragmentation. (Bottom Left) Michael addition that forms the UV transparent leucodopaminochrome and the oxidation of Fe(OH)₂ that forms the FeOOH.
9.8 Dopamine Conclusion

The degradation process can be slowed slightly by the addition of a large ligand through the terminal amine, but is also detrimental since a greater presence of the dopamine quinone can be cytotoxic. Thus we concluded that the use of dopamine as a robust anchor for iron oxide or iron oxide shell particles will not fulfill the need for stable dispersions for use in most biomedical applications.

9.9 Cysteine Trials

Another functional ligand that was used in functionalization for MRI trials in the subsequent chapter is the amino acid cysteine. This ligand offers two advantages; one advantage is that the ligand being an amino acid already exhibits basic biocompatibility; the other advantage is the three different possible interacting functional groups being a carboxylic acid, amine, and sulfide. The fact that cysteine possesses these three functional groups allows for the possibility of multiple binding methods to the surface of an iron or iron oxide nanoparticles. Other carboxylic acids have been used to coordinate to the surface of iron oxide nanoparticles with success in ferrofluid formation with oleic acid. For the particles synthesized in chapter 8 via thermal decomposition of Fe(CO)$_5$ using TOP as a capping agent, cysteine was chosen for the potential of displacing the similar Fe-phosphide interaction at the surface for a Fe-sulfide type interaction.

In order to attempt to force the Fe-sulfide interaction, the cysteine was introduced to the nanoparticles in an aqueous and high pH environment (pH > 10). This would
ensure that all of the function groups would exist in higher concentration in the
deprotonated form. Once this step was performed concurrently with sonication, the
particles that were insoluble while capped with the TOP, became dispersed and formed a
clear blue solution. At this step the particles were still able to be slowly magnetically
separated. To then ensure that the particles would not aggregate when in the presence of
a magnetic field, a diacid terminated polyethylene glycol (diacid-PEG) was added until
the blue color turned yellow and a pH nearer to neutral was obtained. At this point, the
particles were no longer able to be magnetically extracted, thus suggesting that the amine
end of the cysteine was now tethered to the diacid-PEG through an amide bond. This
also suggests that the most likely arrangement or attachment to the particle is through the
sulfide since this would allow for the amine to be more accessible. On the other hand, if
the carboxylic acid was coordinated to the particle, the amine would either be involved in
the attachment or more so sterically unavailable. TEM analysis revealed the presence of
particles after the functionalization and concentrations of Fe were obtained by ICP-OES
for a common comparison point for the MRI analysis.

9.10 Polyethylene Glycol Ferrofluid Functionalization

The polyol synthetic method is a well established means to produce nanoparticles.
Since the solvent is also the capping agent for reaction in glycol, there is the possibility to
use the polyol synthetic method to also incorporate a polyethylene glycol (PEG)
functional ligand to the surface of iron/iron oxide nanoparticles synthesized therein. This
is primarily done by a two step method; firstly producing an iron/iron oxide core by
means of a standard polyol method; then follow up with the subsequent addition and further reaction with a PEG solution produced from the same glycol used in the nanoparticles synthesis. This type of coating process gives the advantage of producing more uniformly coated particles since the polymer synthesis growth stage was performed in situ with the nanoparticles. Also, PEG’s biocompatibility has already been established.

As with all of the samples prepared for MRI in chapter 10, they must exhibit that they will not aggregate and pull out of solution when in the presence of a high magnetic field. A good ferrofluid should be the perfect colloidal system to use in with MRI since the particles should not be able to be extracted from the solution.

Fig. 9.11. (left) Aqueous ferrofluid prepared by modified polyol technique. (right) Same aqueous ferrofluid in the presence of a magnet.
This is clearly illustrated with the ferrofluid in Fig. 9.11 because the magnet will pull the entire solution (when concentrated) and not pull any individual particles out. This shows that the particles are isolated from each other and the colloidal dispersion is not compromised. Then upon dilution the particles remain dispersed and a clear solution is produced without visible signs of particles (by eye). The TEM image in Fig. 9.12 shows the size and morphology of the particles.

Fig. 9.12. TEM image of the iron oxide aqueous ferrofluid after dilution for MRI. This solution was further diluted for MRI studies.
This aqueous ferrofluid synthesis has yielded two variations of material composition.

One variation of the synthesis yields particles comprised of both metallic iron and iron oxide, where the other yields iron oxide. This was verified by powder XRD and the diffraction pattern shown in Fig. 9.13 which is for the sample with both metallic iron (α-Fe) and iron oxide. The peaks for the metallic iron have the pointed to with arrows for illustration purposes.

![Fig. 9.13. Powder XRD pattern showing the presence of iron oxide and metallic iron in one of the ferrofluids synthesized.](image)

This XRD pattern was obtained from dried ferrofluid after being initially dispersed in water. The other ferrofluid only revealed peaks on XRD that were representative of iron
oxide. These two ferrofluids will be a good point of comparison for determining whether or not metallic iron or iron oxide is better for MRI contrast enhancement.

9.11 Conclusion

These functionalization methods presented have illustrated several points. The ability to use several methods to produce colloidal dispersions that will not allow for magnetically induced aggregation is one of the basic points shown. Also, this chapter has illustrated the importance of stability studies and further investigations to ensure biocompatibility of possible byproducts from the decomposition of the particles and ligands.
Chapter 10: Material Application in Magnetic Resonance Imaging

Inspiring Thoughts #10

“The truth shall set you free.”
10.1 Introduction

In order to enhance MRI contrast, it is necessary that the material shorten the longitudinal ($T_1$) and transverse ($T_2$) relaxation times. In general, the static magnetic field produced by the MRI magnet causes the protons in water and tissue, or other spin $1/2$ or magnetic nuclei, to align in a given direction ($z$-axis). A radio frequency (RF) pulse is applied to the aligned protons which causes a change to an excited state. The frequency of irradiation that is absorbed is equal to the Larmor frequency, or frequency of nuclei rotation about the $z$-axis. $T_1$ describes relaxation back to the original $z$-axis alignment and $T_2$ describes the relaxation back to the original procession state. The basic principle then for all MRI contrast agents can be thought of as dissipation of the energy introduced by the RF-pulse into the system, quickly returning back to original orientation in the static magnetic field.

10.2 Enhanced Ferrite Study with MRI

10.2.1 Introduction

Metal oxides such as ferrites are of particular interest for therapeutic and diagnostic medical applications due to their relative inertness and properties that can be tailored by changing synthesis parameters. These ferrites have found application as contrast agents for magnetic resonance imaging (MRI) due to enhancement of relaxivity, in ferrofluid technology for MRI monitoring in hypothermia, and in cancer tumor detection via SQUID magnetometry. The high magnetic moment of ferrites can be enhanced through the use of doping metals like nickel, cobalt, etc. Nickel
ferrites have been used in many of the above mentioned applications due to the superior magnetic properties. Magnetic studies of ferrofluids based on nickel ferrite nanoparticles, synthesized by several different methodologies, have been investigated in great detail. Reverse micelle synthesis has been the method which makes the most stable ferrofluid dispersion which is more suitable for biomedical applications. Reverse micelles techniques also have the added benefit of being compatible for sequential synthesis leading to core-shell nanoparticles which have enhanced magnetic properties.

10.2.2 Experimental

Along with the application, we will discuss the synthesis and characterization of the material used in these first MRI measurements. The synthesis of enhanced nickel ferrite nanoparticles was carried out via reverse micelle methods used in core shell techniques utilizing nonionic surfactants. The enhancement to the ferrite comes from the formation of a core with more superior magnetic properties, followed by subsequent oxidation for the formation of the ferrite shell. The structure of the nanoparticles was confirmed by x-ray absorption spectroscopy. The resulting nanoparticle, while having a nickel ferrite shell, has minimal nickel concentrations which should be at an acceptable level for medical applications.

To give further information, a basic synthesis will now be described in further detail. The nonionic surfactants used were nonylphenoxy poly(ethylenoxy)ethanols known by product names IGEPAL CO-520 (NP5) for a chain length of five and IGEPAL
CO-630 (NP9) for a chain length of nine and were received from Rhodia Incorporated. Surfactant solutions were prepared by dissolving 6.857 g of NP5 and 20.571 g of NP9 in 123.23 mL of cyclohexane. In a typical synthesis, two surfactant solutions were required. One solution was placed into a 1000 mL three neck round bottom flask under magnetic stirring and degassed for 20 minutes with nitrogen through Schlenk line techniques. The other surfactant solution was stirred vigorously while slowly adding 6.857 mL of a 0.35 M Ni$^{2+}$(aq). Once the solution formed micelles and became clear, it was placed in an addition funnel above the round bottom flask and degassed in the same manner.

Next, 6.857 mL of 0.70 M Fe$^{2+}$(aq) was added to the first surfactant solution, stirred until it became a clear pale green, and degassed for 5 minutes. Then 0.365 g of NaBH$_4$ was added to the flask and allowed to react for 20 minutes, at the end of which the micelle solution in the addition funnel containing the Ni$^{2+}$ was added to the reaction for 5 minutes. The reaction was quenched by the addition of 100 mL of chloroform and 100 mL of methanol and subsequently washed with methanol and magnetically separated in a separation funnel three times. After washing was complete the remaining methanol was decanted and the particles were dried in a vacuum desiccator. Once exposed to air the particles were aged for one week to ensure oxidation had occurred.

10.2.3 Structural Results

XAS analysis suggests that the iron exists partially in the form of a ferrite, and partially in the form of an amorphous iron boride compound. As in Ref. 25, the x-ray absorption near-edge structure (XANES) was used to estimate the ratio of these two
phases. A simultaneous fit on both edges was performed, using Feff6 to calculate theoretical standards for iron nickel boron ferrite and amorphous iron boron. Because the nickel edge was much smaller and had to be deglitched, the iron edge was weighted by a factor of ten in the fitting process (roughly the ratio of the size of the edge jumps).

Results and constraints are shown in Table 10.1. As can be seen from the table, the fit is considerably better for the iron edge (R-factor 0.009) than for the nickel edge (R-factor 0.052). The excellent agreement between fit and data for the iron edge, as well as the physically reasonable values found in Table 10.1, confirm that the spinel/iron boron model is appropriate for the iron. The lower quality of the nickel factor is probably attributable to a combination of three types of effect: the lower signal-to-noise ratio of the nickel data; the lower weighting given to the nickel data in the fitting process; and some fraction of the nickel atoms not being present in a spinel environment. It is difficult to judge the relative importance of these factors, but in any case the agreement between data and model is good enough to assert that a large fraction of the nickel is present in a spinel environment.

We speculate that this unique structure can be explained by investigating the major differences between this synthesis and other wet chemical methods of fabricating nickel ferrites. In a typical procedure the metals are all dissolved in a single aqueous solution and then precipitated together by adjusting the pH according to Pourbaix diagrams. Our synthesis first reduces the Fe$^{2+}$ to form Fe nanoparticles in the absence of oxygen. Then before all of the NaBH$_4$ is reacted, the addition of Ni$^{2+}$ drives for the production of a core shell type structure.
Table 10.1. Results of EXAFS fit. Uncertainties in the least significant digit are given in parentheses.

<table>
<thead>
<tr>
<th>Fitted Parameters:</th>
<th>Constrained Parameters:</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta E_0 ) Nickel</td>
<td>8(3) eV</td>
</tr>
<tr>
<td>( \Delta E_0 ) Iron</td>
<td>6(7) eV</td>
</tr>
<tr>
<td>Spinel lattice constant</td>
<td>8.37(18) Å</td>
</tr>
<tr>
<td>Spinel oxygen parameter</td>
<td>0.38(2)</td>
</tr>
<tr>
<td>Spinel MSRD</td>
<td>0.060(20) Å²</td>
</tr>
<tr>
<td>Ni-O MSRD</td>
<td>0.003(3) Å²</td>
</tr>
<tr>
<td>Fe-O MSRD</td>
<td>0.019(4) Å²</td>
</tr>
<tr>
<td>Fraction iron octahedral</td>
<td>38(3)%</td>
</tr>
<tr>
<td>Fe-Fe distances in iron boron</td>
<td>2.53(3) Å</td>
</tr>
<tr>
<td>First Fe-Fe MSRD in iron boron</td>
<td>0.021(4) Å²</td>
</tr>
</tbody>
</table>

The Ni\(^{2+}\) is allowed into the reverse micelles with the Fe nanoparticles by the aid of the NP5 component of the surfactant solution. It is known that NP5 has a hydrophilic to hydrophobic surface area ratio that is close to one which has been shown to allow for the formation of open water channels in the microemulsions.\(^{94}\) It is this feature that we speculate drives the incorporation of nickel into the particle, and then after exposure to oxygen, the particle slowly oxidizes and the two metals distribute themselves in this particular fashion.

10.2.4 Magnetic Characterization
The magnetic characterization as determined by SQUID magnetometry demonstrates that the particles exhibit superparamagnetic behavior with the blocking temperature \((T_B)\) being dependent on the magnetization of the measuring field. \(T_B\) shifts from a value above 300 K at 100 Oe to 120 K at 1000 Oe. The susceptibility plot at 100 Oe can be seen in Fig. 10.1 and the plot at 1000 Oe can be seen in Fig. 10.2. The high blocking temperature at 100 Oe as compared to other nano-nickel ferrites is due to the increase in blocking temperature with increasing size.\(^95\)

Fig. 10.1. Zero field cooled and field cooled plots of the nickel ferrite particles. Data was collected at a measuring field of 100 Oe.
TEM revealed that the particles are 10 -15 nm in size which would be expected to have a blocking temperature above 300 K. To further characterize the particles we employed a method as shown in the literature to estimate the magnetic size. The hysteresis plot seen in Fig. 10.3 shows a saturation magnetization ($M_s$) of 68 emu/g and reveals relatively small coercivity not larger than 200 Oe. The saturation magnetization in this case being higher than other values reported for nano nickel ferrites of similar size is easily explained by the structure as determined by EXAFS confirming the presence of a FeB core.
Fig. 10.3. Plot of magnetization versus applied field for the nickel ferrite particles. Data was collected at temperature of 10 K. The inset plot reveals relatively small coercivity.

The magnetic size estimate uses the slope (dM/dH) near zero field, which in this case is 0.0425 emu/g Oe. Plugging this into Eq. 10.1 along with $M_s$, Boltzmann’s constant ($k$), the density of Fe$_2$O$_3$ ($\rho = 4.9$ g/cm$^3$), and the temperature ($T = 10$K), we calculate a magnetic diameter ($d_m$) of 2.5 nm.

$$d_m = \left[ \frac{18kT}{\pi} \left( \frac{dM}{dH} \right)_{H \rightarrow 0} \right]^{1/3}$$

(10.1)

The difference between $d_m$ and the visually observed diameter by TEM ($d_{TEM}$) is due to the magnetically “dead” space of varying thickness reported to be present in all spherical particles. The incorporation of boron by this reduction synthesis method has
been well studied,\textsuperscript{99,100} and thus could also explain the large difference in $d_m$ and $d_{TEM}$ due to greater distortion in the crystal lattice by the boron.

10.2.5 Functionalization for MRI

In looking at the medical applications for which these particles can be used, it is important to be able to form stable aqueous solutions. In order to disperse the nanoparticles, a ferrofluid was created using a surface functionalization. The surface was treated with dopamine hydrochloride\textsuperscript{65} which was first treated with diacid PEG-600 to prevent aggregation in the high magnetic field of the MRI, and slow the degradation process of the nanoparticle as before mentioned.\textsuperscript{78} Fig. 10.4 shows a cartoon representation of the coating and functionalization process employed.

![Fig. 10.4. Cartoon representation of the coating process for MRI functionalization.](image-url)
When a sample of the functionalized enhanced ferrite particles were placed in water, a homogenous, clear blue-green solution was formed. The TEM image as seen in Fig. 10.5 shows that the particles are still present and dispersed after functionalization. The concentric rings visible on the TEM image from different layers of electron density show great correlation with the graphical representation in Fig. 10.4. This also showed that particles were still present after the functionalization process.

![TEM image of PEG/Dopamine coated particles taken at 120 kV illustrating the core-shell structure and dispersion.](image)

Fig. 10.5. TEM image of PEG/Dopamine coated particles taken at 120 kV illustrating the core-shell structure and dispersion.
10.2.6 MRI Application Experimental

The dispersed solution of particles was then used in a MRI study to determine the T1 and T2 relaxation times and their potential use as contrast agents. The magnetic resonance imaging/spectroscopic experiments were performed by a collaborator and the experimental details can be found in the literature, but are also given here for ease of reference. The magnetic resonance imaging/spectroscopic experiments were performed on a 2.4 T/40 cm bore MR system (Biospec/Bruker). Spectroscopic T1 and T2 1H relaxation measurements of saline solutions of the nickel ferrite nanoparticles were conducted at 2.4 T using an inversion recovery sequence with 8 inversion times (TI) and repetition times (TR) at least 5 times the expected T1. For the T2 measurements a multi spin-echo CPMG sequence was employed with several echo times (TE) and TR values at least 5 times the expected T1. The relaxation times were computed from least-squares fitting of the exponentially varying signals using analysis routines available at the MR system. Relaxivities were extracted from graphs of relaxation rates (1/T1 and 1/T2) versus concentration. The concentration range used for the relaxivity measurements was in the range 0.0022-0.0714 μM. Vials of different contrast concentrations were imaged in a phantom to obtain T1-weighted (TR/TE 700/10 ms) and T2-weighted (TR/TE 3000/100 ms) images.
10.2.7 MRI First Results

In Fig. 10.6, the relaxation rates $R_1=1/T_1$ and $R_2=1/T_2$ are shown as a function of concentration of the enhanced ferrite nanoparticles. The relaxivities $R_1$ and $R_2$, representing the slopes of these curves, are $71.9 \text{ sec}^{-1}\text{mM}^{-1}$ and $99.6 \text{ sec}^{-1}\text{mM}^{-1}$ respectively.

![Fig. 10.6. Relaxivity plot for first MRI measurements.](image-url)
These values are in terms of µM of nanoparticles as estimated from size calculations done by using the TEM and ICP results. These values could be compared with relaxivities approximately 4-5 sec⁻¹mM⁻¹ corresponding to the commonly used commercial gadolinium chelate contrast agents in human MR examinations. The difficulty in the comparison is that the materials are different and thus it is not clear what the best comparison units should be. This point will be discussed further in subsequent sections.

Fig. 10.7. Image of phantom cells with varying concentration of the enhanced ferrite nanoparticles: T₁-weighted image. The sample concentrations from top to bottom are 0.0714 µM, 0.0357 µM, 0.0179 µM, 0.0089 µM, 0.0045 µM, and 0.0022 µM in terms of nanoparticles.
Fig. 10.8. Image of phantom cells with varying concentration of the enhanced ferrite nanoparticles: $T_2$-weighted image. The sample concentrations from top to bottom are 0.0714 µM, 0.0357 µM, 0.0179 µM, 0.0089 µM, 0.0045 µM, and 0.0022 µM in terms of nanoparticles.

The $T_1W$ and $T_2W$ images are shown in Fig. 10.7. The expected intensity changes with increasing concentration are seen: signal increases at the highest concentrations in $T_1W$ images due to shortening of the $T_1$ and corresponding signal losses in $T_2W$ images due to $T_2$ shortening.
10.2.8 Conclusion I

The success in MRI contrast enhancement is clearly illustrated in the phantom cell experiments in Fig. 10.7 and Fig. 10.8. The difficulty once again is determining the best method to compare between contrast agents. This first study though was able to give us a better focusing point for our next set of MRI experiments. It will be easier to compare results between common materials, thus we will next present results of comparing various structures of iron compounds. This will allow for a better conclusion toward which structure of iron would be the optimal MRI contrast agent.

10.3 MRI Studies Comparing Iron Structures
10.3.1 Introduction

In order to reveal whether structure or magnetization is the primary property of a material that enables contrast enhancement in MRI, we must first be able to directly compare MRI results between samples. When searching through the literature one finds many different units of concentration, magnetic fields of the MRI, and capping or dispersing ligands used. In some sources in the literature, it is not clear if proper dispersions are used and thus aggregation can lead to improper results. Also, many MRI experiments currently done to determine relaxivity are performed at very high magnetic fields, some of which are not often used for MRI due to issues with RF penetration into the body tissue. When each experiment is done differently it is difficult to discern what type of iron will make the best contrast agent.
Literature on MRI contrast agents goes into great detail about the $T_1$ relaxation process and how different $T_1$ contrast agents work through inner-sphere mechanisms. The inner-sphere relaxation involves only the waters of solvation that are directly coordinated to the contrast agent complex.\textsuperscript{16,102} The outer-sphere processes are then considered to be affecting the rest of the solvent molecules in second solvation shells and beyond or bulk solvent.\textsuperscript{16,102} In a practical sense I believe that most of the contrast enhancement, especially in the body tissue, is due to outer-sphere or bulk processes. This area however is somewhat glossed over due to the lack of understanding and inability to know how many water molecules are to be considered in each solvation shell.\textsuperscript{16} Nanoparticles used as contrast agents should only act by outer-sphere or bulk processes since their size is large relative to the individual atom and the solvation waters typically interact with some type of functionalization ligand in maintaining the stable dispersion. This then leaves the fundamental way that MRI contrast agents work unknown and overlooked.

10.3.2 Hypothesis Behind MRI Enhancement With Iron/Iron Oxide Nanoparticles

My hypothesis for how magnetic nanoparticles improve contrast in MRI involves two separate properties. Firstly, a magnetic nanoparticle in the presence of the static MRI magnetic field may increase the local magnetic field in the body. This could conceptually lead to a $T_1$ enhancement by allowing for further penetration of the magnetic field into the body, thus helping the proton spins in tissue to realign with the
static field. The real question though is whether or not the magnetic field in the body is large enough to allow for the nanoparticle to shorten $T_1$ better than a spin only contribution from a complex such as Gd$^{3+}$. $T_1$ can also depend on many other features such as viscosity in the tissue itself and in the practical range of MRI from 0.5-3T, (which is due to RF penetration into the body) $T_1$ may not differ much between paramagnetic, superparamagnetic, or ferromagnetic materials.

My hypothesis for $T_2$ enhancement however, involves a different property of magnetic nanoparticles. The ability of iron oxides to absorb RF frequencies and produce heat is of great interest in many areas of drug delivery and tumor treatment. I hypothesize that this property is also what gives iron oxides a much higher $T_2$ enhancement as opposed to more metallic particles as shown in the literature. Thinking simply about the $T_2$ relaxation process, the proton that is processing at the Larmor frequency first absorbs the energy from the RF pulse that is equal to the Larmor frequency, thus going to a higher energy state. This energy must be released in order to relax back to its original procession. The addition of iron oxide to the system, which can absorb readily in the RF range to produce heat gives a perfect pathway for relaxation and limits re-absorption of this energy by other protons in tissue, thus greatly shortening $T_2$.

10.3.3 Further MRI Studies

In attempting to prove or disprove the hypotheses presented for how MRI contrast agents work, we will first list the common comparison units that will be used for these
results. Although it has been speculated, recent literature illustrates that the size of the nanoparticles does affect the contrast enhancement abilities. The literature reports that greater enhancement is found for larger particles. I find this contrary to suspecting that the enhancement comes from protons directly coordinated to the chelate or other contrast agent since smaller particles should have a greater surface area to concentration ratio, thereby interacting with more water molecules. On the other hand, this more so illustrates a bulk like or outersphere relaxation mechanism is at work and contributing to the MRI enhancement. These next presented results focus only on the structure without looking into size implications, but will involve two comparisons of different compositions between similarly sized and synthesized particles.

The first comparison of MRI results is between the iron based nanoparticles synthesized via thermal decomposition of Fe(CO)$_5$ in trioctylphosphine and hexadecane from chapter 9. The two particles of interest from these synthesis are the primarily cementite nanoparticles with oxide shell and the more so core-shell type with an $\alpha$-Fe core, followed by a cementite layer with an oxide surface. These particles are good for structure comparison due to three similar factors: similar size of around 5 nm, similar synthetic route, and the similar functionalization ligand cysteine as described in chapter 9. Before presenting the results, we will establish the units for comparison. Since the particles being directly compared will have similar size and capping ligand, the resulting relaxivities $R_1$ and $R_2$ will be reported in terms of mM concentration of Fe. To illustrate how the differences in units can affect the results, Fig. 10.9 shows $R_1$ and $R_2$ corrected in terms of mM Fe as determined by ICP-OES.
Fig. 10.9. Plot of $1/T_1$ and $1/T_2$ versus concentration in mM of Fe. This data is from the enhanced ferrite study previously discussed in this chapter but has been transformed from units of concentration in terms of nanoparticles, to concentration of only Fe.

The R1 and R2 shown here are 0.848 and 1.175 sec$^{-1}$mM$^{-1}$ Fe which can be compared to 71.9 and 99.6 sec$^{-1}$µM$^{-1}$ in terms of concentration of nanoparticles. This clearly demonstrates the importance of a common unit of comparison when searching for the best MRI agent in any form.

The results shown below in Fig. 10.10 are for the $\alpha$-Fe/Fe$_3$C/FeOx nanoparticles.
Fig. 10.10. Plot of $1/T_1$ versus $1/T_2$ versus concentration of Fe (mM) for the as prepared for MRI $\alpha$-Fe/Fe$_3$C/FeOx nanoparticles.

Though not a proper comparison, the fact that $R_1/R_2$ ratio is different for this sample as compared to the one in Fig. 10.9 gives first evidence of a structural dependence. The resulting $R_1$ and $R_2$ of 0.5 and 1.7 $\text{sec}^{-1}\text{mM}^{-1}$ Fe can be directly compared however to and $R_1$ and $R_2$ of 0.2 and 0.9 $\text{sec}^{-1}\text{mM}^{-1}$ Fe for the Fe$_3$C/FeOx nanoparticles as measured by our collaborator. The best way to compare these values is to look at the amount that $R_1$ and $R_2$ differ between samples. If you divide the $R_1$ of the $\alpha$-Fe/Fe$_3$C/FeOx by the $R_1$ of the Fe$_3$C/FeOx, you obtain a value of 2.5, while dividing the $R_2$’s in the same
manner gives 1.9. One can infer from this that overall the sample with more metallic core in the BCC phase is stronger toward R1 or longitudinal relaxation enhancement. This also correlates to a higher saturation magnetization which is suggested to have a more pronounced effect on T1, although both samples showed fairly low enhancement most likely due to their small size.

The next comparison involves the aqueous ferrofluid samples prepared by the polyol method as mentioned in Chapter 9. These samples are larger in size and will illustrate the difference between an entirely iron oxide sample and a combination of metallic and oxide. The metallic iron and iron oxide combination sample yielded an R1 value of 8.6 sec\(^{-1}\)mM\(^{-1}\) Fe and an R2 of 382.2 sec\(^{-1}\)mM\(^{-1}\) Fe. Values obtained for the primarily oxide sample were an R1 of 7.8 sec\(^{-1}\)mM\(^{-1}\) Fe and R2 of 494.6 sec\(^{-1}\)mM\(^{-1}\) Fe. If we compare these values in a similar manner as before, we obtain a ratio of R1’s from more metallic to oxide of 1.1 and a ratio of R2’s of 0.77. Here again the sample with more metallic phase shows a slight improvement in R1. Also, the previous comparison showed that R2 did not improve as much for the more metallic sample, but in this case between the metallic and oxide samples there is a drop in R2 enhancement with the more metal presence. Therefore, the oxide form of iron yields the best R2 enhancement. Even though R1 was improved slightly for the metallic as opposed to the oxide, R2 was affected in a greater manner. This is primarily due to the mechanism of transverse relaxation and further investigation and inquire into Larmor frequencies in structures should be performed.
10.4 Conclusion

The results presented in this chapter show successful MRI measurements with various functionalization techniques of nanoparticles. The main conclusion though is that looking into a correlation between the internal Larmor frequency of a given material and the MRI contrast enhancement may lead to the optimal R2 contrast agent. Also, if a reasonable spin moment or saturation magnetization can be maintained, the R1 enhancement would be acceptable and comparable to current contrast agents. This is the path to the optimal contrast agent which is contrary to much work being done in the current literature.
Chapter 11: Conclusions

Inspiring Thoughts #11

“Good to Go!”
This work has focused on addressing several areas of nanoparticle research that would have an impact on the understanding of current research and provide a clearer direction for future endeavors. The development of characterization methods that are rapid and bench top is vital to understanding how synthesis parameters affect the resultant nanoparticle. A correlation of results was established between time consuming and costly beamline techniques of XANES and EXAFS and another readily available spectroscopy technique of Fourier transform infrared spectroscopy. The detail of cation occupancy in manganese zinc ferrite can be determined well enough to quickly investigate multiple synthetic procedures efficiently. This now makes it possible to better tailor nanoparticle synthesis to yield desired materials. This can also impact laboratories that would otherwise be unable to ever investigate cation occupancies in manganese zinc ferrite.

The development of this rapid FT-IR characterization technique enabled us to investigate the coprecipitation reaction to form manganese zinc ferrite and determine how the initial $\text{Fe}^{3+}/\text{Fe}^{2+}$ ratio affected the resultant particle. It was found that with this one synthesis parameter the $\text{Zn}^{2+}$ incorporation and occupancy site distribution of $\text{Mn}^{2+}$ could be altered, thereby showing that soluble complexes formed and charge and site deficiencies in the precipitating hydroxide drive site occupancies and $\text{Mn}^{2+}$ and $\text{Zn}^{2+}$ incorporation levels. Without such a quick feedback loop for analysis, such synthetic parameters would be very difficult to investigate in a timely or cost efficient manner. It also gives insight into the synthesis of other mixed metal ferrite systems involving zinc or manganese.
The ability to alter or specifically target desired cation occupancy in ferrites by synthesis parameters allow for optimal materials to be prepared for various electronic and magnetic applications. The understanding gained from the unique characterization technique yielded various cation distributions in the manganese zinc ferrite system and various saturation magnetization values. Utilizing the correct $\text{Fe}^{3+}/\text{Fe}^{2+}$ ratio will consistently produce mixed metal ferrites of either high magnetic saturation or more $\text{Mn}^{2+}$ involved in octahedral or tetrahedral sites. Such information and ability drives ferrite research and pushes toward atomic level design of nanomaterials.

Novel particle synthesis was also successfully performed and investigated in this work. It is known that nanoscale synthesis can often have an effect on the structure of materials, and thus also affect many properties of the material. In the case of magnetic nanoparticles, structure plays a major role in the magnetic properties and thus can open the door to new applications that were not possible when limited to properties similar to bulk materials. Novel synthesis techniques often result in or allow for new methods of passivation against oxidation or corrosion of magnetic materials, thus resulting in longer retention of magnetic properties. The novel synthesis utilizing TOP and hexadecane allowed for both of these initiatives to be met. The dilution of TOP in hexadecane allowed for a stronger capping barrier, slowing the growth and promoting the formation of the thermodynamic product of $\alpha$-$\text{Fe}$ in the core. The higher TOP concentrations allowed for quick growth and the formation of the kinetic product $\text{Fe}_3\text{C}$. The variation of this synthesis parameter yielded higher concentrations of two iron based structures in the same core-shell nanoparticle. Also, the $\text{Fe}_3\text{C}$ being a major component in carbon steel
shows resilience to oxidation and corrosion which stabilizes the nanoparticles in multiple media.

Functionalization of nanoparticles for aqueous dispersions and ferrofluids has varying degrees of importance, depending on the application. In applications such as MRI where the targets are biological systems, it is important to produce solutions that will not aggregate in the magnetic field of the MRI. It is also vital to characterize decomposition mechanisms and products that would be presented to the body after use as a contrast agent. This work has provided insight into both the preparation of magnetic samples for MRI applications and implications of the biocompatibility of reactive and decomposition products. All three methods of forming dispersions that would not aggregate in the high magnetic field of the MRI were successful. The cysteine and PEG coating of the ferrofluid showed the best stability and therefore no evident byproducts that could be harmful to the body. Further studies should be done to analyze the uptake and interaction with cells to better characterize possible decomposition in the body.

The dopamine studies on the other hand, while providing a good dispersion, the reactivity of iron with dopamine formed dopamine quinone that has shown cytotoxicity and ultimately led to the destruction of the nanoparticles. Even though this functionalization had difficulties with biocompatibility, the coupling of dopamine to PEG allowed for slower decomposition and the ability to perform MRI contrast measurements. Using all three types of dispersions, the MRI measurement concluded with iron oxide yielding the highest R2 enhancement. Though samples solely comprised of α-Fe remain somewhat elusive, the core-shell samples synthesized in this work allowed for the
conclusion that other factors besides saturation magnetization have a greater effect on contrast enhancement, especially in R2. The higher saturation magnetization of the samples with more α-Fe was able to enhance R1 as opposed to the less magnetic oxide samples, but this enhancement was on a lower scale. The R1 achieved by the iron oxide ferrofluid sample was comparable and or better than many commercially available R1 agents with the advantage of vastly improved R2. Therefore, a drive toward new materials with high absorption of Larmor frequency energies could be the direction of future research.
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