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**THE
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Development of New Silica and Magnetic-Luminescent Silica Nanostructured Materials

Gemma-Louise Davies

A thesis submitted to the University of Dublin, Trinity College for the
degree of Doctor of Philosophy.

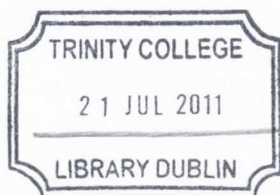
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DECLARATION

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Summary

The main aim of this project is to develop a series of nanocomposite materials based on silica and magnetic-luminescent silica nanoparticles. The work involves the synthesis and characterisation of silica nanoparticles, rare earth-based metallasiloxane materials, magnetic nanocomposites and magnetic-fluorescent nanostructures.

Chapter 1 provides background information relating to nanotechnology, introduces relevant nanomaterials and describes their properties, the techniques used to synthesise these nanomaterials and their current applications. This chapter also provides motivation for our interest in silica and magnetic nanocomposite materials and our aims.

The experimental procedures and techniques which are used for synthesis of the materials are described in Chapter 2. The various characterisation techniques, including FTIR and Raman spectroscopy, X-ray diffraction, magnetisation measurements, electron microscopy, photon correlation spectroscopy, zeta potential measurements, UV-vis and photoluminescence spectroscopy, nuclear magnetic resonance and dispersion techniques and thermogravimetric analysis are also discussed.

Chapter 3 discusses the optimised preparation of silica nanoparticles of small sizes using statistical analyses called 2^2 factorial designs. Such designs allow the variation of more than one experimental parameter, resulting in an assessment of the interaction between these factors. The resulting nanoparticles have been characterised and 3-D surface contour plots, which can be used as 'maps' to prepare tailor-made silica nanoparticles of a specific size, were generated. In addition, luminescent silica nanoparticles have been prepared which display strong broad white emission upon excitation. This chapter also discusses the formation of multi-layered onion-like nanostructures with interesting hollow morphologies.

The preparation of rare earth metallasiloxane materials has been investigated in Chapter 4. These compounds have been utilised as precursors in the preparation of luminescent rare earth doped silica nanoparticles using thermal decomposition techniques.

Chapter 5 describes the synthesis and characterisation of new polyelectrolyte-stabilised magnetic nanocomposites, which are based on ferrite materials. The magnetic

properties of these stable aqueous suspensions of ferrofluids have been investigated in detail using the nuclear magnetic resonance dispersion technique, demonstrating their efficacy as potential contrast agents for MRI.

Chapter 6 deals with multimodal nanocomposites with multiple functionalities, including magnetism and luminescence. The interesting structural features of some of these composite materials are examined in detail. In addition, this chapter discusses the formation of oxide-coated linear 1-dimensional magnetic nanowires using a novel method which is currently under patentation.

Finally, Chapter 7 provides the conclusions of this work and the outlook of further studies which are planned for the future.

Overall, a number of interesting silica and silica coated magnetic nanomaterials, including nanoparticles, nanoshells, nanorattles and nanowires have been prepared and characterised. We believe that many of these materials may have exciting potential applications in the emerging relevant fields of nanotechnology and nanomedicine.

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Abbreviations

Am^2	Ampere metre squared
Am^2/kg	Ampere metre squared per kilogram
APTES	Aminopropyltriethoxysilane
a.u.	atomic units
B_0	applied magnetic field
$^{\circ}\text{C}$	degrees Celcius
ccp	cubic close packed
C_6D_6	deuterated benzene
C_7H_8	toluene
$\text{C}_4\text{H}_8\text{O}$	tetrahydrofuran
cm^{-1}	wavenumbers
CoFe_2O_4	Cobalt ferrite
cy	cyclohexyl
DCM	dichloromethane
DLS	Dynamic Light Scattering
DNA	Deoxyribose Nucleic Acid
d_{hyd}	average hydrodynamic radius according to PCS
d_{TEM}	average diameter according to TEM
DTGA	Derivative thermogravimetric analysis
ΔE_{anis}	change in anisotropy energy
EDC	N-[3-Dimethylaminopropyl]-N'-ethylcarbodiimide-hydrochloric acid
EELS	Electron Energy Loss Spectroscopy
Fe_3O_4	Magnetite
FITC	fluorescein isothiocyanate
FTIR	Fourier Transform Infrared Spectroscopy
g	grams
H	applied magnetic field
HAADF	High Angle Annular Dark Field

JCPDS	Joint Committee on Powder Diffraction Studies
KBr	Potassium bromide
LbL	layer-by-layer
M	Magnetisation
M_0	longitudinal magnetisation
M_s	saturation magnetisation
MHz	Megahertz
mL	millilitres
mM	millimolar
$MnFe_2O_4$	Manganese ferrite
MRI	Magnetic Resonance Imaging
mT	milliTesla
mV	milliVolts
NH_4OH	ammonium hydroxide solution
nm	nanometres
NMR	Nuclear Magnetic Resonance
NMRD	Nuclear Magnetic Resonance Dispersion
Oe	oersted
PCS	Photon Correlation Spectroscopy
PDI	Poly Dispersity Index
Ph	phenyl substituent
PL	photoluminescence
PSSS	Poly (sodium-4-styrene) sulfonate
QD	Quantum Dot
R_1	Spin-lattice relaxation time
R_2	Spin-spin relaxation time
r_1	relaxivity
RE	Rare Earth
SEM	Scanning Electron Microscopy
SiO_2	silicon dioxide (silica)
SQUID	Superconducting Quantum Interference Device

STEM	Scanning Transmission Electron Microscopy
T	Tesla
T_1	Longitudinal relaxation time (or spin-lattice relaxation time)
T_2	Transverse relaxation time (or spin-spin relaxation time)
T_C	Curie temperature
T_N	Néel temperature
TEM	Transmission Electron Microscopy
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
UV	Ultraviolet
XRD	X-Ray Diffraction
λ_{em}	wavelength of emission
λ_{ex}	wavelength of excitation

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Table 2.1 Reactant volumes used to prepare PSSS-CoFe₂O₄ nanocomposites.

Chapter 3 Preparation and Optimisation of Silica Nanoparticles

Figure 3.1 TEM images of silica nanoparticles prepared according to Table 3.1 as labelled. Samples shown at x20,000 magnification; scale bar 100 nm.

Figure 3.2 Graph showing increasing nanoparticle size with increasing ammonium hydroxide concentration.

Figure 3.3 Histograms showing size distribution of nanoparticles prepared according to Table 3.1.

Figure 3.4 TEM images of samples prepared according the statistical study 1, shown at x50,000 magnification; scale bar 100 nm.

Figure 3.5 Histograms showing size distribution of nanoparticles prepared according to statistical study 1.

Figure 3.6 TEM images of samples prepared according the statistical study 2, shown at x50,000 magnification; scale bar 100 nm.

Figure 3.7 Histograms showing size distribution of nanoparticles prepared according to statistical study 2.

Figure 3.8 3-D surface contour models of the first (1) and second (2) statistical studies where reagent concentrations were chosen as factors to be varied.

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Figure 3.10 TEM images of samples corresponding to samples A-E in Table 3.4, scale bar 100 nm.

Figure 3.11 Histograms of size distribution of samples A-E according to Table 3.4.

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Figure 3.13 Solid state photoluminescence spectra of samples prepared by ultrasonic tapered tip (A), microwave (B) and stirring (C); inset shows close-up of samples B and C, $\lambda_{ex} = 457$ nm.

- Figure 3.14** Lifetime measurement of sample A, prepared using the ultrasonic tapered tip; $t_1 = 0.84$ ns; $t_2 = 10.5$ ns.
- Figure 3.15** Sample prepared using ultrasonic tapered tip (a) TEM image; (b) HAADF STEM image; (c) SEM image showing the nanoparticulate nature of the particles when dried to the solid state; (d) Light microscope image; (e) Bright white emission can be seen when illuminated with light (λ_{ex} 510 nm).
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- Scheme 3.2** Presentation of the first statistical design of optimisation model for the preparation of small sized silica nanoparticles by the classical Stöber method.
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- Table 3.1** Reagent ratios, resulting particle size and standard deviation of experiments carried out.
- Table 3.2** Relative amounts of reagents in reaction and resulting nanoparticle sizes – statistical study 1.
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- Table 3.5** Samples prepared using ultrasonic tapered tip and resulting nanoparticle sizes.

Chapter 4 Rare Earth Metallasiloxanes as Precursors for Luminescent Silica Nanoparticles

- Figure 4.1** Structure of incompletely condensed trisilanol ligand $[R_7Si_7O_9(OH)_3]$, where $R = c\text{-C}_6\text{H}_{11}$ (**Ligand A**).
- Figure 4.2** The structure of lithium-ytterbium metallasilsesquioxane derivative (Cy = cyclohexyl).⁵
- Figure 4.3** ^{29}Si NMR of $[\text{Eu}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 2**) showing one peak at 54.78 ppm.
- Figure 4.4** ^{29}Si NMR of $[\text{Yb}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 5**) showing a peak at -19 ppm.

- Figure 4.5** ^{29}Si NMR of **Compound 6**, showing peaks at -69.5, -69.2, -67.9, -67.21, -67.15, -67.0, -66.7, -60.0, -58.4, -57.3, -55.6, -21.67, 11.39 ppm, insets show close-up of the peaks representing the structure of **Compound 6**.
- Figure 4.6** ^{29}Si NMR of **Compound 8**, displaying peaks at -67.11, -66.98 and -58.18 ppm.
- Figure 4.7** ^{29}Si NMR of **Compound 10**, showing peaks at -73.77, -70.08, -69.23, -65.56, -64.75, -61.11, -58.77 and -50.35 ppm.
- Figure 4.8** Thermal decomposition graph showing the weight loss and derivative curve of **Compound 4** after thermal treatment to 900 °C and 300 °C.
- Figure 4.9** TEM images of **Compound 4** after 300 °C thermal treatment; a), b) and c) at x50,000 magnification; d) at x25,000 magnification.
- Figure 4.10** Histogram showing size distribution of nanoparticles formed by thermolysis of **Compound 4** to 300 °C.
- Figure 4.11** Solid state photoluminescence spectra of **Compound 4** before (black) and after (red) thermolysis treatment to 300 °C, $\lambda_{ex} = 457$ nm.
- Figure 4.12** Thermal decomposition graph showing the weight loss and derivative curve of **Compound 6** after thermal treatment to 900 °C and 350 °C.
- Figure 4.13** TEM images of **Compound 6** after 350 °C thermal treatment; a) and b) at different magnifications.
- Figure 4.14** Histogram showing size distribution of nanoparticles formed by thermolysis of **Compound 6** to 350 °C.
- Figure 4.15** Solid state photoluminescence spectra of **Compound 6** before (black) and after (red) thermolysis treatment to 350 °C, $\lambda_{ex} = 488$ nm.
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- Scheme 4.1** Synthesis of lanthanide disiloxanediolates *via* the ‘silylamide’ route.¹⁴
- Scheme 4.2** Schematic presentation of the preparation of **Compound 1** [$\text{Ph}_2\text{Si}(\text{OLi})_2$].
- Scheme 4.3** Schematic presentation showing the preparation of $[\text{Ln}(\text{N}(\text{SiMe}_3)_2)_3]$, where $\text{Ln} = \text{Eu}$ (**Compound 2**) and Yb (**Compound 3**).
- Scheme 4.4** Schematic presentation of the reaction between **Compound 1** and $\text{Ln}(\text{OSO}_2\text{CF}_3)_3$, where $\text{Ln} = \text{Eu}$ or Yb , forming $[\text{Eu}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 4**) and $[\text{Yb}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 5**) in two separate experiments.
- Scheme 4.5** Schematic presentation of the synthesis of **A**: trisilanol ligand ($\text{R} = c\text{-C}_6\text{H}_{11}$); and **B** and **C**: its by-products.
- Scheme 4.6** Preparation of **Compound 6** (suggested structure), using trisilanol **Ligand A**, where $\text{R} = c\text{-C}_6\text{H}_{11}$, $n = 1, 2$.
- Scheme 4.7** Preparation of **Compound 7**, a suspected bimetallic cage structure, using **Compound 6** and **Compound 3**, where $\text{R} = c\text{-C}_6\text{H}_{11}$, $n = 1, 2$.
- Scheme 4.8** Preparation of lithiated silsesquioxane structure (**Compound 8**), Yb -silsesquioxane complex (**Compound 9**) and Yb-Eu -silsesquioxane cage structure (**Compound 10**), where $\text{R} = \text{cyclohexyl}$.

Chapter 5 Magnetic Nanomaterials as Potential MRI Contrast Agents

- Figure 5.1** (a) Scheme showing the preparation of polyelectrolyte-stabilised magnetite nanoparticles;⁹ (b) and (c) TEM images of the polyelectrolyte-stabilised magnetite nanoparticles in the presence of an external magnetic field.⁸
- Figure 5.2** (a) and (b) TEM images, (c) and (d) AFM images of the magnetic wire-like structures stabilised with a positively charged polyelectrolyte poly(2-vinyl N -methylpyridinium iodide).¹⁹
- Figure 5.3** Structure of poly(sodium-4-styrene) sulfonate (PSSS), $n=70,000$.
- Figure 5.4** (a) and (b) TEM images and (c) histogram showing size distribution of cobalt ferrite nanoparticles prepared using heat and magnetic stirring; (d) and (e) TEM images and (f) histogram showing size distribution of cobalt ferrite nanoparticles prepared using ultrasonic treatment.
- Figure 5.5** Raman spectra of samples of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red).

- Figure 5.6** XRD pattern of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red) which correspond with the JCPDS database for CoFe_2O_4 .
- Figure 5.7** Magnetisation curves of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red); inset shows close-up of hysteresis loop.
- Figure 5.8** TEM images of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1: (a) Sample 1; (b) Sample 2; (c) Sample 3; (d) Sample 4; (e) Sample 5; (f) close-up of sample 2 showing vesicle arrangement.
- Figure 5.9** Histograms showing size distribution of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1; (a) to (e) represent samples 1-5 sequentially.
- Figure 5.10** Graph showing increasing primary particle size with increasing metal to monomer ratio.
- Figure 5.11** TEM images of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1 in the presence of a magnetic field at x 10,000 magnification: a) Sample 1; b) Sample 2; c) Sample 3; d) Sample 4; e) Sample 5; f) Sample 4 at x 400 magnification.
- Figure 5.12** FTIR spectra of PSSS-cobalt ferrite nanocomposites samples 1-5, prepared according to Table 5.1.
- Figure 5.13** Raman spectra of PSSS-cobalt ferrite nanocomposites samples 1-5, prepared according to Table 5.1.
- Figure 5.14** Typical XRD pattern for sample of PSSS-stabilised cobalt ferrite nanoparticles which corresponds with the JCPDS database for CoFe_2O_4 .
- Figure 5.15** Typical magnetisation curve of sample of PSSS-stabilised cobalt ferrite nanoparticles.
- Figure 5.16** ^1H NMRD profiles for the stable CoFe_2O_4 suspensions: samples 1 (■), 2 (●), 3 (▲), 4 (◆) and 5 (◀), prepared according to Table 5.1. The relaxivities have been calculated in terms of the iron content of the samples (according to Equation 1).

- Figure 5.17** Low frequency relaxivity of the suspensions plotted as a function the hydrodynamic size as measured by PCS: samples 1 (■), 2 (●), 3 (▲), 4 (◆) and 5 (◄). The error bars represent one standard deviation in d_{hyd} . The straight line is a least squares fit to the data; $y = -0.72(9)x + 343(25)$, $R^2 = 0.95$.
- Figure 5.18** (a) and (b) TEM images and (c) histogram showing size and size distribution of manganese ferrite nanoparticles.
- Figure 5.19** Raman spectrum of manganese ferrite nanoparticles prepared by co-precipitation.
- Figure 5.20** XRD pattern of manganese ferrite nanoparticle prepared by co-precipitation which corresponds with the JCPDS database for MnFe_2O_4 .
- Figure 5.21** Magnetisation curve of manganese ferrite nanoparticles prepared using co-precipitation.
- Figure 5.22** (a) and (b) TEM images of PSSS-manganese ferrite nanocomposite at different magnifications and (c) histogram showing the size distribution of the sample.
- Figure 5.23** (a) and (b) TEM images of PSSS-manganese ferrite nanocomposite in the presence of a magnetic field at different magnifications.
- Figure 5.24** Raman spectrum of PSSS-manganese ferrite nanocomposite.
- Figure 5.25** XRD pattern of PSSS-manganese ferrite nanocomposite which corresponds with the JCPDS database for MnFe_2O_4 .
- Figure 5.26** Magnetisation curve of PSSS-manganese ferrite nanocomposite.
- Figure 5.27** ^1H profile of the stable MnFe_2O_4 suspension. The relaxivity has been calculated in terms of the iron content of the sample (according to Equation 1).
- Figure 5.28** NMRD profiles for PSSS-magnetite nanoparticle suspensions with diameters of 6.5 ± 1 nm (■), 7.0 ± 1.1 nm (○) and 7.1 ± 1 nm (△), solid line represents a simulation for a superparamagnetic nanoparticle dispersion with $d_{\text{TEM}} = 12$ nm, $\Delta E_{\text{anis}} = 1$ GHz, and $M_s = 49 \text{ Am}^2/\text{kg}$.⁹

Scheme 5.1 Reaction sequence showing the preparation of cobalt ferrite nanoparticles using co-precipitation.

Scheme 5.2 Reaction sequence showing the preparation of manganese ferrite nanoparticles using co-precipitation.

Table 5.1 Characteristics of PSSS-stabilised cobalt ferrite nanocomposite samples.

Table 5.2 Relaxivity values, r_1 , at 20 MHz for commercially available MRI contrast agents compared to our polyelectrolyte stabilised nanocomposites.

Chapter 6 Multimodal Magnetic Core-Shell Nanostructures

Figure 6.1 (a) Preparation of magnetic nanowires and (b) schematic representation of the structure of magnetic nanowires stabilised with a polyelectrolyte.¹⁹

Figure 6.2 TEM images of (a) hollow silica shells with magnetite nanoparticle core and (b) hollow silica shells with silica nanoparticle core prepared using vesicle templating method.²⁰

Figure 6.3 TEM images (a) and (b) magnetite nanoparticles, (c) sample 1, (d) sample 2 and (e) sample 3, prepared according to Table 6.1.

Figure 6.4 Histograms showing size distribution of (a) magnetite nanoparticles; (b) sample 1; (c) sample 2 and (d) sample 3, prepared according to Table 6.1.

Figure 6.5 XRD pattern for magnetite nanoparticles synthesised by co-precipitation, which corresponds with the JCPDS database for Fe_3O_4 .

Figure 6.6 Magnetisation curves of samples of magnetite and silica coated magnetite nanoparticles at 293 K; inset shows absence of hysteresis, demonstrating superparamagnetism. Samples prepared according to Table 6.1.

Figure 6.7 TEM images of (a) cobalt ferrite nanoparticles; (b) sample 4 and (c) sample 5, prepared according to Table 6.2.

Figure 6.8 Histograms showing size distribution of (a) cobalt ferrite; (b) sample 4 and (c) sample 5, prepared according to Table 6.2.

Figure 6.9 TEM images of (a) manganese ferrite nanoparticles and (b) sample 6, prepared according to Table 6.2.

- Figure 6.10** Histograms showing size distribution of (a) manganese ferrite nanoparticles and (b) sample 6, prepared according to Table 6.2.
- Figure 6.11** XRD patterns for cobalt ferrite (black) and manganese ferrite (red) nanoparticles prepared by co-precipitation, which correspond to the JCPDS database for CoFe_2O_4 and MnFe_2O_4 respectively.
- Figure 6.12** Magnetisation curves for cobalt ferrite and silica coated cobalt ferrite at 293 K; inset (a) shows very narrow hysteresis loop for all samples; inset (b) shows the saturation magnetisation difference between samples with different size silica shells. Samples prepared according to Table 6.2.
- Figure 6.13** Magnetisation curves for manganese ferrite and silica coated manganese ferrite (sample 6) at 293 K; inset shows absence of hysteresis loop for both samples. Samples prepared according to Table 6.2.
- Figure 6.14** TEM images of (a) silica coated magnetite; (b) FITC-linked silica coated magnetite; (c) silica coated cobalt ferrite; (d) FITC-linked silica coated cobalt ferrite; at x50,000 magnification.
- Figure 6.15** UV-visible absorption spectra of samples of FITC-bound silica coated magnetic nanoparticles and free FITC dye.
- Figure 6.16** Photoluminescence spectra of samples of FITC-bound silica coated nanoparticles and free FITC dye, $\lambda_{\text{ex}} = 488 \text{ nm}$.
- Figure 6.17** Electron microscope images of A549 cells incubated with $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites ($53 \pm 11 \text{ nm}$); images (a) to (i) at different magnifications; arrow indicates particles inside various organelles.
- Figure 6.18** Confocal images of A549 cells incubated with $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites ($53 \pm 11 \text{ nm}$).
- Figure 6.19** (a) TEM image and (b) HAADF STEM image of ‘nanorattle’ structures.
- Figure 6.20** ‘Hollow’ structure: (a) HAADF STEM image with red arrow across which EELS linescan experiment was carried out; (b) Graph showing intensity of Si (blue line), C (green line) and O (red line) signals across the linescan experiment; (c) STEM signal graph showing intensity of signal.

- Figure 6.21** ‘Non-hollow’ structure: (a) HAADF STEM image with red arrow across which EELS linescan experiment was carried out; (b) Graph showing intensity of Si (blue line), C (green line) and O (red line) signals across the linescan experiment; (c) STEM signal graph showing intensity of signal.
- Figure 6.22** TEM images of PSSS-stabilised cobalt ferrite nanoparticles before coating showing monodispersity and no intrinsic alignment in the absence of a magnetic field.
- Figure 6.23** (a) and (b) Silica coating on cobalt ferrite nanoparticles – nanowires have been formed and coated with silica; (c) Silica coated nanowires which show non-parallel arrangement; and (d) Silica coated nanowires which have been aligned parallel to one another in the presence of an external magnetic field.
- Figure 6.24** TEM images of silica coated nanowires formed: (a, b, c) using sample 1 PSSS-CoFe₂O₄ (images taken at different magnifications); and (d, e, f) using sample 2 PSSS-CoFe₂O₄ (images taken at different magnifications) which produce nanowires which have a higher aspect ratio and a more ordered appearance. Nanowires prepared using samples of PSSS-CoFe₂O₄ according to Table 6.3.
- Figure 6.25** (a) and (b) Titania coating on cobalt ferrite nanoparticles – nanowires have been formed and coated with titania; (c) Titania coated nanowires which show non-parallel arrangement; and (d) Titania coating nanowires which have been aligned parallel to one another in the presence of an external magnetic field.
- Scheme 6.1** Reaction sequence showing the preparation of magnetite nanoparticles using co-precipitation.
- Scheme 6.2** Representation of preparative procedure used to coat magnetic nanoparticles with a silica shell.
- Scheme 6.3** Preparation of FITC-APTES fluorescent moiety.
- Scheme 6.4** Covalently linked FITC molecule on silica coated magnetic nanocomposite.

- Scheme 6.5** Experimental setup for the preparation of magnetic nanowires from magnetic nanoparticles using magnets. The inset shows the alignment of the magnetic nanoparticles into nanowires and their coating which occurs by a chemical reaction initiated at the interface, triggered by the movement of the magnetic particles through the interface. DCM is dichloromethane solvent and NH_4OH is ammonium hydroxide solution.
- Table 6.1** Characteristics of magnetite and silica coated magnetite with different shell thicknesses.
- Table 6.2** Characteristics of ferrite and silica coated ferrite nanoparticles with different shell thicknesses.
- Table 6.3** Details of PSSS-stabilised CoFe_2O_4 nanoparticles, their composition and characteristics.

Chapter 7 Conclusions and Future Work

- Figure 7.1** SEM image of single silica coated magnetite nanoparticle (indicated by the arrow) on a nano-SQUID machine (at x 50,000 magnification).

Appendix 1

- Figure A1.1** FTIR spectra of samples A-E prepared according to Table 3.1, Chapter 3.
- Figure A1.2** FTIR spectra of samples prepared according to the statistical study 1.
- Figure A1.3** FTIR spectra of samples prepared according to the statistical study 2.
- Figure A1.4** FTIR spectra of samples A-D prepared according to Table 3.5, Chapter 3.

Appendix 2

- Figure A2.1** ^7Li NMR of **Compound 1** showing peaks at 1.56 and -0.20 ppm in a ratio of approximately 5:1.
- Figure A2.2** FTIR spectra of diphenylsilanediol and **Compound 1**.
- Figure A2.3** FTIR spectra of **Compounds 2** and **3**.
- Figure A2.4** FTIR spectra of **Compounds 4** and **5**.
- Figure A2.5** FTIR spectrum of $(c\text{-C}_6\text{H}_{11})_7\text{Si}_7(\text{OH})_3$ **Ligand A**.

Figure A2.6 ^1H NMR spectrum of **Compound 6**.

Figure A2.7 ^{13}C NMR spectrum of **Compound 6**.

Figure A2.8 FTIR spectrum of **Compounds 6** and **7**.

Figure A2.9 FTIR spectrum of **Compounds 8** and **10**.

Figure A2.10 Thermal decomposition graph showing the weight loss and derivative curve of trisilanol **Ligand A** [$(\text{c-C}_6\text{H}_{11})_7\text{Si}_7(\text{OH})_3$].

Figure A2.11 FTIR spectra of **Compound 4** before and after thermolysis to 300 °C.

Figure A2.12 FTIR spectra of **Compound 6** before and after thermolysis to 350 °C.

Figure A2.13 FTIR spectra of **Compound 7** before and after thermolysis to 300 °C.

Figure A2.14 Raman spectra of **Compound 6** before and after thermolysis to 350 °C.

Figure A2.15 Raman spectra of **Compound 7** before and after thermolysis to 300 °C.

Figure A2.16 Raman spectra of **Compound 4** before and after thermolysis to 300 °C.

Appendix 3

Figure A3.1 FTIR spectra of CoFe_2O_4 nanoparticles prepared by co-precipitation using heat and mechanical stirring (black) and ultrasound treatment (red).

Figure A3.2 FTIR spectra of MnFe_2O_4 nanoparticles prepared by co-precipitation using heat and mechanical stirring.

Figure A3.3 FTIR spectra of PSSS- MnFe_2O_4 nanoparticles prepared by co-precipitation.

Appendix 4

Figure A4.1 FTIR spectra of magnetite and silica coated magnetite nanocomposites, samples 1, 2 and 3, prepared according to Table 6.1, Chapter 6.

Figure A4.2 Raman spectra of magnetite and silica coated magnetite nanocomposites, samples 1, 2 and 3, prepared according to Table 6.1, Chapter 6.

Figure A4.3 FTIR spectra of cobalt ferrite and silica coated cobalt ferrite nanocomposites, samples 4 and 5, prepared according to Table 6.2, Chapter 6.

Figure A4.4 FTIR spectra of manganese ferrite and silica coated manganese ferrite nanocomposites, sample 6, prepared according to Table 6.2, Chapter 6.

- Figure A4.5** Raman spectra of cobalt ferrite and silica coated cobalt ferrite nanocomposites, samples 4 and 5, prepared according to Table 6.2, Chapter 6.
- Figure A4.6** Raman spectra of manganese ferrite and silica coated manganese ferrite nanocomposite, sample 6, prepared according to Table 6.2, Chapter 6.
- Figure A4.7** FTIR spectra of cobalt ferrite nanoparticles used to prepare the nanowires, silica coated magnetic nanowires, samples 1 and 2 of magnetic nanowires prepared according to Table 6.3, Chapter 6, and titania coated magnetic nanowires.
- Figure A4.8** Raman spectra of cobalt ferrite nanoparticles used to prepare the nanowires and titania coated magnetic nanowires.

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Chapter 1

Introduction

1.1 The Best Things Come in Small Packages – Why Nanomaterials are the Next ‘Big’ Thing

The last two decades have seen an increasing demand for a new generation of high technology materials.¹ Nanoscale structures and materials have been the focus of attention for many years, thanks to their wide range of applications in many interdisciplinary domains including chemistry, physics, materials science, engineering, biology and medicine. The term ‘nanomaterial’ refers to any material which has at least one dimension less than 100 nanometres in size; a nanometre is one billion times smaller than a metre. To put this minute scale into perspective, we can compare some familiar items. For instance, a tennis ball is around 100 million times smaller than the Earth; similarly, nanomaterials are around 100 million times smaller than the size of a tennis ball. This can be seen in the schematic representation of a scale bar below (Figure 1.1).

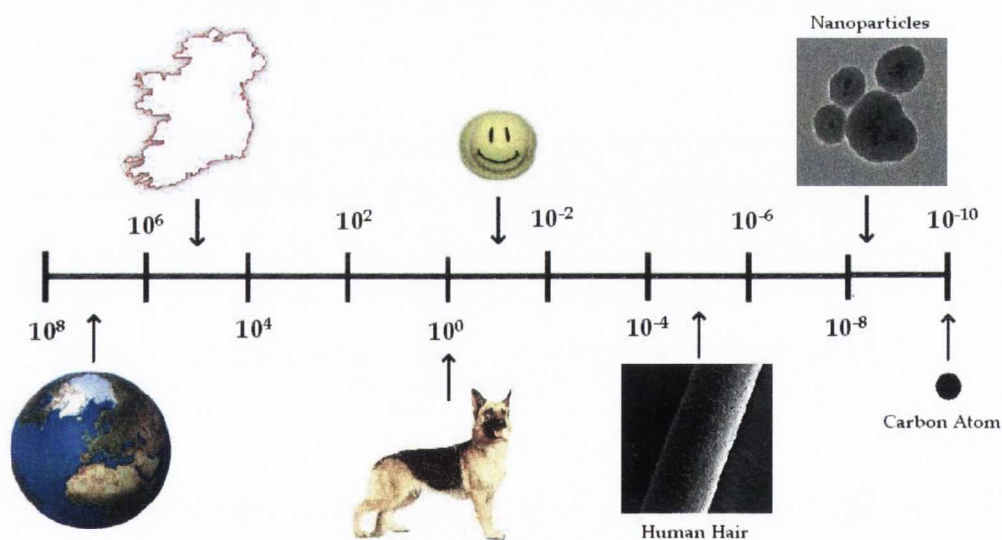


Figure 1.1: Schematic representation of a scale bar demonstrating the scale of nanomaterials.

Nanoscale materials can have controllable sizes, which can be tuned to the dimensions of cells (10-100 μm), viruses (20-450 μm), proteins (5-50 μm) or even genes (2 nm in width and 10-100 nm in length).² This makes them potentially extremely useful for biological applications, where nanomaterials can ‘get close’ to an object or site of interest and can be tailored to carry out specific tasks.

The properties and functions of nanostructures often differ drastically from their bulk counterparts. This can be due to their high surface area-to-volume ratio, surface tailorability, multifunctionality and improved solubility, all of which open a multitude of new possibilities for a wide variety of applications in different fields of science and technology. The intrinsic structural, optical, magnetic and biological properties of nanomaterials offer remarkable opportunities to study and regulate processes in an unprecedented manner.³

Nanostructures can be made from a wide variety of different materials, including oxides, metals and semiconductors.^{4,5} Their unique, often size-dependent properties can prove advantageous in a range of applications. For example, silica nanoparticles, which can be tuned to have variable porosity and architectures, have been developed as tools in molecular engineering and drug delivery,^{6,7} as well as separation technology.⁸ Iron oxide nanoparticles, such as magnetite (Fe_3O_4), possess a magnetic property called superparamagnetism, which makes them useful in drug delivery, magnetic resonance imaging and hyperthermic cancer treatment.⁹⁻¹¹ Other types of magnetic particles, such as FePt, have been used in high-density recording devices.^{12,13} Gold and silver nanostructures have proven useful as molecular sensors, catalysts and antibacterial agents.^{14,15} Semiconductor quantum dots (QDs) represent another class of nanostructures which have found uses in biomedicine, thanks to their size dependant characteristic spectral emission which is tuneable across a range of wavelengths. This allows them to be used as biolabels in fluorescent biological imaging.^{4,16} They have also been used as tumour targeting nanoparticles.¹⁷

Importantly, some nanomaterials have already been commercialised and utilised in industry. One example of this is Invitrogen, a company which manufactures non-toxic semiconductor QDs. These QDs emit light of a specific wavelength when excited; the wavelength of the light they emit is size-dependent and hence, colour-specific dots can be

prepared. These quantum dots can be used in a variety of applications, such as cell tracing, flow cytometry and *in vivo* and *in vitro* imaging.

1.2 Silica Based Nanomaterials

Silicate materials, which include both bulk and nanostructures, are those which consist of elements of silicon and oxygen. Elemental silicon does not occur freely in nature, but its compounds, silica and silicates, are abundant in the forms of sand, flint clay, slate *etc.* It is so plentiful that silicon is second only to oxygen in weight percentage of the earth's crust.^{18,19} Within the silicon group of compounds, there are a large variety of silicate materials, in which the SiO_4^{4-} tetrahedron is the basic unit. The Si^{4+} ion is coordinated by four ions in a tetrahedral coordination mode to form a SiO_4^{4-} ionic compound. The SiO_4^{4-} tetrahedra are linked together and only corner oxygens will be shared with other SiO_4^{4-} groups (Figure 1.2). If all the corner oxygens are shared with another SiO_4^{4-} tetrahedron, a framework structure develops with the basic structural group becoming SiO_2 . The minerals quartz, cristobalite, and tridymite are all based on this structure. Silicates can occur in many structures; they can occur singly or can connect by sharing oxygen atoms. This enables the formation of various structures, including chains, layers, rings or cages.

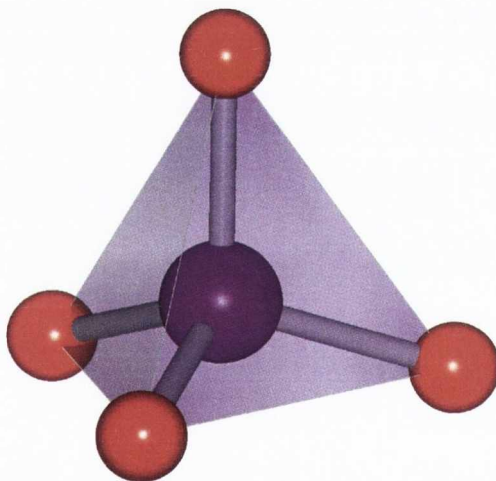


Figure 1.2: Structure of SiO_4^{4-} tetrahedron: purple sphere represents Si^{4+} ; red spheres represent O^{2-} .

Silicate-based materials are hence very attractive and thoroughly researched throughout the literature thanks to their profusion and hence low costs. In addition, their relative ease of preparation and their useful surface functionalities makes them an ideal starting point for further manipulation.

1.2.1 Silica Nanoparticles

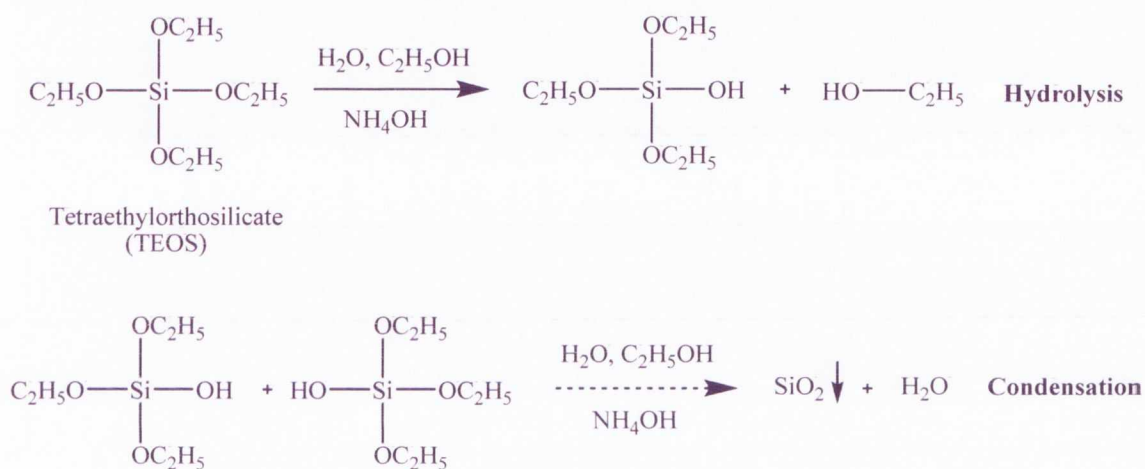
Silica nanoparticles occupy a prominent position in scientific research and in various industrial applications, such as catalysis,²⁰ electronic and thin film substrates,¹² electronic and thermal insulators,²¹ as well as humidity sensors.²² Amorphous silica, otherwise known as silica “gel”, is used when dehydrated as a drying agent, and a chromatographic and catalyst support material¹⁹ and is well documented both in research and industrial applications. The quality of many of these products is highly dependent on the structure, size and size distribution of the particles.

As silica (SiO_2) is generally believed to be a non-toxic material²³ and can be readily modified with various functional groups, it also carries great potential for use in biomedical applications.²⁴ For example, the surface of the silica can be modified to allow effective cellular transport, enabling drug delivery.²⁵ Surface modifications of the outer silica shell can also improve the particles’ ability to bind electrostatically to DNA, allowing it to be further used in drug delivery techniques.²⁶ As is the case in most nanoparticle applications, the particles’ morphology, average size, size distribution, and phase composition are considered to be the key properties that must be controlled.²⁷

1.2.2 Synthesis of Silica Nanoparticles

Silica nanoparticles have been synthesised in diameters ranging from nanometres to several microns. There are several different synthetic techniques which can be used to prepare nanoparticles. These include water-in-oil microemulsion,⁷ stirred bead milling,²⁸ synthesis by ‘fumed’ silica nanoparticles,²⁹ flame spray pyrolysis,²⁷ reverse micelle and sol-gel processing,³⁰⁻³² continuous microwave hydrothermal synthesis,³³ and self-assembly in basic solutions of organic and inorganic cations.³⁴ These techniques can yield nanoparticles which are small in size and have narrow size distributions. However, many of these can prove to be inefficient and costly processes. For this reason, the well-

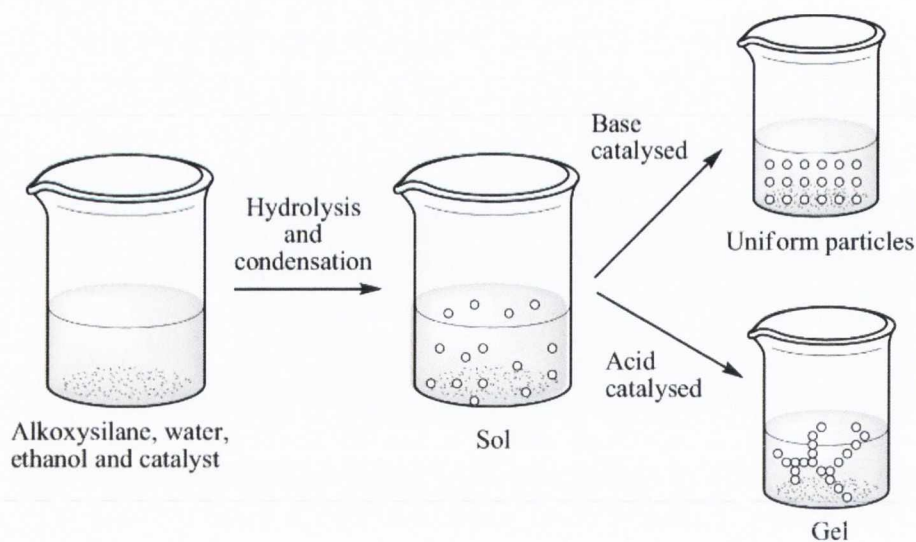
documented and less expensive Stöber method is the most widely-used approach for the fabrication of silica nanoparticles which are stable in aqueous suspension.³⁵ The Stöber method is a one-pot technique which involves the hydrolysis and condensation reaction of an alkoxy silane, typically tetraethylorthosilicate (TEOS), in ethanol and water, using an acidic or a basic catalyst (Scheme 1.1). The hydrolysis step of this reaction involves the partial hydrolysis of the alkoxy silane. Condensation occurs when two partially hydrolysed molecules link together. This part of the reaction can continue to build a larger and larger siloxane matrix *via* a polymerisation-style procedure.



Scheme 1.1: Preparation of silica nanoparticles (SiO_2) by hydrolysis and condensation of an alkoxy silane using a basic catalyst.

It is widely accepted that condensation takes place in such a way as to maximise the number of Si-O-Si bonds and minimise the number of terminal hydroxyl groups.³⁶ Therefore, rings of siloxanes are formed, followed by the addition of monomers to these and so, three-dimensional ‘nuclei’ particles are prepared – a silica sol. The behaviour of the silica sol during the subsequent polymerisation-style stage can differ depending on whether the pH is above or below 7, *i.e.* the reaction takes place in a basic or an acidic medium. In basic solution, the silica particles are appreciably more ionised and therefore particle growth occurs without aggregation or gelation. The three-dimensional nuclei particles undergo Ostwald ripening, which causes their subsequent growth in size and the

production of distinct uniform particles. In acidic solution, the silica particles aggregate into three-dimensional networks and form gels (Scheme 1.2).³⁶



Scheme 1.2: Preparation of a silica sol by hydrolysis and condensation and the subsequent formation of uniform silica particles or a gel in the presence of a basic or acidic catalyst, respectively.³⁶

In this thesis, we are interested in the preparation of nanoparticles of silica using the base catalysed hydrolysis and condensation reaction. This method generally yields silica nanoparticles which are between 100 nm and 1 μm in diameter. The resulting particle size and distribution of silica nanoparticles prepared in this way can be affected by several experimental parameters, including reactant concentration, heat and agitation.^{37,38,39} Reactant concentration is very important, as altering the concentration of the alkoxysilane, the catalyst or the water can affect the growth of the nanoparticles.⁴⁰ Stöber's original 1968 paper was the first to investigate this variation, noting that increasing the ammonium hydroxide concentration led to larger particle sizes.³⁵ Following this, Bogush and co-workers⁴¹ as well as other groups^{22,38} investigated further in order to establish a range of reagent concentrations which yield monodisperse silica particles.⁴¹ These reports offer a variety of results, many of which are contradictory. Similarly, increasing the temperature of the reaction and introducing different methods of agitation of the silica sol can alter the particles' growth. It has been shown that agitation can play a large role in the nucleation and growth of silica nanoparticles during their synthesis.³⁷ All these factors play important parts in the formation of silica nanoparticles and can affect the resultant particle size.

Reactant choice is also an important consideration. Indeed, the length of the alkoxy chain of the silane can have steric and inductive effects on the rate of condensation.³⁶ Similarly, it has been found that variation of solvents can affect the rate of the reaction. Short chain alcohols were found to have the fastest reaction rates.³⁵

The optimisation of the Stöber synthesis for the preparation of silica nanoparticles and nanostructures is still a hotbed of controversy. Reproducibility of many procedures in the literature are problematic, particularly for the synthesis of small sized (<100 nm) silica particles, which are advantageous for biomedical applications, such as drug delivery and as biomarkers. Therefore, this remains an interesting subject of investigation, as elucidation of a method to define appropriate parameters for the preparation of tailored particles could not only be used for silica, but could be broadened to an enormous variety of nano and microparticles and their properties.⁴²

Hollow nanostructures have become more prevalent in the literature in recent years, with the modification of well-known techniques to prepare them. Hollow silica spheres can be prepared using various procedures which can be broadly categorised into templated, self-templated and non-templated methods. Templated techniques rely on the initial preparation of a core-shell structure, whose internal core is subsequently dissolved or destructed by physical or chemical means. For example, such core-shell structures can be made with polymer or calcium carbonate core inside a silica shell, which can be calcined in order to remove the core.^{43,44} Self-templated mechanisms use their own internal structures as a 'template'. Hollow silica nanostructures made in this way begin as amorphous silica colloids which undergo a spontaneous morphology change from solid to hollow spheres due to their environment.^{45,46} Non-templated methods rely on the synthetic mechanism or procedure only. Hollow nanocrystals can be prepared through a mechanism analogous to the Kirkendall effect. The Kirkendall theory traditionally describes the formation of alloyed materials by atomic diffusion through vacancy exchange.⁴⁷ Prior to this, it was thought that atomic diffusion occurred *via* a direct exchange or a ring mechanism (Figure 1.3).⁴⁸

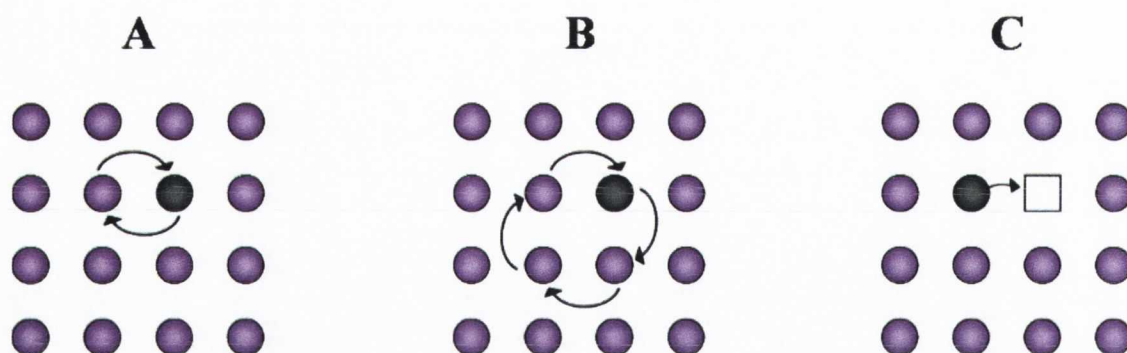


Figure 1.3: The atomic diffusion mechanism showing: a) direct exchange mechanism; b) ring mechanism and c) Kirkendall's vacancy mechanism.⁴⁸ Purple spheres represent atoms, grey spheres represent the atom undergoing diffusion, square represents a vacancy, arrows indicate movement of atoms during diffusion.

Kirkendall's theory shows the net directional flow of matter is balanced by an opposite flow of vacancies, which can condense into pores or voids.⁴⁹ Yin and co-workers used this idea to prepare hollow cobalt oxide nanocrystals from cobalt particles by relying on the diffusion of atoms to the surface and the formation of voids in the centre of these particles.⁴⁹ Hollow nanostructures may find a range of applications in fields such as catalysis and drug delivery as well as being highly useful as anti-reflective coatings on surfaces.^{45,50}

1.2.3 Luminescent Silica Nanoparticles

The synthesis of small silica nanoparticles is of particular importance due to their potential biological applications, where small, biocompatible particles (< 50 nm) are required. One application of such particles is biological labelling using fluorescent nanoparticles. A well-known example of bright, commercially available nanoparticles is the semiconductor QD. QDs have characteristic emission wavelengths and are quite photostable when compared to organic dyes, however, their toxicity restricts their use in many applications. Fluorescent silica nanoparticles encapsulating organic dyes present a less toxic alternative to these QDs. A wide variety of commercially available organic dyes make such fluorescent particles a credible alternative (Figure 1.4).⁵¹

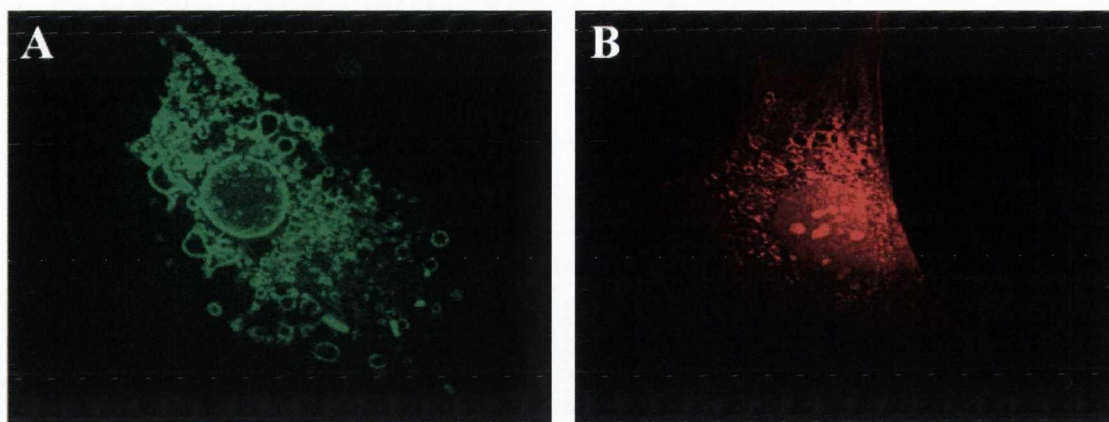
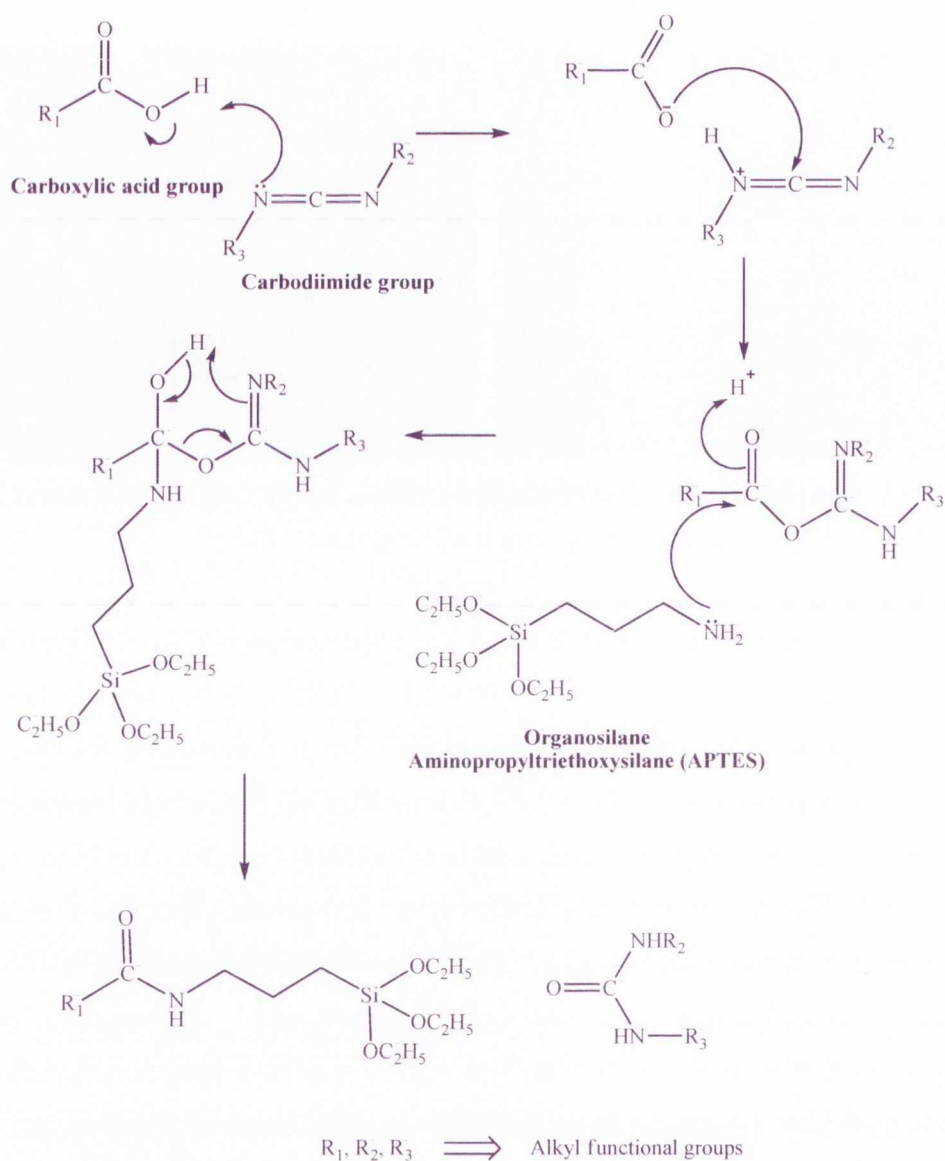


Figure 1.4: a) Confocal microscope image of QDs in live THP-1 cell;⁴ b) Confocal microscope image of porphyrin doped nanoparticles in osteoblast cells.⁵²

Hybrid organic/inorganic nanoparticles consisting of an organic dye with a silica shell have been the subject of research for many years. This is due to silica's stable shell which serves to protect the inner organic dye from external dangers and also provides a biocompatible and easily functionalised shell. One method used to incorporate a dye within a silica particle is by physical encapsulation, typically carried out using reverse microemulsion.⁵³ The drawback of this method is the non-covalent attachment of the dye, which often leads to subsequent leaking of dye, decreasing the luminescent intensity of the particle and exposing the dye to the surrounding environment.⁶ Alternatively, covalent attachment of the dye molecule by coupling the dye to a reactive organosilane group can be carried out – this can potentially avoid the issue of dye leakage. One of the first to demonstrate the incorporation of fluorescein dye into a silica particle *via* coupling to an organosilane was van Blaaderen and co-workers.⁵⁴ They have shown that the dye can be placed on the outer surface of particles or internally within layers of 'pure' silica. A series of dyes have since been incorporated into silica particles by this method.^{55,56} These dye-doped silica nanoparticles can be used as fluorescence nanosensors for metal ions, for cell tracking and have also been used as biomarkers.^{57,58}

Organic dyes can be attached to an organosilane group *via* a carbodiimide coupling reaction (Scheme 1.3). This mechanism involves the formation of a stable urea group (N-C=O) with the assistance of a carbodiimide molecule.



Scheme 1.3: Carbodiimide coupling mechanism of an organosilane to a carboxylic acid functional group.

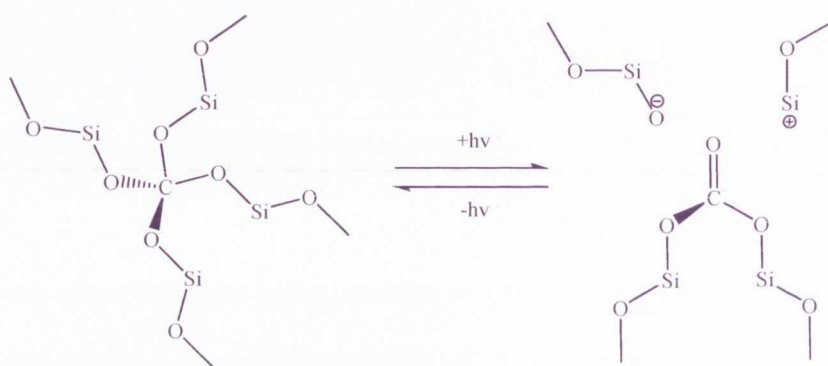
The use of silicon-based materials is synonymous with optoelectronic and photonic devices, with silicon dioxide being the most common material used in optical fibres. Silicon oxides do not, however, possess direct electron band transitions, and are therefore not luminescent.⁵⁹ Doping with appropriate materials can produce luminescent silicates capable of emission. Rare earth (RE) metals could be used to prepare such materials, since they possess some advantages over using traditional organic dyes, such as superior luminescent properties, including very long decay times, greater resistance to

photobleaching and sharp emission profiles.⁶⁰ Despite this, there appear to be few reports on the successful synthesis of fluorescent RE doped silica particles.^{61,62}

The luminescent properties of RE ions in a silica host matrix are of interest for both fundamental aspects and for the numerous applications concerning optoelectronics and optical communication technology as well as potential biomedical techniques. For example, RE doped glasses are used as optical fibres, amplifiers, and solid state lasers.^{63,64} Most of the applications of these materials are based on the unique fluorescence emission of RE ions related to the closed 4f electronic configuration of RE elements. However, the clustering of RE dopant ions in glass hosts frequently results in self-quenching of the fluorescence. RE ions have high coordination numbers and must share the limited number of oxygen atoms in the silica matrix. Clusters formed through RE-O-RE bonding facilitate energy dissipation and cross relaxation resulting in non-radiative recombination at many sites in the glass. This clustering restricts the RE doping level in silica based materials and thereby limits their applications.^{65,66} Within the silica matrix, some of the silicon atoms may be replaced by aluminium atoms, this type of structure is called an aluminosilicate, examples of which include feldspars and zeolites, which are widespread in nature. The aluminosilicate template is one method of preparing RE doped silica-based materials. The addition of alumina to the silica matrix improves its properties and facilitates the incorporation of RE metals by preventing their clustering and preventing formation of RE-O-RE bonds.⁶⁷

As previously discussed, luminescent silica nanoparticles can be made from a host of different materials, however these offer unique benefits but also disadvantages. Organic dyes are plentiful, low cost, can be chosen according to specific emission characteristics and offer the potential for modification if necessary. They do, however, photobleach and can leak from host particles. RE metals possess strong emission, long decay times and are more resistant to photobleaching. Their downfalls lie in their potential toxicity if free ions enter the body, as well as their high cost and complexity of synthesis. The solution to these problems would be to use a material with an intrinsic or defect emission which cannot leak out or be photobleached and possesses long term stability. QDs have such intrinsic luminescence, but are so inherently toxic to cells that they are unlikely to ever be used as a viable medical tool.

Some bulk silica gels possessing strong emission have been prepared by several groups.^{68,69} These bulk silica matrices are prepared by the acid catalysed hydrolysis and condensation of an alkoxy silane, followed by high temperature sintering to prepare silicate glasses. Green *et al.* have prepared such materials from various alkoxy silane precursors which are highly emissive.⁶⁸ They attribute this photoluminescence to a carbon substitutional defect within the silica matrix, formed due to the high heat treatment used during preparation (Scheme 1.4).



Scheme 1.4: Carbon substitutional defect in silica matrix responsible for the bright white luminescence observed by Green *et al.*⁶⁸

The nature and origin of the photoluminescent centre is still the subject of great debate. The carbon defect theory postulated by Green *et al.* in 1997 has not yet been confirmed and is not the only suggestion. Other theories which have been hypothesised and investigated include non-bridging oxygens and oxygen vacancies,⁷⁰ triplet and singlet states of Si-OH,⁷¹ hydrogen related centres,⁷² hydrocarbon contamination,⁷³ dioxasilirane [$=\text{Si}(\text{O}_2)$] and silylene [$=\text{Si}:$] centres,^{74,75} and silicon carbide defects.^{69,73}

Nanostructures such as nanotubes have been prepared using this sol-gel method which show similar emission.^{76,77} In addition, this phenomenon has been reported in nanoparticles which were commercially sourced and subsequently sintered at high temperatures.^{78,79} However, these particles were not structurally characterised after heat treatment and therefore are not credibly still nanostructures, despite their emission characteristics. Aqueous-based silica nanoparticles with such emission properties have not been reported to date. Nevertheless, such strong, non-photobleaching, non-toxic silicate

materials present an excellent opportunity for the development of silica nanostructures for a wide variety of applications, not only for optics, but as tools in biomedicine.

1.3 Silanols

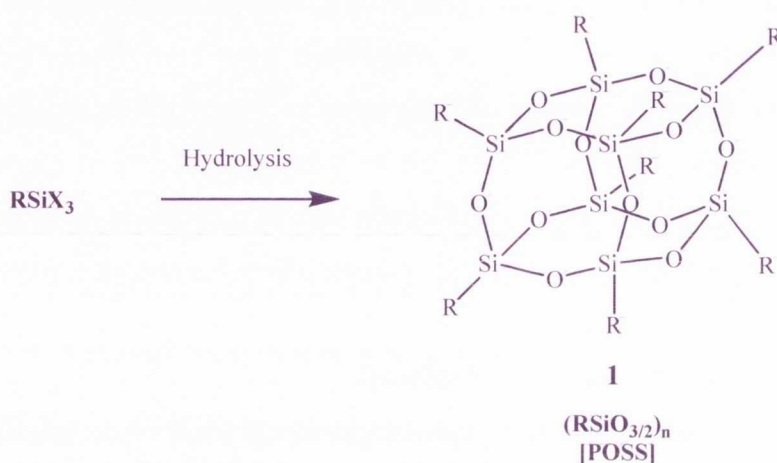
Silanols are organosilicon compounds containing the Si-OH functionality. Organosilanols are analogous to alcohols, the most common being simple silanols, e.g. triorganosilanols [R_3SiOH], silanediols [$R_2Si(OH)_2$] and silanetriols [$RSi(OH)_3$] (where R is an organic group). These classes of compounds have been widely studied and are precursors to materials with a variety of important uses, which will be highlighted later.^{80,81} Compounds containing the silanol group are well-known not only in nature, but also in industrial processes in which polymeric materials such as polydimethylsiloxanes (silicones) and silica gels are produced by condensation reactions of a reactive silanol species.

1.3.1 Structure and Preparation of Silanols

Silanediols can be prepared by the straight-forward hydrolysis reaction of a silane such as dichlorodimethylsilane. Silanediols have been used to prepare a multitude of metallasiloxane materials, as the presence of a metal in the siloxane framework can enhance its catalytic and conductive properties.⁸² Of the known silanediols, the compounds [$Ph_2Si(OH)_2$] and [$t-Bu_2Si(OH)_2$] are most frequently used for the preparation of metallasiloxanes. Although the silanol functional groups are found in a wide variety of situations, compounds containing such groups are relatively rarely isolated as discrete molecular species, but can exist as hydrogen-bonded molecules.⁸³

Polyhedral oligosilsesquioxane (POSS) compounds are a particularly interesting class of three dimensional silsesquioxanes of the general formula $(RSiO_{1.5})_n$ (where n is an even number and R can be many different groups, either organic or inorganic). Since their discovery in 1946,⁸⁴ many stoichiometrically well-defined POSS frameworks have been reported,⁸⁵ including a wide variety of frameworks with synthetically useful functional groups. Interest in polyhedral silsesquioxanes has greatly intensified over the past 20 years, as new methods have been devised for preparing useful compounds and the pool of known frameworks is ever expanding.^{81,86,87}

These POSS cage compounds can be prepared by the hydrolysis of trifunctional organosilicon monomers, such as $[\text{RSiCl}_3]$ or $[\text{RSi(OMe)}_3]$ (Scheme 1.5).⁸⁴ These monomers undergo polycondensation in solution to yield completely condensed POSS cage frameworks with *closo*-cubic geometry, resembling a sphaerosilicate molecule. POSS (**1**) is an important compound as it can be used as a building block for a variety of silica-based materials, such as polymeric rubbers.

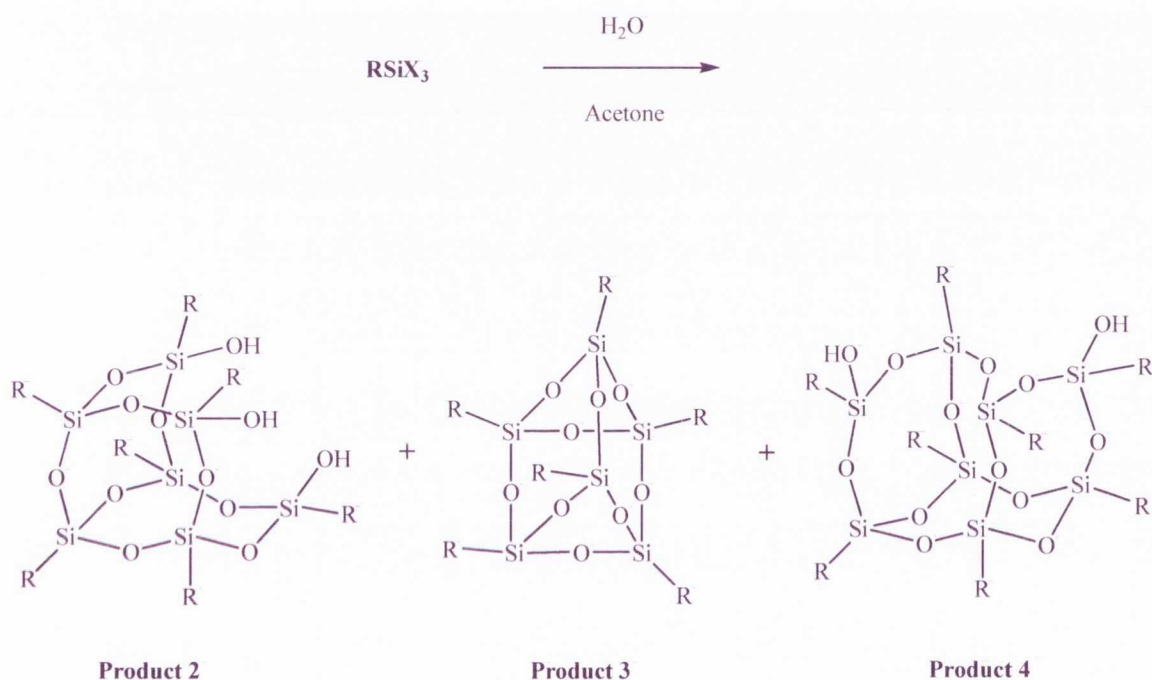


Scheme 1.5: Synthetic route for the preparation of polyhedral oligosilsesquioxanes (POSS), where **R** = any organic or inorganic functionality, **X** = Cl or OMe, **n** = degree of polymerisation.

Two distinct framework structures of these silsesquioxane cages can be formed: ‘fully condensed’ or ‘incompletely condensed’. Fully condensed silsesquioxane cages are closed structures, with no active surface silanol functional groups, such as the one shown in Scheme 1.5 above. Incompletely condensed silsesquioxane cages resemble their fully condensed counterparts, but with one dramatic difference in terms of their structure and chemical formula. Incompletely condensed frameworks are ‘missing’ a corner or section of their framework and thus possess reactive Si-OH groups which are potentially capable of forming additional Si-O-Si linkages through the elimination of water. These cage structures can be prepared by the controlled hydrolytic condensation of RSiX_3 and careful isolation of the products (Scheme 1.6). The formation of POSS compounds is dependent on a series of factors, including the concentration of monomer, the solvent, the nature of the R and X functional groups and the reaction temperature. Due to the strong mutual effects

of many of these factors, it is difficult to elucidate the complex mechanism of their formation.

The preparation of incompletely condensed silsesquioxane cages was first reported by Brown *et al.* in 1965, who isolated a series of polyhedral silsesquioxanes of $R_7Si_7O_9(OH)_3$, where R = cyclohexyl or phenyl, bearing three free Si-OH groups (Scheme 1.6).^{88,89} Further work on this preparative strategy by Feher and co-workers yielded a detailed investigation into the products yielded by the hydrolysis method and their reactivity with various metals.⁸⁶ The procedure which yields the highly useful trisilanol ligand (Scheme 1.6, Product 2), however, possesses the drawback of taking up to three years to proceed to completion, due to its kinetically controlled mechanism of formation. Alternatively, the corresponding cyclopentyl and cycloheptyl derivatives of these siloxanes can be obtained in relatively shorter periods of time.⁹⁰



Scheme 1.6: Synthetic route for the production of incompletely condensed trisilanol ligand (2) and the by-products produced (3, 4), where R = cyclohexyl, X = Cl or OMe.

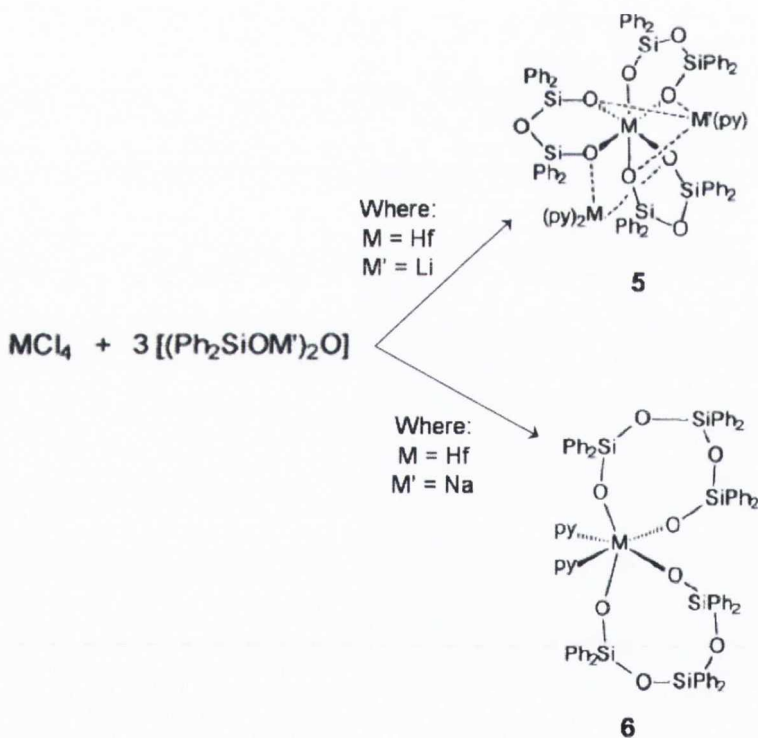
The reactive silanol functional groups as well as the flexible nature of the Si-O-Si backbone of incompletely condensed silsesquioxanes make these compounds very

important, especially when considering the preparation of completely condensed metallasilsesquioxanes.

1.3.2 Structure and Preparation of Metallasiloxanes

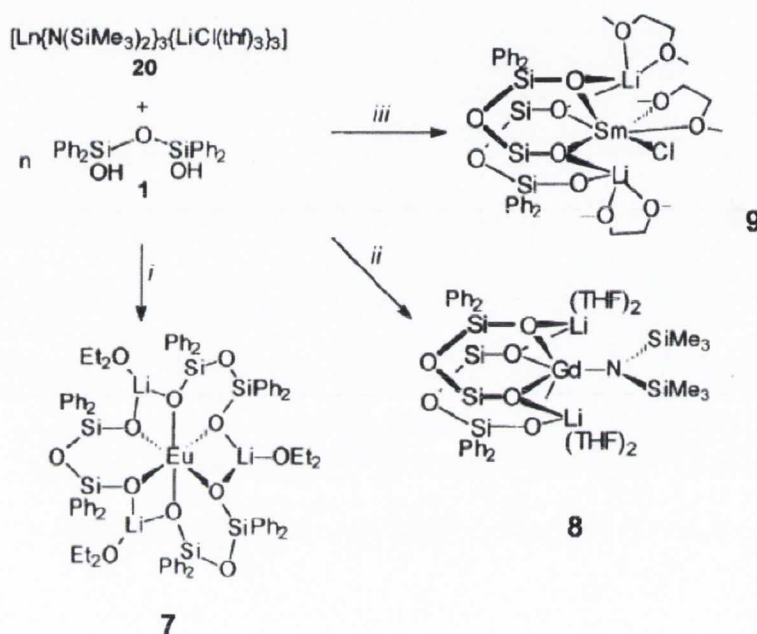
Metallasiloxanes contain Si-O-M groups (where M is a main group metal, transition metal or f-element). Metallasiloxanes with a variety of structures have been derived from silanediols, including those with alkali metals, main group metals and transition metals at their centres.⁸²

Metallasiloxane complexes can adopt various structures which are dependent on the nature of the siloxane ligand used and the preferred coordination of the metal centre. For example, the heterobimetallic complex (**5**) was produced upon reaction of HfCl_4 with $\text{Ph}_2\text{Si}(\text{OLi})\text{OSiPh}_2(\text{OLi})$; whereas the complex $[\text{Ph}_2\text{Si}(\text{OSiPh}_2\text{O})_2]_2\text{Hf}(\text{py})_2$ (**6**) was the only product when HfCl_4 was treated with $\text{Ph}_2\text{Si}(\text{ONa})\text{OSiPh}_2(\text{ONa})$ (Scheme 1.7).⁹¹



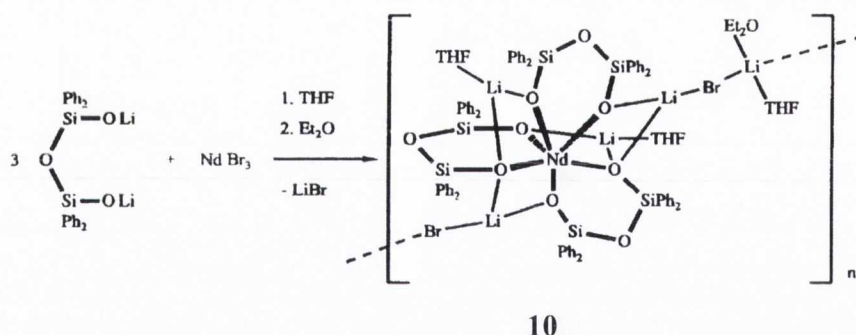
Scheme 1.7: Preparation of Group 4 metal disiloxanediolates.⁹¹

Research into lanthanide based siloxane derivatives has become more prevalent and over the last two decades, various f-element based metallasiloxanes have been prepared. The ‘silylamide’ route was found to be the method of choice for making such species.⁹¹ Firstly, silylamide precursors containing f-elements can be prepared readily *via* the reaction of anhydrous lanthanide trichlorides with three equivalents of $\text{LiN}(\text{SiMe}_3)_2$ in a dry organic solvent. The silylamide precursors $\text{Ln}[\text{N}(\text{SiMe}_3)_2]_3[\text{LiCl}(\text{thf})_3]_3$, where Ln = any lanthanide metal, can then be employed to prepare lanthanide-based metallasiloxanes (Scheme 1.8).⁹²



Scheme 1.8: Synthesis of lanthanide disiloxanediolates using the ‘silylamide’ route; complexes 7-9, Reaction *i*: Ln = Eu, $n = 3$, toluene- Et_2O solvent; reaction *ii*: Ln = Gd, $n = 2$, THF solvent; reaction *iii*: Ln = Sm, $n = 2$, DME solvent (four phenyl groups have been omitted from the structures of **8** and **9** for clarity).⁹²

Another route to prepare these metallasiloxane materials is through the reaction of anhydrous lanthanide trihalides with the $\text{Ph}_2\text{Si}(\text{OLi})\text{OSiPh}_2(\text{OLi})$ ligand. The preparation of a heterobimetallic neodymium disiloxanediolate (**10**) using this method is shown in Scheme 1.9.⁹¹



Scheme 1.9: Preparation of a neodymium disiloxanediolate (**10**) using the $\text{Ph}_2\text{Si}(\text{OLi})\text{OSiPh}_2(\text{OLi})$ ligand.⁹¹

1.3.3 Structure and Preparation of Metallasilsesquioxanes

Metallasilsesquioxanes containing Si-O-M groups (where M is the main group metal, transition metal or f-element) have been envisaged as molecular analogues of metal silicates due to their astonishing geometrical relationship.^{82,91,93}

Silsesquioxane complexes with trivalent M^{3+} ions in their structure show varied coordination chemistry. The capping undertaken by the incompletely condensed trisilanol ligand (**2**) has the ability to dictate unusual coordination geometries, often forming dimers.⁹⁴ Depending on the metal centre and its coordination requirements, metallasilsesquioxanes can adopt different structures, as shown in Figure 1.5 below. Many M^{3+} ions adopt the dimer structure **A**, with a coordination number of 4. Cleavage of a dimer can yield structure **B**. Some metals can assume the dimer structure **C**, where the metal exists with a coordination number of 6. Very large M^{3+} ions achieve a coordination number of 6 through coordination with framework oxygen atoms, as in structure **D**. In addition, structure **E** is undertaken when π -interactions favour a trigonal geometry. These are amongst the simplest geometries that metals can take on within dimers, others can involve complexation and coordination to other ions and solvent molecules.

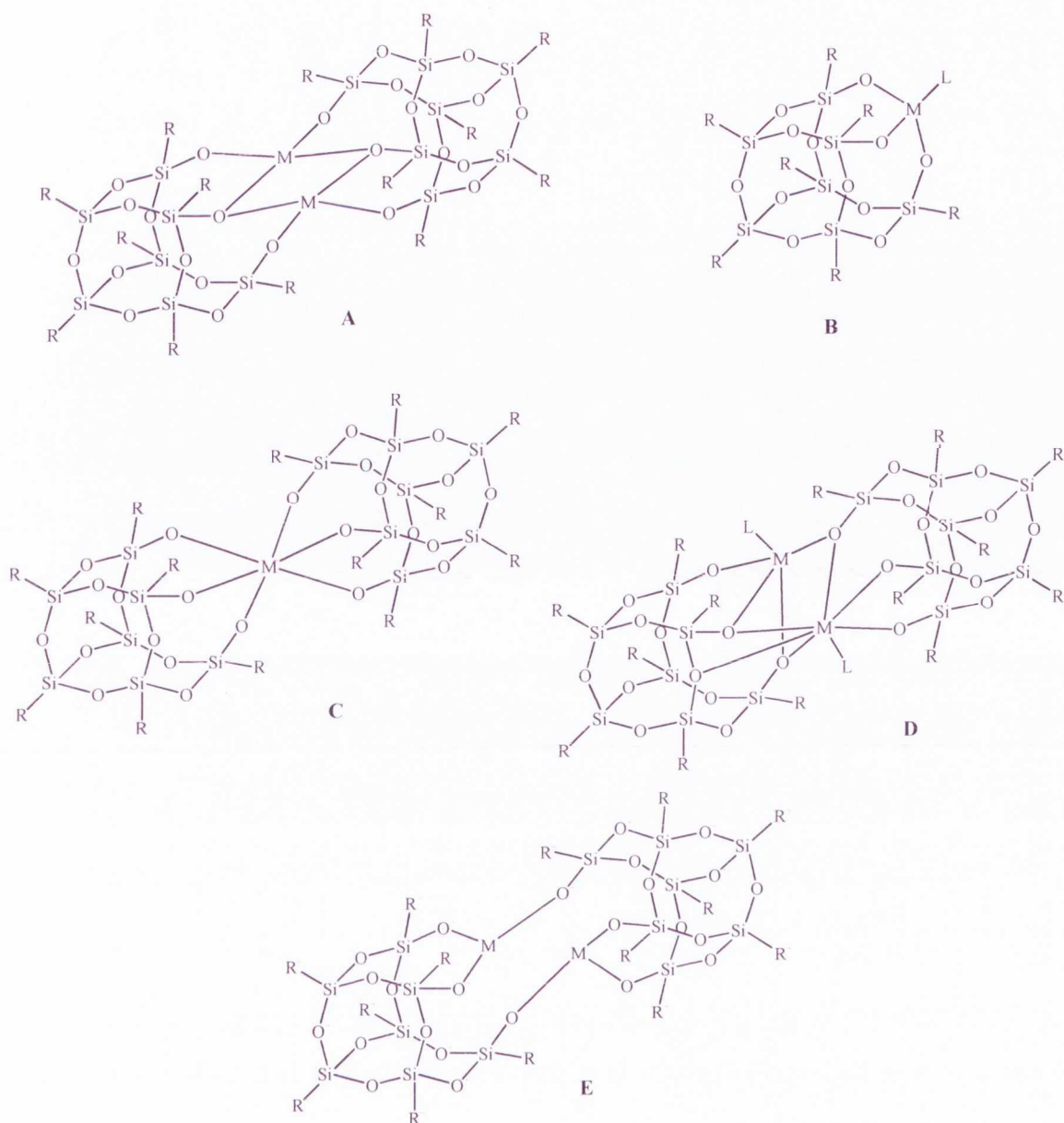


Figure 1.5: Possible structures of incompletely condensed trisilanol ligand with metals with different coordinations, where M = trivalent metal ion, R = any organic group, L = ligand.⁹⁴

A host of metallasilsesquioxanes have been prepared over the last two decades, incorporating main group, transition and lanthanide metals into their structures.⁹⁵ One generally acceptable route to rare earth metal based metallasilsesquioxanes involves the treatment of the silanol ligand (2) with lanthanide trichlorides in the presence of triethylamine. However, the ‘silylamide’ preparative strategy is the most popular, whereby metal silylamide groups are reacted with the silanol ligand (2).⁹⁶ Some examples of

metallasilsesquioxanes prepared using these methods are shown in Figure 1.6 and include complexes such as the heterobimetallic metallasilsesquioxane $[[[(c\text{-C}_6\text{H}_{11})_7\text{Si}_7\text{O}_{12}]\text{Li}(\text{OCMe}_2)_2\text{Zr}]]$ (**11**),⁹⁶ the vanadyl compound $[\text{Cy}_7\text{Si}_7\text{O}_{12}\text{VO}]$ (**12**),⁹¹ and the bis(silsesquioxane) titanium complex, $[\text{Cy}_7\text{Si}_7\text{O}_{11}(\text{OSiMe}_3)]_2\text{Ti}$ (**13**).⁹¹

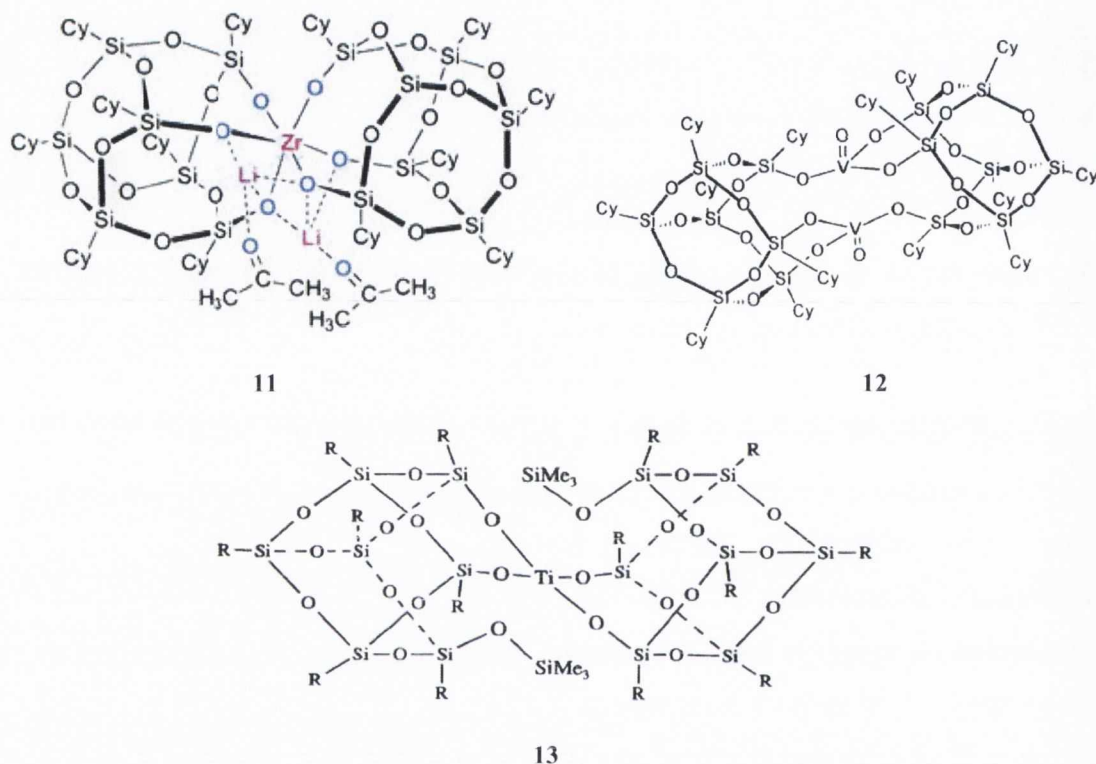


Figure 1.6: Examples of metallasilsesquioxane complexes which have been prepared using different methods: $[[[(c\text{-C}_6\text{H}_{11})_7\text{Si}_7\text{O}_{12}]\text{Li}(\text{OCMe}_2)_2\text{Zr}]]$ (**11**);⁹⁶ $[\text{Cy}_7\text{Si}_7\text{O}_{12}\text{VO}]$ (**12**);⁹¹ $[\text{Cy}_7\text{Si}_7\text{O}_{11}(\text{OSiMe}_3)]_2\text{Ti}$ (**13**).⁹¹

It is widely accepted that structural characterisation of metallasiloxanes, especially complex cage-based structures, is a difficult task in the absence of X-ray crystallographic data.⁹⁷ Often, due to the sensitive nature of the compounds and solvent solubility issues, crystal growth can be a challenge. The use of nuclei-specific NMR spectroscopy, for example ^{29}Si NMR, offers the potential to assist characterisation of such structures. Despite the promise of this widely used technique, issues can still arise. In particular, should a complex contain a paramagnetic metal ion, unpredictable NMR spectral shifts can occur, making analysis and assignment of peaks problematic. The use of a glass NMR tube

is the norm for spectral acquisition, however the large signal that this possesses due to its composition can often mask weak signals from a sample. As a result, investigations into the use of other techniques, such as heteronuclei and solid state NMR are of great importance.

1.3.4 Applications of Metallasiloxanes

Silica supported metal complexes are very important due to their use in catalysis.⁸⁶ In fact, metallasilsesquioxane materials have been used as catalysts for many years, with the first report in 1991 of a catalytically active metallasilsesquioxane being a vanadium-based compound which catalyses olefin polymerisation.⁹⁸ Titanium silsesquioxanes also display catalytic activity, where they have been shown to be reactive in the epoxidation of cyclohexane.⁹⁹ Lanthanide metal based catalysts could hold advantages over using traditional transition metal-based catalysts such as Group 4 and 5 derivatives, which are active catalysts for alkene polymerisation, due to their resistance to the harsh conditions of activation.¹⁰⁰

The use of silica-supported catalysts is widespread in heterogeneous catalysis.¹⁰¹ For example, chromium-based silicate catalysts are used for the coordination of the polymerisation of ethylene¹⁰² and silica-supported metallocenes can catalyse olefin polymerisation.¹⁰³ Due to their importance and wide-spread use in commercial and industrial applications, an understanding of the chemistry of catalysts such as these at a molecular level is extremely important. However, this can prove difficult due to the lack of structurally relevant, well-defined homogeneous model systems. The incompletely condensed trisilanol ligand (**2**) bears a close symmetrical similarity to silica and silaceous compounds, such as cristobalite and tridymite forms of SiO_2 .⁹³ Therefore, this class of compounds is a very useful model for silica surfaces. In addition, by virtue of these similarities, it is expected that metallasiloxanes derived from these silanols could serve as excellent homogeneous model systems for many heterogeneous silica-supported catalyst systems. This offers an opportunity to develop a molecular level understanding of heterogeneous catalysts which could lead to better strategies for control of selectivity, activity and catalyst lifetime.^{82,93}

Photoluminescent silsesquioxane complexes have applications in optics as well as biomedical applications. POSS-derived compounds have been used in organic light emitting diodes (OLEDs), where they can be employed as an electron and hole carrier transport layer or as the light emitting portion of the OLED device.⁹⁵ In addition, POSS-molecules can behave as insulating or packing materials to modify or enhance the behaviour of systems; one example of this the use of a POSS-derivative to prevent the diffusion of quantum dots into polyelectrolyte multi-layers.¹⁰⁴ Some POSS derivatives have even been used as additives in inks, where they serve to improve certain properties, such as hydrophobicity or abrasion.⁹⁵

POSS-based compounds have also proven to be useful biomaterials, finding applications in areas of medicine such as anti-bacterial agents, bypass grafts, DNA detection probes and have even shown potential as drug delivery systems.⁹⁵

The inorganic nature and multiple reactive functionalities of POSS make these compounds ideal for use in the construction of organic-inorganic hybrid nanomaterials.¹⁰⁵ Materials such as these can be produced by mixing POSS with a polymer or covalent bonding onto a polymer backbone. In addition, the relative ease of functionalisation of the POSS molecule with a wide variety of functional groups allows its use as a cross-linking agent in polymeric systems.

It is well-known that the decomposition of fully condensed oligosilsesquioxanes using thermal treatment yields SiO_2 . In fact, thin films of SiO_2 have been grown by CVD methods.¹⁰⁶ Materials such as these could be used in semiconductor technology, where films of this nature are often used as protective shields against environmental factors, for electrical isolation and for anti-reflective coatings. As such, the preparation of nanostructured materials based on these POSS structures could open up a new avenue for the preparation of nanomaterials with a variety of properties.

Greater exploitation of these unique oligosilsesquioxane compounds has in the past been severely restricted by the limitation of the synthetic routes followed. Unfortunately, many routes of preparation employ multi-step procedures using a large excess of silane, long reaction times and then provide very low yields of the desired products. Recently however, silsesquioxanes have attracted new interest, largely because new synthetic

strategies have drastically reduced the reaction times, the number of steps involved, and have improved their yields.

With this vast range of important potential applications and unique characteristics, there has been much research on the chemistry of silanols and their metal derivatives.^{80,81} A wealth of novel Si-O-M based polyhedral frameworks have been uncovered over the last two decades and exciting supramolecular assemblies are emerging. These compounds are proving to be ideal starting materials for the next generation of two- and three-dimensional metallasiloxanes and nanomaterials with novel structural features and interesting properties.

1.4 Magnetic Nanoparticles

Magnetic nanomaterials represent an extremely popular field of nanotechnology with very promising prospects in a variety of applications due to their unique size-dependent magnetic properties, which differ from their bulk counterparts. Magnetic materials are currently employed in technology such as magnetic recording devices, where information can be stored on nanometre-sized magnetic grains.^{107,108} The preparation of smaller sized magnetic grains means stored data takes up less space, which is one of the main objectives of the billion-dollar computer and microchip industries. Magnetic nanomaterials also offer exciting opportunities in biomedical research. In particular, they have the potential to improve the quality of magnetic resonance imaging (MRI), by providing a new class of contrast agents which provide enhanced imaging capabilities. Magnetic nanoparticles which heat up when subjected to an alternating magnetic field could be used for hyperthermic cancer treatment.¹¹ External magnetic fields could bring magnetic nanoparticles internalised in the body to a site of interest to allow site-specific drug delivery.⁹

The magnetic nanoparticles which will be synthesised and investigated in this project include magnetite (Fe_3O_4), cobalt ferrite (CoFe_2O_4) and manganese ferrite (MnFe_2O_4). These iron oxide based nanomaterials have many attractive qualities, including their small sizes, magnetic properties, aqueous synthetic preparation and the relative ease with which they can be further functionalised with materials which can provide them with additional useful properties.

1.4.1 Properties of Magnetic Nanoparticles

We will focus mainly on the three types of magnetic nanoparticles of interest to us in this thesis, namely magnetite (Fe_3O_4), cobalt ferrite (CoFe_2O_4) and manganese ferrite (MnFe_2O_4).

1.4.1.1 Structure

Many iron oxides, including magnetite (Fe_3O_4), cobalt ferrite (CoFe_2O_4) and manganese ferrite (MnFe_2O_4), belong to the ferromagnetic oxide (or ferrite) family. Ferrites exist as ionic compounds, consisting of arrays of positively charged iron and metal ions and negatively charged oxygen ions. Ferrites adopt a spinel structure based on a cubic close packed (ccp) array of oxide ions. The ccp structure consists of three layers, each geometrically distinct from one another (ABCABC...). The third layer (C) is placed in the octahedral holes created from the stacking of layers A and B. In this way, the octahedral and tetrahedral holes alternate throughout the structure (Figure 1.7). These spinel structures can be classified into two types, depending on how the divalent ions occupy the structure. If the divalent ions occupy only tetrahedral sites, it is referred to as a 'normal' spinel structure; if they occupy only octahedral sites, then the spinel is said to be 'inverse'.

Magnetite (Fe_3O_4) contains both Fe^{2+} and Fe^{3+} ions and has an inverse spinel structure, where the divalent Fe^{2+} ions occupy half of the octahedral (B) sites and the trivalent Fe^{3+} ions occupy the remaining octahedral (B) sites and all the tetrahedral (A) sites. Cobalt ferrite (CoFe_2O_4) also has an inverse spinel structure. In its case, the Co^{2+} ions occupy the octahedral (B) sites and the Fe^{3+} ions occupy the remaining octahedral (B) sites and all the tetrahedral (A) sites. In both instances, the inverse framework is adopted due to the larger divalent ions' preference to occupy the roomier octahedral positions. The adopted structure of manganese ferrite has been a source of controversy,¹⁰⁹ but it is now agreed that manganese ferrite exists as a mixed spinel structure, with a large percentage being normal and the rest being inverse.¹¹⁰ The percentage of inversion can be affected by the synthetic method used.¹¹¹ The normal spinel structure of MnFe_2O_4 would have Mn^{2+} ions occupying the tetrahedral (A) sites and Fe^{3+} ions occupying the octahedral (B) sites.

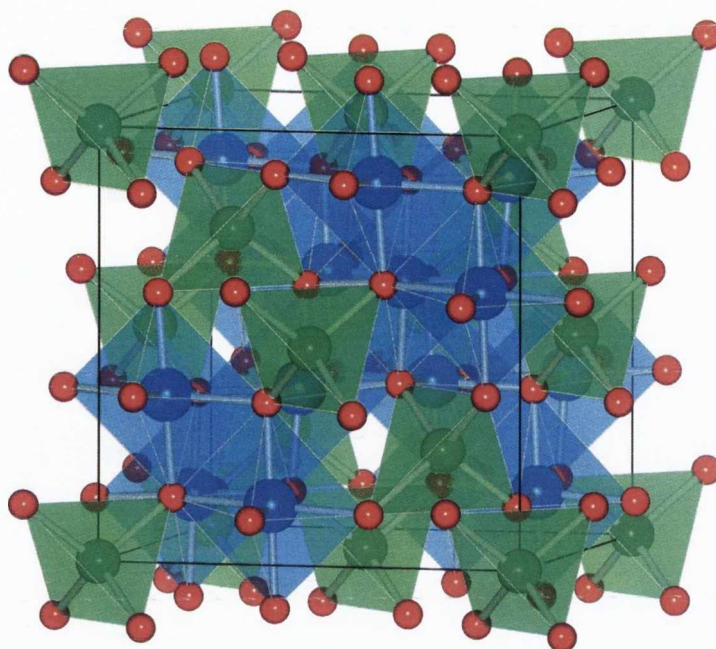


Figure 1.7: Spinel structure of an iron oxide lattice. Red spheres represent oxygen atoms, green spheres represent tetrahedral (A) sites and blue spheres represent octahedral (B) sites.

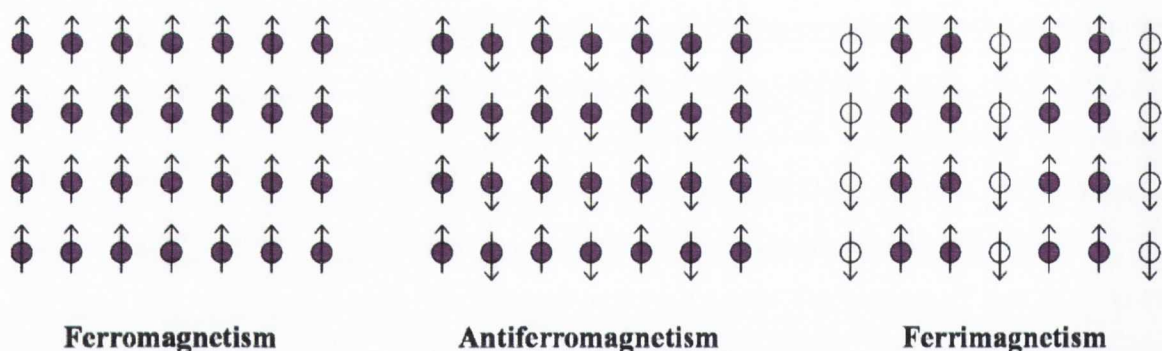
1.4.1.2 Magnetism

Magnetism was first observed up to 2500 years ago, with legends originating from ancient Greece, China and India describing a strange phenomenon of black stones which attracted iron.¹¹² The discovery of their distinctive north and south polarity lead to their use as a primitive compass and the name lodestone or ‘leading stone’. We refer to this now as magnetite. The magnetic field surrounding magnetic materials such as magnetite can be represented by invisible field lines and other objects can respond to that field.

Magnetism arises from the intrinsic spin property of electrons, which results in every electron possessing its own spin magnetic moment as well as an orbital magnetic moment due to the movement of the electrons within orbitals. Within any given atom, two electrons occupying an atomic orbital must have opposite spins and therefore their magnetic moments cancel each other out. This is the case for diamagnetic materials, which possess no unpaired electrons and hence no atomic magnetic moments, therefore displaying no magnetism in the absence of an applied magnetic field. When a magnetic field is

applied, a small negative moment is induced (-10^{-6}); removal of the field immediately reduces this induced moment.

Paramagnetic materials possess unpaired electrons which are randomly oriented throughout the sample. Application of a magnetic field causes the magnetic moments to align in the direction of that field and proportional to it. Iron oxides undergo a transition to a magnetically ordered state below a certain temperature; they become ferromagnetic, antiferromagnetic or ferrimagnetic.¹¹³ The temperature at which this transition occurs is termed the Curie temperature (T_C) for ferro- and ferrimagnetic substances or the Néel temperature (T_N) for antiferromagnetic substances. Ferro- and ferrimagnetic materials are strongly attracted by a magnetic field due to interactions between neighbouring spins causing the moments of their unpaired electrons to be aligned even in the absence of an applied magnetic field. Ferromagnetic materials have an overall net magnetic moment due to the parallel alignment of the electron spins. Antiferromagnetic materials have spins which are aligned anti-parallel to one another, leading to an overall magnetic moment of zero. Ferrimagnetic materials also have spins aligned anti-parallel to one another; however, the different spins have unequal magnetic moments, giving these materials a net magnetic moment. An illustration of the different spin states giving rise to these magnetic behaviours is shown in Scheme 1.10.



Scheme 1.10: Illustration of the varieties of magnetic order. Purple and white spheres represent Fe atoms with unequal magnetic moments, arrows indicate spin orientation.¹¹³

Ferro-, antiferro- and ferrimagnetic materials all possess a domain structure. A domain is defined as a region in which all the spins are either parallel or antiparallel and neighbouring domains have different spin orientations. The application of a large enough

magnetic field causes the spins in the domains to become aligned in the same direction. The point at which all of the domains are parallel to each other is termed saturation magnetisation. Graphical representation of a material’s magnetisation (σ) against the strength of an applied magnetic field (H) gives rise to magnetisation curve with a characteristic sigmoidal shape, where the saturation magnetisation is reached if the applied magnetic field is large enough (Figure 1.8). The two branches of the curve correspond to the magnetisation and demagnetisation processes. The term coercivity refers to the strength of the reverse field required to demagnetise a ferro- or ferrimagnetic material. Remanence refers to the residual magnetisation of a material at 0 applied magnetic field. Ferro- and ferrimagnetic materials often display hysteresis due to their overall net magnetic moments. For nanomaterials, the shape of the magnetisation curve is often dependent on the nanoparticle size. If particles are of a large size (1 μm), hysteresis is observed, while for smaller sizes ($< 10\text{ nm}$), no hysteresis is observed due to a phenomenon called superparamagnetism. Superparamagnetic materials are those which behave as ferro- or ferrimagnets in the bulk state, but below sizes of 20 nm, they consist of individual magnetic domains. Superparamagnetism arises as a result of magnetic anisotropy, *i.e.* the spins are aligned along a preferred crystallographic direction. If enough energy is supplied, magnetism can be reversed along this axis, therefore no hysteresis is observed.

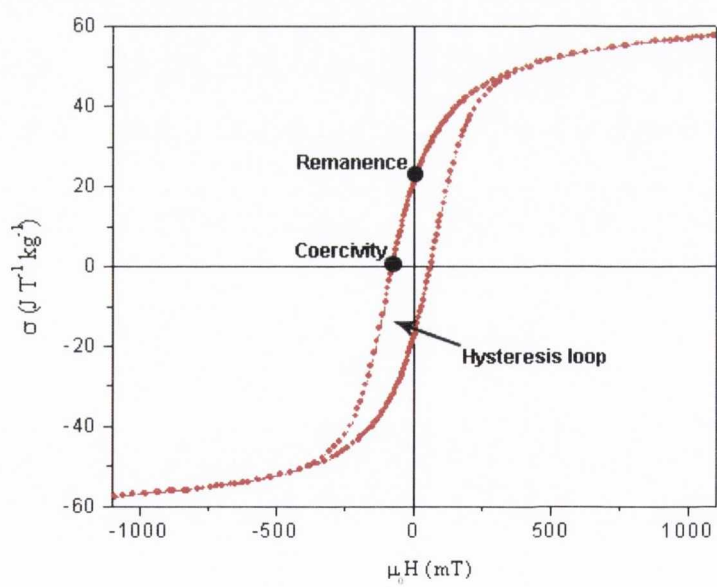


Figure 1.8: Magnetisation curve of ferromagnetic cobalt ferrite nanoparticles displaying a hysteresis loop.

1.4.2 Synthesis of Magnetic Nanoparticles

The importance of magnetic nanoparticles in a variety of fields has led to numerous investigations into different preparative strategies over the last two decades. Consideration of the synthetic procedure is of vital importance depending on the application of the nanoparticles. For example, ferrofluids of magnetic nanoparticles can be used in high powered loudspeakers or motors, where they remain in a confined space between moving machinery. For such applications, nanoparticles should be suspended in synthetic oil. On the other hand, ferrofluids for medical applications, such as MRI contrast agents, are required to be in a biocompatible solvent, such as water. For both these applications, long-term stability is vital, as precipitation of the particles can clog up and damage delicate machinery and blood vessels and organs in the body. As such, it is necessary to tailor their preparation specifically for these purposes.

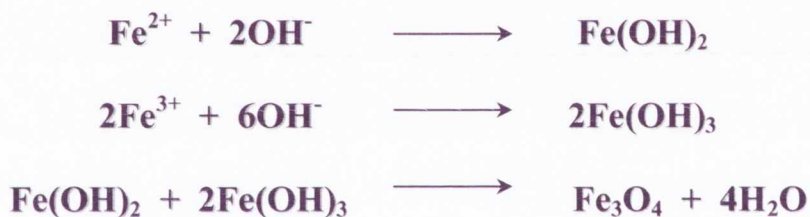
There are currently a plethora of synthetic methods which have been developed to prepare shape-controlled, highly stable, and monodisperse magnetic nanoparticles. These include micelle syntheses,¹¹⁴ microemulsions,¹¹⁵ sol-gel syntheses,¹¹⁶ sonochemical reactions,¹¹⁷ hydrothermal reactions,¹¹⁸ thermal decomposition,¹¹⁹ high temperature solution phase reaction,¹²⁰ flow injection syntheses,¹²¹ and co-precipitation.¹²²

Co-precipitation is a facile and convenient route to iron oxides such as Fe₃O₄ from aqueous salt solutions by the addition of a base in an inert atmosphere at room temperature or higher (Scheme 1.11).¹²³ The first controlled preparation of Fe₃O₄ by co-precipitation in the absence of stabilisers was carried out by Massart in 1981.¹²⁴ The experimental procedure for the preparation of iron oxide based ferrites is relatively straight forward. It involves the precipitation of M²⁺ and Fe³⁺ salts in a strict ratio of 1:2 in deoxygenated water by the addition of a base, such as ammonium hydroxide or sodium hydroxide (where M²⁺ is a divalent metal, such as Fe²⁺, Co²⁺ or Mn²⁺). It is important to carry out the co-precipitation in an inert environment to prevent the oxidation of M²⁺ before required. It is also important to use the metal salt solutions immediately to prevent aging of Fe³⁺ to goethite (α-FeOOH).¹²⁵



Scheme 1.11: Co-precipitation technique to produce iron oxides, where M = Fe²⁺, Co²⁺, Mn²⁺ or other divalent metal ion.

The size, shape and composition of the nanoparticles produced depends upon the salts used, the M^{2+}/Fe^{3+} ion ratio (where M^{2+} is a divalent metal ion), the reaction temperature and pH, as well as the ionic strength of the medium. Once these parameters are fixed, high quality, reproducible nanoparticles can be prepared. Particle size distribution within a sample, however, can be more difficult to control by this method. It is well-known that the co-precipitation mechanism proceeds by two steps: a short burst of nucleation, followed by slow particle growth.^{113,126} Nucleation occurs when the concentration of the metal ions reaches critical supersaturation levels. The subsequent growth step is rate determining as it is limited by the rate of diffusion of solutes to the crystal surface. At high pH, the precipitation of Fe^{2+} to Fe^{3+} can be broken down into a multiple-step scheme (Scheme 1.12).¹²⁷ The preparation of various ferrites follows this scheme, such as $CoFe_2O_4$ and $MnFe_2O_4$, where the divalent ion is Co^{2+} or Mn^{2+} respectively.



Scheme 1.12: Preparation of magnetite nanoparticles *via* co-precipitation.¹²⁷

The co-precipitation technique provides a one-step method which can be used to synthesise iron oxide based nanoparticles with various divalent metals in their structure. One of the advantages of this technique is the large quantities in which the magnetic nanoparticles can be produced. The resulting nanoparticles can be easily stabilised with ligands or surfactants to provide stable colloidal suspensions of magnetic particles.

1.4.3 Coating Magnetic Nanoparticles

Despite the significant volume of research into the synthesis of magnetic nanoparticles of different compositions and sizes, their long-term stability in suspension without aggregation and precipitation is often problematic. In fact, upon formation,

precipitated ferrite particles tend to aggregate quickly. The most popular method to guard against this difficulty is surface modification. Surface modification can be carried out during the synthesis of the nanomaterial, or can be added subsequently.

The use of a surfactant or polymer is the most common technique to stabilise nanoparticles in suspension. Surfactant or polymer stabilisers can be covalently bound or physically adsorbed onto the surface of a nanoparticle, relying on electrostatic or steric repulsion to ensure that nanoparticles overcome van der Waals and any magnetic interactions to remain stable in a colloidal state.¹²³

Polymers hold a prominent position as stabilising agents due to their biocompatibility. In fact, polymer-coated magnetic nanoparticles have been investigated as potential contrast agents in MRI.^{128,129} Polymers are particularly useful as stabilisers as they provide templates for the production of nanoparticle assemblies and can be added either during or after the synthesis of the nanoparticles.¹³⁰⁻¹³³ Hybrid aggregates comprising charged co-polymers and nanoparticles as well as polyelectrolyte-stabilised nanomaterials have been reported.¹³³⁻¹³⁵ Polyelectrolytes have been a popular template choice for the preparation of self-assembled nanostructured materials,¹³⁶ and specifically for aqueous magnetic nanoparticle suspensions.¹³⁷⁻¹³⁹ This is due to their flexible chemistry and ability to direct a 1-D nanoparticle arrangement with a high aspect ratio.^{129,140} Recently, this has been shown with DNA and the polyelectrolyte poly(sodium-4-styrene) sulfonate (PSSS); where the polyelectrolytes act as assembly directors and aqueous colloidal stabilisers (Figure 1.9).^{128,129}

Another advantage of a stabilising agent is its ability to provide a protective barrier around a nanoparticle, acting as a shield against environmental factors which could cause degradation or damage to the material. However, polymer stabilisers are not ideal for this role, as they do not provide a robust impenetrable shell; additionally, their susceptibility to degradation at high temperatures limits their use.

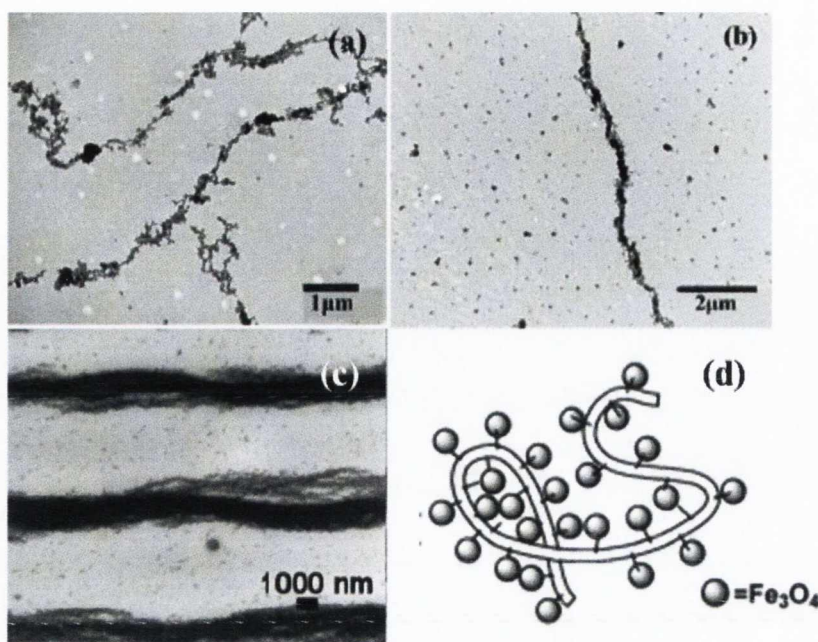


Figure 1.9: a) TEM image of single-stranded DNA stabilised Fe_3O_4 nanoparticles; b) TEM image of single stranded DNA stabilised Fe_3O_4 nanoparticles in the presence of an applied magnetic field;¹⁴¹ c) PSSS-stabilised Fe_3O_4 nanoparticles in the presence of an applied magnetic field¹²⁸ and d) schematic presentation of PSSS-stabilised Fe_3O_4 .¹²⁹

An alternative coating material is metal. Recent research has shown that nanoparticles can be coated with a layer of metal, which serves to protect and stabilise. For example, Ban and co-workers have coated Fe nanoparticles with a thin layer of Au to reveal nanocomposites with a core-shell structure.¹⁴²

By far the most prevalent material that is used to stabilise nanoparticles is silica. Silica as a coating material offers an unparalleled opportunity for the enhancement of colloidal properties and functions, offering so-called core-shell designs and vast synthetic versatility. It has been used to encapsulate many different colloidal systems, including nanoscale metals, semiconductor QDs, magnetic and ceramic nanoparticles.^{6,143} Its popularity is due to its high stability, especially in aqueous solutions, its strength, versatility, optical transparency, porosity and processability, allowing further modification. When employed in core-shell coatings, it not only offers its cargo protection from external influences, but it prevents leaching of it to the immediate environment and helps to avoid unwanted interactions. The most well-known core-shell structure is that of the Earth, whose outer crust is made up primarily of silica (~61 % of its total weight contribution).¹⁴³

It is a prime example of a protective shell, which maintains the physical integrity of our quasi-spherical planet, in addition to protecting us from outer influences and providing an adequate platform for the development of life as we know it.

1.4.4 Methods of Silica Coating Magnetic Nanoparticles

The traditional Stöber or sol-gel processing technique is a straight forward and inexpensive route to preparing a silica coating which is suitable for many colloidal nanoparticle systems.¹⁴⁴ It involves the hydrolysis and condensation of a silicon alkoxide such as tetraethylorthosilicate (TEOS) in the presence of a suspension of the particles of interest. A modification of this method involves the addition of a silane precursor, such as aminopropyltriethoxysilane (APTES). This method holds advantages over other techniques due to its aqueous system and the ability to tune the silica shell thickness through the variation of the TEOS and/or catalyst concentration. However, it remains a challenge to control the shell thickness to nanometres.

Another approach used in the preparation of core-shell nanostructures with thin silica shells is the microemulsion technique. Firstly, this involves the formation of an emulsion consisting of an organic and an aqueous phase containing the particles to be coated and the silica source. Next, the catalyst is introduced, allowing initiation of the condensation of the silica onto the surface of the particle.¹⁴⁵ The main disadvantage of this method is the high concentrations of surfactants associated with the microemulsion system.¹⁴⁶

1.4.5 Multimodal Nanomaterials

Multimodal or multi-functional nanomaterials are those which possess multiple desirable modalities; for example, these can include magnetism, definite UV-vis absorption and photoluminescence and specific biomarkers. Multi-functional materials can provide excellent opportunities, particularly for molecular imaging and targeted drug delivery. Whilst combining multiple modalities in one probe is not necessary for all applications, there can be advantages to this arrangement, in particular in inducing less stress on the body's clearance systems.¹⁴⁷

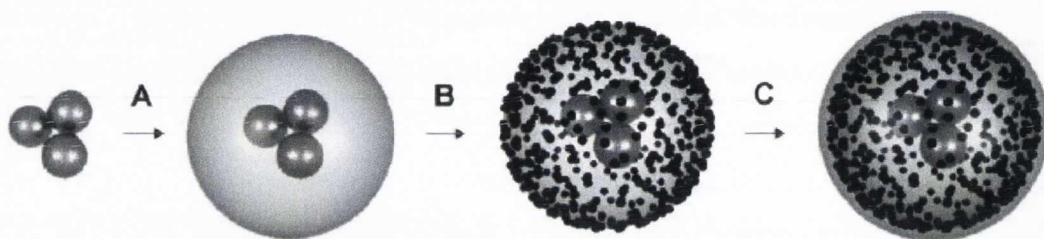
The techniques which can be used to prepare probes with multiple modalities are numerous, ranging from encapsulation to synthetic conjugation. One of the simplest methods of preparing multi-functional materials is through encapsulation, with some of the earliest examples involving lipid systems, or liposomes.¹⁴⁷ Since then, a range of other encapsulating materials have been investigated, including, but by no means limited to, polyelectrolytes, styrene/acrylamide co-polymers and silica nanomaterials.^{6,148,149} The encapsulation procedure is efficient when dealing with aqueous materials, as they can be encased within layers through self-assembly. However, the drawback of this approach is the propensity of materials to easily leak from the layered shell.¹⁴⁷

The use of nanomaterials in the preparation of multi-functional materials is one of the most popular due to their small, controllable sizes and their facile manipulation which lends them to multi-component compositions. Many methods of preparation of nanomaterials are fast, relatively straight-forward and allow a modular approach to their design. The two main approaches of preparing multimodal nanomaterials include using an existing nanoparticle base and building onto it. In this way, the functionalities can be separated from one another to prevent any unwanted interactions. Alternatively, nanomaterials with multiple functionalities can be embedded into the same core matrix through a one-step procedure.

Magnetic-fluorescent nanocomposites can be made from a variety of materials. These can take the form of a magnetic core with some surface stabiliser or coating which can be functionalised with a fluorescent moiety. Alternatively, they could have a fluorescent core with an external shell which can be decorated with magnetic materials. Both composites achieve their goal of providing a multi-functional material, but inevitably possess their own individual advantages and drawbacks. Magnetic materials commonly used to prepare composites of this type include magnetite (Fe_3O_4), maghemite ($\gamma\text{-Fe}_2\text{O}_3$) and other ferrite materials which exhibit strong magnetisation and are usually superparamagnetic. Superparamagnetism is an important characteristic, especially for biomedical applications, where aggregation due to magnetic interaction effects is undesirable. Additionally, for magnetic separation techniques and targeting, a strong response to a magnetic field is attractive. Fluorescent moieties are plentiful, with semiconductor QDs and fluorescent dyes being the most widely used materials due to their

characteristic emission and specific wavelength of excitation, which can be tuned according to size and choice of fluorophore, respectively.

Nanocomposites consisting of magnetic and QD cores have been prepared by dual encapsulation of these nanoparticles inside a shell of silica to provide a robust, chemically and physically stable coating.¹⁵⁰ A major disadvantage of this method is the possibility of the proximity of the QD to the magnetic core causing quenching of the luminescent emission. Alternatively, a multi-step coating approach can be adopted, similar to one demonstrated by Salgueiriño-Maceira and co-workers (Scheme 1.13).²⁴



Scheme 1.13: Preparation of magnetic-fluorescent nanocomposites by a) initial coating of magnetic nanoparticles with silica; b) deposition of QDs onto the silica shell by electrostatic interaction; and c) outer coating with a silica shell.²⁴

The incorporation of an organic dye into a magnetic nanocomposite can offer an alternative to using QDs. In these procedures, the magnetic component is often at the core of a silica shell into which a dye can be incorporated during synthesis. Alternatively, the dye can be coupled with or conjugated onto the shell afterwards.¹⁴⁷ Coupling sometimes relies on ionic interactions between the dye and the silica surface and can be carried out by modifying the surface charge of the materials. For example, the silica shell can be modified to possess a cationic charge to which a negatively charged dye, such as fluorescein isothiocyanate (FITC), will be electrostatically bound.¹⁵¹ On the other hand, chemical conjugation of an organic dye to the silica shell ensures strong covalent chemical bonding, preventing leaking of the dye molecule to the surroundings. A variety of organic dyes can be used, including rhodamine-B, rhodamine-G, FITC and Alexa dyes.^{147,152} Zhang *et al.* used the conjugation approach to prepare FITC-bound silica coated Fe_3O_4

nanoparticles which proved a useful bi-functional probe which demonstrated luminescence and T_2 relaxivity.¹⁵²

Finally, an inorganic synthetic route can be taken to prepare dimers of nanoparticles consisting of a QD and a magnetic nanoparticle. For example, Gu *et al.* prepared FePt nanoparticles and deposited amorphous CdS onto their surface to produce a heterodimer of FePt and CdS nanocrystals attached through a small interface.¹⁵³ These dimers retain their discrete magnetic and luminescent characteristics and illustrate a new route to multimodal nanocomposites.

Multimodal nanocomposites occupy an active area of research, with a variety of synthetic routes which can be manipulated to achieve similar goals of discrete particles with multiple characteristics. They have shown tremendous potential, especially with regard to biological imaging and targeting and they represent the ambitious future of nanotechnology in medicine.

1.4.6 Applications of Magnetic Nanoparticles

Iron oxides have been used for thousands of years in the form of pigments and have been also developed for their uses as catalysts, abrasives and in water purification.¹¹³ Magnetic nanoparticles themselves have found applications in a diverse range of fields, including data storage,¹⁰⁷ catalysis,¹⁵⁴ environmental remediation¹⁵⁵ and engineering, where ferrofluids based on magnetic nanoparticles can be used to provide a reliable seal and can protect mechanical and electronic parts from contamination.¹¹³ Of particular interest are the uses of nanomaterials in biotechnology and biomedicine.

Small sized particles have been used in biomedicine and *in vitro* diagnostics for almost half a century.¹⁵⁶ This is due to their unique properties, their high surface area-to-volume ratio and their ability to access tissues and infiltrate cells. In particular, magnetic nanoparticles possess unique characteristics which have proven useful in specific biomedical techniques, such as MRI and drug delivery. One of the most simple applications of magnetic nanoparticles in biotechnology and biomedicine is magnetic separation, which can be used as a quick and simple method for the efficient and reliable capture of specific proteins or other biomolecules.¹²³

1.4.6.1 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a powerful non-invasive technique in medical research that can provide images of the anatomy and physiology of living subjects by rapidly mapping out the spatial distribution of the proton (^1H) signal intensity. It was originally named nuclear magnetic resonance imaging and works by exploiting the phenomenon of nuclear magnetic resonance (NMR). This technique makes use of the reaction of atomic nuclei to a strong magnetic field, which absorb and re-emit electromagnetic waves at a characteristic radio frequency (RF). Despite the lack of known adverse effects from strong magnetic fields or radio waves, the negative implications associated with the term ‘nuclear’ caused the technique to be renamed in the 1970’s to magnetic resonance imaging.

The basis of NMR is derived from the fact that certain nuclei, possessing unpaired protons or neutrons, have small magnetic moments. For MRI, the most important of these nuclei is hydrogen, as it is present throughout the body in water and fat. The spin of these nuclei precess around an axis producing a very low magnetic moment.

Nuclei such as ^1H have two possible spin arrangements, either aligned ‘with’ (α) or ‘against’ (β) an applied magnetic field (B_0), generating two spin states which can be described using the Boltzmann equation (Equation 1).

$$\frac{N_\beta}{N_\alpha} = e^{\frac{-\mu B_0}{kT}} \quad (1)$$

Where N_α and N_β are the numbers of spin arrangements α and β , μ is the nuclear magnetic moment, B_0 is the magnetic field strength, k is the Boltzmann constant and T is the sample temperature. At equilibrium, multiple nuclei precess about B_0 with random phases, producing no net transverse magnetisation. However, slightly more of the nuclei are oriented α (‘with’) the field than β (‘against’) it, giving rise to a small net longitudinal magnetisation, M_0 (Figure 1.10).¹⁵⁷

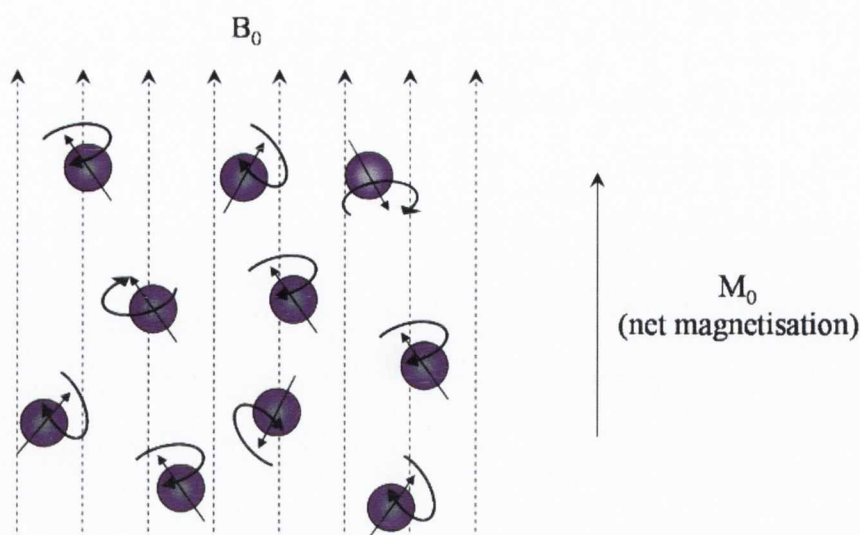


Figure 1.10: Nuclei (purple spheres) at equilibrium, precessing about B_0 with random phases producing no net transverse magnetisation, but a small net longitudinal magnetisation.¹⁵⁷

The application of a pulse of RF causes the longitudinal magnetisation to be shifted from the z-axis to the transverse x-y plane. The excess nuclei that had been aligned with B_0 at equilibrium then precess in this direction in harmony and therefore emit a detectable signal. After the cessation of the RF pulse, this transverse magnetisation slowly realigns itself with the z-axis and its equilibrium state in a process called relaxation. There are two mechanisms by which relaxation can occur, namely longitudinal relaxation (T_1) or transverse relaxation (T_2). T_1 is the time it takes for the net magnetisation to return to its equilibrium state, aligned with the z-axis. T_2 refers to the loss of phase coherence and the decrease in the transverse magnetisation. T_1 and T_2 are the characteristic times for the recovery of the magnetisation to the equilibrium value. T_1 relaxation involves the loss of energy through the interactions of nuclei with their surroundings (the ‘lattice’), thus it can also be referred to as spin-lattice relaxation. T_2 relaxation is a result of energy exchange between other nuclei which are precessing or ‘spinning’, and can also be called spin-spin relaxation. T_2 relaxation generally proceeds more quickly than T_1 .

The presence of a large number of protons, such as in an environment like the human body, provides a measurable effect in the presence of a large magnetic field. Therefore, MRI can be useful in imaging the musculoskeletal system of humans and animals. MRI is regarded as a powerful imaging tool thanks to its non-invasive nature,

high spatial resolution and tomographic capabilities, but its low signal sensitivity has been a major limitation. The use of contrast agents can enhance the image quality by reducing T_1 and T_2 relaxation times and altering the NMR signal intensity of the water in the body tissues containing the agent.² The most common contrast agents currently used are paramagnetic gadolinium ion complexes (Gd^{3+}). These gadolinium chelates can enhance the signal in T_1 -weighted images.¹⁵⁸ However, free Gd^{3+} is toxic and gadolinium chelates can accumulate in the liver.¹⁵⁶ Therefore, colloidal iron oxides have been the subject of investigation as they can provide strong contrast in T_2 -weighted images and additionally have enhanced cellular internalisation and slower clearance from the tumour site.^{10,159,160}

The nanoparticulate nature of iron oxide nanoparticles can present benefits over traditional chelate materials as they hold opportunities for surface modification, allowing easy chemical distribution and biological transportation. MRI contrast depends on the variations in agent uptake in different tissues and the efficacy of contrast agents often depends on their size and surface chemistry. Surface chemistry can play a role not only in ensuring stability of the nanoparticle in biocompatible media, but it can enhance the benefits of the nanomaterials, allowing them to be utilised in targeting and cell tracking.^{2,156}

One of the first examples of magnetic nanoparticle-based contrast agents were dextran coated iron oxides (Fe_3O_4 or $\gamma-Fe_2O_3$) over 20 years ago.¹⁵⁹ They have been shown to dramatically shorten T_2 relaxation times in the liver, spleen, and bone marrow (Figure 1.11).¹⁶⁰ Since then, numerous studies have been conducted to develop new MRI contrast agents based on magnetic nanoparticles made from core materials with improved magnetic properties and surface characteristics.^{135,159,161-163} Other types of iron oxide-based nanoparticles which have been investigated include ferrites such as MFe_2O_4 , where $M = Mn, Fe, Co$ or Ni .¹⁶⁴ These materials, in particular $MnFe_2O_4$, had considerably enhanced sensitivity for cancer cell detection and also made the *in vivo* imaging of small tumours possible.

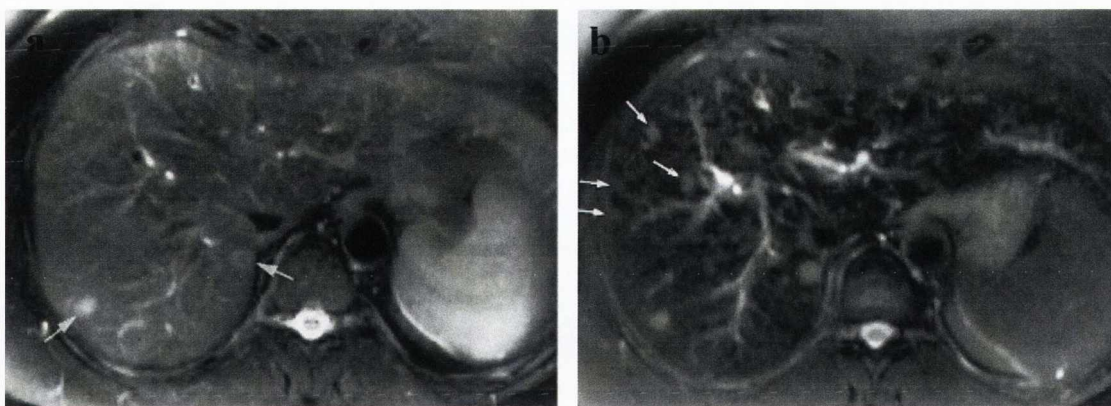


Figure 1.11: T₂-weighted MR images of liver metastases: a) before and b) after magnetic fluid administration, showing liver metastases to be more conspicuous after (indicated by arrows).¹⁶⁰

Iron oxide nanoparticles have been successfully used to image tumours without targeting probes, a procedure referred to as passive targeting.¹⁰ Active targeting is the objective of the next generation of contrast agents, where iron oxide nanoparticles can be conjugated with active targeting probes, such as antibodies, proteins or anticancer drugs.¹⁶⁵ Some research in this area has shown successful results. For example, Hu and co-workers demonstrated that Fe₃O₄ nanoparticles coupled with a specific cancer-targeting antibody can be used as effective MRI contrast agents for cancer diagnosis.¹⁶⁶

Magnetic nanoparticles are undergoing significant testing as possible MRI contrast agents, however it is likely to be many years before their widespread use in clinical medicine, as their toxicological effects and long-term stability are among the issues which must be successfully addressed.

1.4.6.2 Drug Delivery

Nanotechnology has the potential to improve upon the traditionally used pharmaceutical delivery of drugs in many ways. In particular, poorly water-soluble drugs may find improved delivery; drugs may be targeted to specific tissues or cells; drugs may assume more effective movement; and more than one drug could be delivered for combination therapy. In addition, the process of drug delivery could be visualised through the incorporation of additional imaging modalities and could allow the possibility of real-time monitoring of the efficacy of therapeutic agents in *in vivo* systems.¹⁶⁷

One of the main problems with drug administration in the medical field is the lack of drug localisation towards a specific pathological site. As a result, elevated doses are often necessary to achieve high local concentrations, bringing with them a host of problems, including toxicity and patient side-effects. Drug targeting aims to resolve many of these problems by providing enhanced drug specificity.¹⁵⁶

One of the most exciting applications of nanomaterials in biomedicine is drug delivery. The concept of 'magnetic drug delivery' was first proposed in the 1970's by Widder.¹²³ The idea is based upon the magnetic attraction to a specific site of a nanoparticle functionalised with or encapsulating a drug molecule. Once there, it can be held in place until the therapy is complete, after which, the nanoparticle can be removed. The interest in this idea stems from the fact that the particle can be tailored to a specific size so it can move through spaces within the body. In addition, the drug load per particle could potentially be very high, thanks to the high surface area to volume ratio due to the particles' small sizes.

There are a number of important considerations in the development of targeted drug delivery agents. The use of biocompatible agents which allow assembly or conjugation of functional materials is vital. Most importantly, optimisation of the materials for the vast number of biological, physiological and chemical parameters which could come into play in the biological environment for which they are being designed must be thoroughly investigated.¹⁶⁷ The effectiveness of magnetic drug delivery for targeted therapy is dependent on several parameters. These include the field strength and magnetic properties of the particles, as well as their hydrodynamic properties, such as blood flow rate, ferrofluid concentration, infusion route and circulation time.² One of the main drawbacks to the use of magnetic carriers for drug therapy is the toxic responses of the body and its cells to the magnetic particles. However, it is possible to overcome these limitations.²

There have been several advances in the magnetic drug-delivery concept over the last decade. In fact, there are numerous nanotechnology-based therapeutic products which are being developed and to date, several have been approved for clinical usage.¹⁶⁸ A number of research groups have prepared superparamagnetic iron oxide nanoparticles loaded with drug molecules, such as anti-cancer drugs and monitored their delivery to specific sites in the body and drug release.¹⁶⁵ The first clinical trials in humans using

magnetic drug targeting were reported by L  bbe *et al.* in 1996.¹⁶⁹ They used a ferrofluid consisting of nanoparticles to which the drug epirubicin (a well-known antibiotic) was chemically bound. The treatment showed initial success, but required further development to improve its efficiency.

Another development of the concept of magnetic drug delivery is the preparation of nanocapsules which are capable of harbouring the drug molecule and allowing controlled release. A good example of this is the work by Kong *et al.*, who have prepared porous hollow silica nanoparticles which encapsulate magnetic nanoparticles and anticancer drugs.¹⁷⁰ These nanocapsules can penetrate the interior of a tumour and the application of a magnetic field allows controllable on-off switchable release of the drug cargo.

Multimodal nanocomposites also hold promise in drug delivery, where magnetic-fluorescent nanoparticles can be conjugated with anti-cancer drugs.¹⁷¹ Their multiple functionalities allow attraction to the site of interest using a magnetic field gradient, fluorescence imaging to monitor movement and importantly, therapeutic capability.

Despite the requirement for a great deal of further research, the progress to date demonstrates the excellent capabilities of nanoparticle-based materials to improve current medical techniques. This is an exciting prospect which has led to a surge in research in this area in recent years and will be intensively investigated in the future.

1.5 Aims and Objectives of the Project

The main aim of the work presented in this thesis is to prepare a series of nanocomposite materials for potential biomedical applications. Silica nanoparticles are fundamentally useful in several areas of scientific research, particularly biomedicine, where small sizes are often important. There is a lack of reliable synthetic procedures in the literature due to the multiple parameters which can affect the resulting particle size using the St  ber method. With this in mind, we plan to develop a statistical analysis to optimise the preparation of small sized silica nanoparticles with narrow standard deviation. Luminescence is a desirable characteristic for particles such as these, and one of the major objectives of our research is to develop new methods of producing luminescent silica nanoparticles. To this end, we plan to prepare a series of new rare earth metal based metallasiloxane precursors and we aim to use these materials to develop new approaches of

preparing rare earth doped silica nanoparticles with characteristic emission properties. We anticipate that these particles will be useful in techniques such as confocal imaging.

Magnetic nanocomposites are attractive due to their applications in many fields of biotechnology and medicine, due to their controllable sizes, biocompatibility, and magnetic properties. In this part of the work, we aim to prepare stable suspensions of iron oxide based nanoparticles and to study their potential as MRI contrast agents. The NMRD technique will be applied to study the efficiency of our particles in an aqueous environment. One major obstacle encountered in the preparation of magnetic fluids is the aggregation of particles. In order to overcome this, we will employ polyelectrolyte stabilisers during the synthesis of the particles. Silica will be employed as a coating material to prepare core-shell nanostructures which can be further modified and functionalised. In addition, we plan to prepare multi-functional magnetic-fluorescent nanocomposites.

In summary, our major scientific and technical objectives are to:

- Optimise the preparation of silica (SiO_2) nanoparticles by the Stöber method using statistical analyses;
- Prepare luminescent silica nanoparticles;
- Prepare new rare earth based metallasiloxane compounds;
- Develop a new method of preparing rare earth doped SiO_2 nanoparticles using metallasiloxane precursors;
- Prepare new stable magnetic fluids based on functionalised iron oxide nanoparticles for MRI and other potential biomedical applications;
- Evaluate these magnetic fluids by measuring the effect of magnetic nanocomposites on the water proton spin–lattice relaxation time using the NMRD technique;
- Develop novel “two-in-one” magnetic-fluorescent nanocomposites for intracellular visualisation, manipulation and diagnostics;
- Characterise the nanoparticles, nanocomposites and magnetic fluids fully using different instrumental techniques (e.g. FTIR, Raman, UV-vis and photoluminescence spectroscopy, electron microscopy, XRD, magnetisation measurements, NMR, NMRD and thermogravimetric analysis).

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Chapter 2

Experimental

2.1 Materials and General Procedures

2.1.1 Starting materials

All starting materials have been supplied by Sigma-Aldrich unless stated otherwise. Ammonium hydroxide (30 w/v%) and water from a Millipore filtration system (operating at 18 MΩ) was used throughout. The silsesquioxane ligand [*c*-(C₆H₁₁)₇Si₇O₉(OH)₃] was prepared according to a procedure previously described by Feher *et al.*¹

2.1.2 Solvents

Organic solvents such as tetrahydrofuran (THF) and diethyl ether were purified by heating under reflux for 2-3 hours over a sodium-potassium alloy and benzophenone, followed by distillation under argon and then condensation into a reaction flask. Benzophenone forms a blue ketyl once the solvent is dry. Toluene and aliphatic (hexane, pentane) solvents were dried by heating under reflux over a sodium-potassium alloy followed by distillation under argon. Millipore water was deoxygenated by bubbling argon through it for ~30 minutes.

2.1.3 Ultrasonic and Microwave Equipment

The ultrasonic bath used was a Grant XB6 operating at 5–60 Hz. The ultrasonic processor was Model GEX-750 fitted with a Model CV33 tip with 1/4 in. tapered tip operated at 20 % of maximum power. A Samsung Microwave Model CE2727N at a power of 100 W was also used.

2.2 Experimental Procedures

2.2.1 Experimental Details for Chapter 3

2.2.1.1 Preparation of Silica Nanoparticles

All procedures were carried out in air. Silica nanoparticles were prepared according to previously published procedures.²⁻⁴ Briefly, tetraethylorthosilicate (TEOS) was mixed with ethanol, Millipore water and ammonium hydroxide solution. The concentrations were varied according to Tables 3.1, 3.2 and 3.3 in Chapter 3 and the mixture was stirred for two hours at 40-50 °C. This procedure yielded a colloidal suspension of silicon dioxide nanoparticles. After precipitation, all samples were washed using centrifugation until pH neutral with Millipore water and acetone before being dried in air at room temperature for 48 hours.

IR (cm⁻¹): 3000-3460 (br), 1020-1120 (s), 948 (w), 790 (w).

2.2.1.2 Preparation of Silica Nanoparticles Using Different Agitation Methods

Tetraethylorthosilicate (15.63 mL, 70 mmol) was mixed with ethanol (23.35 mL, 0.4 mol), millipore water (3.6 mL, 0.2 mol) and ammonium hydroxide solution (0.117 mL, 3 mmol) and the agitation method was varied. This yielded a colloidal solution of silicon dioxide nanoparticles. After precipitation, all samples were washed using centrifugation until pH neutral with Millipore water and acetone before being dried in air at room temperature for 48 h. The agitation methods used included ultrasonic bath, ultrasonic tapered tip and microwave treatment under the conditions described in Table 3.4, Chapter 3. Ultrasonic bath experiments were carried out in air with the time spent in the ultrasonic bath varied from 2 to 30 min. Ultrasonic tapered tip experiments were carried out on samples for between 2 and 15 min with temperature controlled using an ice bath (0 °C). Microwave experiments were carried out on samples for between 1 and 5 min with temperature controlled using an ice bath (0 °C).

IR (cm⁻¹): 3000-3460 (br), 1020-1120 (s), 948 (w), 790 (w).

2.2.1.3 Preparation of Hollow Silica Nanoparticles

Tetraethylorthosilicate (3.5 mL, 15.7 mmol) was mixed with toluene (25 mL) in a round bottomed flask. Ammonium hydroxide (0.05 mL, 0.33 mmol) in water (3.6 mL, 0.2

mol) was placed in a syringe. The ammonium hydroxide solution was added to the TEOS solution with sonication over the course of one hour using a syringe pump (at a rate of 3.65 mL/hour). This yielded a bi-layered solution; the two layers were separated and the aqueous layer containing the silica nanostructures was washed with ethanol using centrifugation.

Incorporation of rhodamine B dye into the nanoparticles was carried out using the same method, with rhodamine B (Sample A: 0.02g, 0.04 mmol; Sample B: 0.04 g, 0.08 mmol) dissolved into the ammonium hydroxide solution prior to injection.

2.2.2 Experimental Details for Chapter 4

The preparation of all metallasiloxanes and metallasilsesquioxanes was carried out under argon using strict Schlenk conditions, using dry organic solvents unless otherwise stated. NMR spectroscopy was carried out on samples in dry THF, dry toluene, dry d-benzene, dry d-chloroform or dry d-pyridine. FTIR spectroscopy was carried out on solid samples in Nujol dried over molecular sieves as soon as prepared.

2.2.2.1 Preparation of $\text{Ph}_2\text{Si}(\text{OLi})_2$ (Compound 1)

Diphenylsilanediol (3.35 g, 0.015 mol) was dissolved in dry THF (35 mL). Butyllithium (19 mL, 0.00304 mol) was added slowly to the stirring solution at 0 °C. The solution was then allowed to reach room temperature and stirred for several days. The white precipitated product of **Compound 1** was allowed to settle before filtration under argon. The white solid was washed with dry hexane and then dried under vacuum and characterised.

^7Li (155.5 MHz, C_7H_8 , 25 °C): $\delta = -0.20, 1.56$ ppm.

IR (Nujol, cm^{-1}): 1425 (s), 1115 (w), 980 (w), 907 (w), 874 (w), 700 (w).

2.2.2.2 Preparation of $[\text{Ln}(\text{N}(\text{SiMe}_3)_2)_3]$ (Compounds 2 and 3)

Anhydrous europium chloride (0.34 g, 1.31 mmol) was dissolved in dry THF (30 mL). $\text{Li}(\text{N}(\text{SiMe}_3)_2)$ (1.04 g, 4.3 mmol) was gradually added to the stirring solution at room temperature. The reaction was stirred at room temperature for several days. The white precipitate was allowed to settle before filtration of the orange liquid containing

Compound 2. The orange liquid was dried under vacuum to a red/orange powder which was then characterised.

^{29}Si (79.5 MHz, C_7H_8 , 25 °C): $\delta = 54.78$ ppm.

IR (Nujol, cm^{-1}): 2880 (w), 1405 (w), 1240 (s), 1180 (s), 1040 (m), 979 (m), 827 (m) 766 (m), 750 (m), 671 (w).

Anhydrous ytterbium chloride (0.29 g, 1.04 mmol) was dissolved in dry THF (45 mL). $\text{Li}(\text{N}(\text{SiMe}_3)_2)$ (0.77 g, 3.1 mmol) was gradually added to the stirring solution at room temperature. The reaction was stirred at room temperature for several days. The white precipitate was allowed to settle before filtration of the yellow liquid containing **Compound 3**. The yellow liquid was dried under vacuum to a yellow powder which was then characterised.

^{29}Si (79.5 MHz, C_7H_8 , 25 °C): $\delta = 2.1$ ppm.

IR (Nujol, cm^{-1}): 2880 (w), 1405 (w), 1240 (s), 1180 (s), 1040 (m), 979 (m), 827 (m) 766 (m), 750 (m), 671 (w).

2.2.2.3 Preparation of $[\text{Ln}(\text{O}_2\text{SiPh}_2)_3]$ (Compounds 4 and 5)

$[\text{Ph}_2\text{Si}(\text{OLi})_2]$ (**Compound 1**) (1.23 g, 5.1 mmol) was dissolved in dry THF (50 mL). Europium trifluoromethanesulfonate (1.01 g, 1.7 mmol) was slowly added to the stirring solution at room temperature. The yellow/orange liquid was allowed to stir overnight at room temperature. The THF solvent was removed under vacuum and dry toluene (40 mL) was added. The solution was stirred for one day and then the white precipitated lithium trifluoromethanesulfonate was allowed to settle. The clear yellow/orange solution containing **Compound 4** was removed by filtration and dried under vacuum to yield a yellow/orange powder which was characterised.

^{29}Si (79.5 MHz, C_7H_8 , 25 °C): $\delta = -42$ (minor impurity), -18 ppm.

IR (Nujol, cm^{-1}): 1273 (s), 1180 (s), 1052 (s), 896 (w), 727 (s), 643 (s).

$[\text{Ph}_2\text{Si}(\text{OLi})_2]$ (**Compound 1**) (0.9 g, 3.75 mmol) was dissolved in dry THF (50 mL). Ytterbium trifluoromethanesulfonate (0.7 g, 1.25 mmol) was slowly added to the stirring solution at room temperature. The yellow liquid was allowed to stir overnight at room temperature. The THF solvent was removed under vacuum and dry toluene (40 mL) was added. The solution was stirred for one day and then the white precipitated lithium

trifluoromethanesulfonate was allowed to settle. The clear yellow solution containing **Compound 5** was removed by filtration and dried under vacuum to yield a yellow powder which was then characterised.

^{29}Si (79.5 MHz, C_7H_8 , 25 °C): $\delta = -19$ ppm.

IR (Nujol, cm^{-1}): 1260 (w), 1181 (w), 1034 (w), 901 (w), 817 (w), 703 (w).

2.2.2.4 Preparation of Trisilanol Ligand A ($c\text{-C}_6\text{H}_{11}$) $_7\text{Si}_7(\text{OH})_3$

The preparation of ($c\text{-C}_6\text{H}_{11}$) $_7\text{Si}_7(\text{OH})_3$ was carried out in ambient conditions, according to published procedure.¹ Distilled water (151 mL) was carefully added to a stirring solution of cyclohexyltrichlorosilane [$c\text{-C}_6\text{H}_{11}\text{SiCl}_3$] in acetone (566 mL). The reaction was sealed and allowed to stand, undisturbed, over several months. The desired product precipitates over a period of 2-36 months as a white microcrystalline solid along with two minor components (Scheme 4.5, Chapter 4) which can be separated. Extraction of the crude product mixture from pyridine separated the insoluble **Product B** from the two silanol-containing products. Separation of **Product A** from **Product C** was effected by fractional crystallisation from diethyl ether. **Product A** is less soluble in ether than **Product C** and precipitated as analytically pure microcrystals upon concentration of hot ether solutions. **Product A** was named trisilanol **Ligand A** and was characterised.

^{29}Si (79.5 MHz, C_6D_6 , 25 °C): $\delta = -69.76, -68.23, -60.34$ ppm

^1H (400 MHz, C_6D_6 , 25 °C): $\delta = 7.28, 2.27, 2.25, 1.93, 1.77, 1.76, 1.74, 1.72, 1.47, 1.45, 1.43, 1.41, 1.39, 1.37, 1.19, 1.17, 1.15, 0.99, 0.58, 0.41$ ppm.

^{13}C NMR (100 MHz, C_6D_6 , 25 °C): $\delta = 27.54, 27.51, 27.38, 27.13, 27.05, 27.02, 26.93, 26.89, 26.84, 24.24, 23.91, 23.42$ ppm.

IR (Nujol, cm^{-1}): 3149 (br), 1443 (w), 1267 (w), 1195 (w), 1085 (s), 890 (s), 846 (w), 824 (w), 750 (w), 677 (w).

2.2.2.5 Preparation of Compound 6

Trisilanol **Ligand A** (0.14 g, 0.13 mmol) was dissolved in dry THF (50 mL). **Compound 2** [$\text{Eu}(\text{N}(\text{SiMe}_3)_2)_3$] (0.04 g, 0.063 mmol) was slowly added to the solution with stirring at room temperature. The solution was refluxed under argon at 70-80 °C for two days. The white precipitate of $\text{HN}(\text{SiMe}_3)_2$ was allowed to settle out and the pale

yellow liquid containing **Compound 6** was removed by filtration. The liquid was dried under vacuum to yield a pale yellow powder which was characterised.

^1H (400 MHz, C_6D_6 , 25 °C): δ = 7.27, 2.20, 1.86, 1.69, 1.37, 1.33, 0.97, 0.38 ppm.

^{13}C NMR (100 MHz, C_6D_6 , 25 °C): δ = 27.52, 27.11, 26.87, 24.96, 24.21, 23.76, 23.37, 1.49, 0.96 ppm.

^{29}Si (79.5 MHz, $\text{C}_4\text{H}_8\text{O}$, 25 °C): δ = -69.5, -69.2, -67.9, -67.21, -67.15, -67.0, -66.7, -60.0, -58.4, -57.3, -55.6, -21.67, 11.39 ppm.

IR (Nujol, cm^{-1}): 2964 (w), 2880 (w), 1446 (w), 1260 (s), 1080 (s), 1025 (s), 800 (s).

2.2.2.6 Preparation of Compound 7

Compound 6 (0.04 g, 0.018 mmol) was dissolved into dry toluene (20 mL). **Compound 3** [$\text{Yb}(\text{N}(\text{SiMe}_3)_2)_3$] (0.02 g, 0.018 mmol) was slowly added to the solution with stirring at room temperature. The solution was stirred at room temperature for several days and refluxed under argon at 110-120 °C for one day. The white precipitate of $\text{HN}(\text{SiMe}_3)_2$ was allowed to settle out and the pale yellow liquid containing **Compound 7** was removed by filtration. The liquid was dried under vacuum to yield an off-white powder which was characterised.

^{29}Si NMR not resolvable.

IR (Nujol, cm^{-1}): 2964 (w), 2880 (w), 1446 (w), 1260 (s), 1080 (s), 1025 (s), 800 (s).

2.2.2.7 Preparation of Compounds 8, 9 and 10

The preparation of **Compound 8** was carried out according to published procedures.⁵ $\text{Li}(\text{N}(\text{SiMe}_3)_2)$ (0.79 g, 3.1 mmol) was dissolved in dry THF (55 mL). Trisilanol **Ligand A** (1.0 g, 1.054 mmol) was added to the stirring solution at room temperature. The solution was stirred at room temperature for one day. The solution containing **Compound 8** was orange and a small portion of this was dried under vacuum to yield an orange solid which was characterised.

^{29}Si (79.5 MHz, $\text{C}_4\text{H}_8\text{O}$, 25 °C): δ = -67.11, -66.98, -58.18 ppm.

IR (Nujol, cm^{-1}): 2940 (w), 2850 (w), 1060 (w), 850 (w).

Anhydrous YbCl_3 (0.14 g, 0.52 mmol) was added slowly to a stirring solution of the orange liquid containing **Compound 8** in dry THF at room temperature. The solution was

stirred at room temperature for one day. The solution containing **Compound 9** was orange and part of this was dried under vacuum to yield an orange solid which was characterised.

^{29}Si (79.5 MHz, $\text{C}_4\text{H}_8\text{O}$, 25 °C): $\delta = -66.69$ ppm.

Anhydrous EuCl_3 (0.13 g, 0.52 mmol) was added slowly to a stirring solution of the orange liquid containing **Compound 9** in dry THF at room temperature. The solution was stirred at room temperature for one day. The solution containing **Compound 10** was orange/yellow and part of this was dried under vacuum to yield an orange/yellow solid which was characterised.

^{29}Si (79.5 MHz, $\text{C}_4\text{H}_8\text{O}$, 25 °C): $\delta = -73.77, -70.08, -69.23, -65.56, -64.75, -61.11, -58.77, -50.35$ ppm.

IR (Nujol, cm^{-1}): 2920 (s), 2848 (s), 1251 (w), 1194 (w), 1110 (w), 1060 (w), 1000 (w), 995 (w), 890 (w), 750 (w).

2.2.2.8 Preparation of Silica Nanoparticles from Metallasiloxanes and Metallasilsesquioxanes

Thermal decomposition studies were carried out on selected metallasiloxanes and metallasilsesquioxanes. Samples were heated using a Perkin Elmer Pyris 1 TGA with a burn rate of 10 °C/min under a nitrogen atmosphere. Samples were retained after burning for further characterisation. Samples studied included **Compounds 4, 6 and 7**.

2.2.3 Experimental Details for Chapter 5

2.2.3.1 Preparation of Cobalt Ferrite Nanoparticles

Cobalt (II) nitrate hexahydrate (0.5812 g, 2 mmol) and iron (II) chloride tetrahydrate (0.7959 g, 4 mmol) were dissolved into 100 mL of deoxygenated water. The solution was allowed to stir for 15 minutes at room temperature to allow full dissolution. Nanoparticles were precipitated by the addition of ammonium hydroxide solution until the solution reached a pH of ~11. The solution was then reacted at 80-90 °C for 1 hour with stirring agitation or ultrasonic bath treatment. The particles were then washed using centrifugation with Millipore water until pH neutral and the strongly magnetic black precipitate was dried under vacuum.

IR (KBr, cm^{-1}): 3440 (br), 670 (w), 570 (s).

2.2.3.2 Preparation of Cobalt Ferrite-Polyelectrolyte Nanocomposites

Cobalt (II) nitrate hexahydrate (0.5812 g, 2 mmol) and iron (II) chloride tetrahydrate (0.7959 g, 4 mmol) were dissolved into 100 mL of deoxygenated water. The solution was allowed to stir for 15 minutes at room temperature to allow full dissolution (referred to as Co/Fe solution). Various concentrations of poly(sodium-4-styrene) sulfonate (PSSS) were made up in millipore water (10 mL) according to Table 2.1. Following this table, the appropriate amount of Co/Fe solution was mixed with the appropriate concentration of PSSS solution and allowed to stir for ~5 minutes. Ammonium hydroxide solution (10 mL) was added in 2 mL aliquots until the pH reached 11-12. The final solution was then stirred at 80-90 °C for 2 hours. The particles were then washed using centrifugation with Millipore water until pH neutral and the strongly magnetic black precipitate was dried under vacuum. The solid and final aqueous washing of the particles were retained for characterisation.

Table 2.1: Reactant volumes used to prepare PSSS-CoFe₂O₄ nanocomposites.

Sample	Co/Fe solution (mL)	PSSS in 10mL
		water (g)
1	25	0.5
2	25	0.1
3	25	0.05
4	25	1.0
5	10	0.1

IR (KBr, cm⁻¹): 3440 (br), 2921 (w), 1633 (s), 1495 (w), 1450 (w), 1410 (w), 1190 (w), 1128 (w), 1040 (w), 1010 (w), 828 (w), 773 (w), 670 (w), 570 (s).

2.2.3.3 Preparation of Manganese Ferrite Nanoparticles

Manganese (II) chloride tetrahydrate (0.3898 g, 2 mmol) and iron (III) chloride hexahydrate (1.083 g, 4 mmol) were dissolved into 100 mL of deoxygenated water. The solution was allowed to stir for 15 minutes at room temperature to allow full dissolution. Nanoparticles were precipitated by the addition of ammonium hydroxide solution until the

solution reached a pH of ~ 11 . The solution was then reacted under reflux at ~ 100 °C for 2 hours with magnetic stirring. The particles were then washed using centrifugation with Millipore water until pH neutral and the strongly magnetic black precipitate was dried under vacuum.

IR (KBr, cm^{-1}): 3440 (br), 2360 (s), 670 (s), 570 (s).

2.2.3.4 Preparation of Manganese Ferrite-Polyelectrolyte Nanocomposites

Manganese (II) chloride tetrahydrate (0.3891 g, 2 mmol) and iron (III) chloride hexahydrate (1.081 g, 4 mmol) were dissolved into 100 mL of deoxygenated water. The solution was allowed to stir for 15 minutes at room temperature to allow full dissolution (referred to as Mn/Fe solution). Poly(sodium-4-styrene) sulfonate (PSSS) (0.1 g) was dissolved in millipore water (10 mL). This was mixed with 50 mL of Mn/Fe solution and allowed to stir for ~ 5 minutes. Ammonium hydroxide solution (10 mL) was added in 2 mL aliquots until the pH reached ~ 11 . The final solution was then reacted under reflux at ~ 100 °C for 2 hours. The particles were then washed using centrifugation with Millipore water until pH neutral and the strongly magnetic black precipitate was dried under vacuum. The solid and final aqueous washing of the particles were retained for characterisation.

IR (KBr, cm^{-1}): 3440 (br), 2360 (s), 1650 (w), 1625 (w), 1560 (w), 1508 (w), 1160 (w), 1040 (w), 670 (s), 570 (s).

2.2.4 Experimental Details for Chapter 6

2.2.4.1 Preparation of Magnetite Nanoparticles

A solution of iron (III) chloride hexahydrate (6.5 g, 0.024 mol) and iron (II) chloride tetrahydrate (2.48 g, 0.012 mol) were made up in 25 mL of deoxygenated Millipore water. This was added dropwise to a 0.5 M sodium hydroxide solution made up in 250 mL of degassed Millipore water at 40 °C. The solution was stirred for 1 hour at this temperature. The particles were then washed using centrifugation with Millipore water until pH neutral and the strongly magnetic black precipitate was dried under vacuum.

IR (KBr, cm^{-1}): 3425 (br), 2350 (w), 1620 (w), 570 (s).

Cobalt ferrite and manganese ferrite nanoparticles were prepared according to the procedure outlined in Sections 2.2.3.1 and 2.2.3.3 respectively.

2.2.4.2 Preparation of Silica Coated Magnetic Nanoparticles with Varying Shell Thickness

A solution containing magnetic nanoparticles (magnetite, cobalt ferrite or manganese ferrite) (0.97 mmol) and citric acid (0.55 g, 2.86 mmol) in 200 mL Millipore water were mixed using sonication until well dispersed. Tetramethylammonium hydroxide (25 v/v%) was added to the suspension until pH neutral.

A solution of ethanol (580 mL, 1.56 mol), Millipore water (180 mL, 10 mol), ammonium hydroxide (45 mL, 1.14 mol), citric-acid stabilised magnetic nanoparticle suspension (45 mL) and tetraethylorthosilicate (varied, see Tables 6.1 and 6.2, Chapter 6) were sonicated in ice for 1 hour. After this time, the solution was reduced to low volume using rotary evaporation and washed using centrifugation with ethanol until pH neutral and the brown precipitate was dried under vacuum. The solid and final aqueous washing of the particles were retained for characterisation.

IR (KBr, cm^{-1}): 3425 (br), 2350 (w), 1620 (w), 1080 (s), 570 (s).

2.2.4.3 Preparation of FITC-Conjugated Magnetic-Luminescent Nanocomposites

A solution of dry THF (~10 mL), fluorescein isothiocyanate (FITC, 0.03 g, 0.077 mmol) and N-[3-Dimethylaminopropyl]-N'-ethylcarbodiimide-hydrochloric acid (EDC, 0.0775 g, 0.5 mmol) were stirred overnight at 0 °C. A solution containing aminopropyltriethoxysilane (APTES, 42 μL , 0.17 mmol) in 1 mL of dry THF was added to the stirring solution at 0 °C and stirred at room temperature overnight. Solid powdered silica coated magnetic nanoparticles (0.05 g) and triethylamine (TEA, 150 μL , 0.0011 mmol) were added to the solution with vigorous stirring and stirred overnight. The brown precipitate was washed with bench THF and Millipore water several times using magnetic separation. This procedure was carried out using silica coated magnetic nanoparticles of magnetite and cobalt ferrite.

2.2.4.4 Preparation of Nanorattle Structures

A solution of FITC-conjugated silica coated magnetic nanoparticles (7 mL, 0.022 mmol) was mixed with ethanol (70 mL), Millipore water (3.5 mL), ammonium hydroxide

(7 mL) and TEOS (0.1 mL, 0.45 mmol) and sonicated at 0 °C for 1 hour. The brown precipitate was washed with ethanol several times using magnetic separation.

2.2.4.5 Preparation of Magnetic Nanowires from Nanoparticles

Stabilised magnetic nanoparticles in aqueous solutions (such as PSSS-cobalt ferrite, prepared as in Section 2.2.3.2) were dispersed in a water/ethanol and ammonium hydroxide (NH_4OH) solution by manual shaking. A solution of dichloromethane (DCM) and silicon or titanium alkoxide precursor (tetraethylorthosilicate [TEOS] or titanium isopropoxide) was prepared in a beaker. The PSSS-stabilised magnetic nanoparticle suspension was then carefully transferred on top of the DCM/precursor solution in order to form a bi-layer. The reaction vessel was then placed on top of a magnet for several hours; until brown magnetic material collected at the bottom of the beaker near the magnetic surface. See Scheme 6.5, Chapter 6 for this experimental setup shown in more detail. The coated magnetic particles were washed with water using centrifugation to remove any unreacted reagents.

2.3 Characterisation Techniques

2.3.1 Infrared Spectroscopy

Infrared spectroscopy is a technique based on the interaction of materials with electromagnetic radiation in the wavelength range approximately 1–300 μm (1 to 10,000 cm^{-1}) (Figure 2.1).⁶

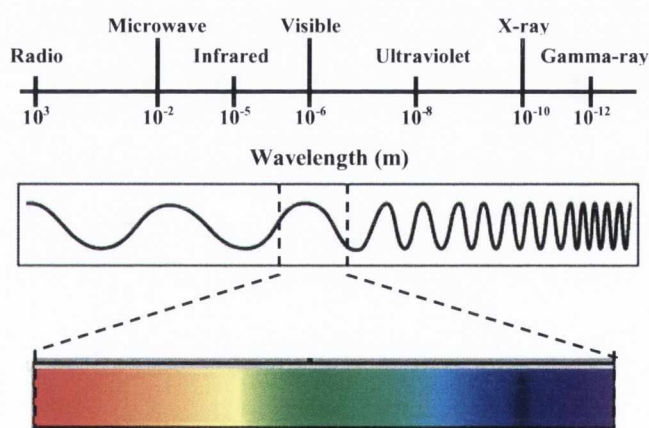


Figure 2.1: Electromagnetic spectrum showing wavelength in metres.

These interactions cause excitation of the vibrational or rotational modes within molecules, which can be detected due to the absorption or transmittance of the infrared radiation. A molecule can be considered as having bonds with spring-like properties. Movement of the bonds between atoms can include stretching (both symmetric and asymmetric) and bending vibrations.⁷ Electromagnetic radiation of a particular frequency can only be absorbed by a molecule if there is a change in the dipole moment associated with the vibrational excitation of the atomic group concerned. Vibrations which show no change in the dipole moment are infrared inactive. A transmission infrared spectrum is a plot of the percentage radiation absorbed versus the frequency of the incident radiation in wavenumbers (cm^{-1}).

In our work, IR spectra ($400\text{--}4000\text{ cm}^{-1}$) were recorded by diffuse reflectance in KBr using a Perkin Elmer Spectrum One FT-IR spectrophotometer. IR spectra ($600\text{--}4000\text{ cm}^{-1}$) were recorded by diffuse reflectance using a Perkin Elmer Spectrum One FT-IR fitted with a ZnSe tip.

2.3.2 Raman Spectroscopy

When electromagnetic radiation interacts with materials, it may be absorbed, emitted or scattered. If the energy of an incident photon corresponds to the energy gap between the ground state and the excited state of a molecule, the photon may be absorbed by the molecule. Raman spectra are the result of the scattering of electromagnetic radiation by molecules of a material. Active Raman vibrations are those which produce a change in the polarisation of the system. This polarisation of a molecule causes the formation of a short-lived state called a 'virtual' state (so called because the energy of these states is determined by the frequency of the light source).⁸ There are several types of scattering processes: elastic Rayleigh scattering, which causes very small frequency changes, and inelastic Raman scattering, which involves energy transfer between the incident photon and the molecule (it can exist as Stokes or anti-Stokes shifts). These different types of scattering are described in Figure 2.2, where a photon with initial energy ($h\nu_0$) may interact with a molecule and proceed with decreased energy (Raman Stokes scattering, $h\nu_{St}$) or increased energy (Raman anti-Stokes scattering, $h\nu_{a-St}$). Alternatively, the energy can remain unchanged (Rayleigh scattering, $h\nu_{Ray}$). Rayleigh scattering results in lines of

strong intensity in the Raman spectrum, often 10^3 - 10^4 times greater than Stokes and anti-Stokes Raman bands. The intensity of the anti-Stokes shift is lower than that of the Stokes shift, therefore, Stokes shift is generally viewed to be more important in Raman spectroscopy.⁹

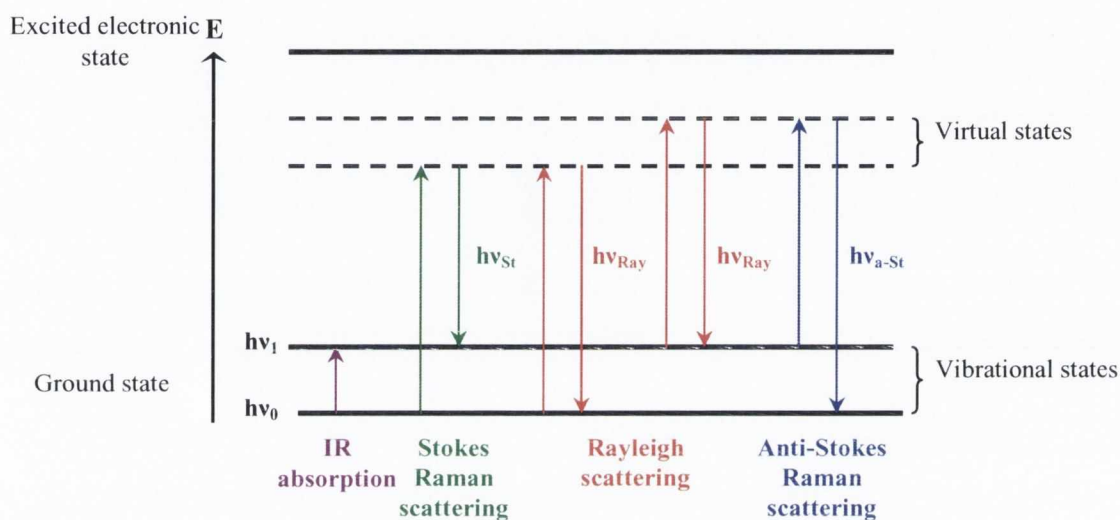


Figure 2.2: Diagram of Rayleigh and Raman scattering processes.⁸

The difference in frequency between the exciting radiation and the scattered radiation is characteristic of the molecule under study and is independent of the frequency of the exciting radiation. The polarisability of any molecule is characteristic of that molecule, as the electric field of an electromagnetic wave can shift the centre of a negative charge in the molecule, therefore inducing a dipole moment, μ_{ind} , which is proportional to the electric field intensity, E (Equation 1).

$$\mu_{ind} = \alpha E \quad (1)$$

Where α is the characteristic polarisability of the molecule, which is reliant on the mobility of the electrons and is always a non-zero value.⁹ Raman spectra consist of a number of bands corresponding to the normal modes of the molecule. Raman spectroscopy offers complimentary information to infrared spectroscopy and both techniques can be used to help provide a complete picture of the vibrational states within a molecule.⁶ To be IR active, the incident light must induce a change in the dipole moment of the molecule. To be Raman active, a change in polarisability in the molecule is required. Although both IR

and Raman spectroscopy arise from the same physical phenomenon (the vibrations of the atoms corresponding to transitions between vibrational energy levels), the interaction between the incident radiation and the sample is different. This can be seen in Figure 2.2. Therefore, the same bonds within a molecule behave differently when investigated by the different techniques. If a molecule possesses a centre of symmetry, a vibration which is IR active will be Raman inactive and *vice versa*. If there is no centre of symmetry within a molecule, a number of vibrations may exist in both spectra.

Raman spectra and solid state photoluminescence spectra were measured with a Renishaw 1000 micro-Raman system with a Leica microscope. The excitation wavelength was 457 nm from an Ar⁺ ion laser (Laser Physics Reliant 150 Select Multi-Line) with a typical laser power of ~10 W cm². The 100x magnifying objective of the Leica microscope was capable of focusing the beam into a spot of approximately 1 μm diameter.

2.3.3 X-Ray Diffraction (XRD)

X-Ray diffraction is a technique which can provide information about the structure of a compound. It involves the interaction of electromagnetic radiation with a wavelength of approx. 0.1 nm with atoms in a solid material of interest. The wavelength of the radiation is comparable with the distances between the atoms in a crystal structure, causing the crystalline phases in the material to diffract the X-rays. A diffraction pattern is formed by the variation in the resulting intensities caused by regions of constructive and destructive interference.⁶ Bragg was the first to show that scattering which leads to the diffraction pattern can be visualised as if x-rays were ‘reflecting’ from planes defined by Miller indices.¹⁰ Miller indices refer to the series of parallel lattice planes within a crystalline material. The x-ray pattern is a plot of the observed diffraction intensity against the Bragg angle (or glancing angle), θ . Each atom plane produces a series of n reflections, depending on the interference conditions. These can be related using the Bragg equation (Equation 2).

$$n\lambda = 2d\sin\theta \quad (2)$$

Where λ is the wavelength of the x-rays and d is the spacing between atomic planes in the crystalline phase. From the diffraction pattern and using the Bragg equation, the interlayer spacings (d) of a material can be calculated. Every compound has a

characteristic set of d values and intensities which allows the diffraction pattern to be used for identification of the material.

The peak widths in XRD patterns are inversely proportional to the crystallite size. Therefore, crystals of a finite size give rise to Bragg peaks of finite widths. In fact, the crystallite size only starts to affect the diffraction pattern when the size (or the scattering domain) becomes smaller than 0.5 μm . In 1918, Scherrer derived an equation to describe the broadening of the diffraction peaks according to the particle size (Equation 3).⁶

$$D = \frac{K\lambda}{B \cos \theta} \quad (3)$$

Where D is the crystallite size, K is a constant (taken as 0.9), λ is the wavelength of the x-rays (for all measurements in this thesis, $\lambda = 1.5406 \text{ \AA}$) and B is the line broadening. This broadening is measured from the peak width at half peak height, obtained from the Warren formula (Equation 4).

$$B = \sqrt{B_m^2 + B_s^2} \quad (4)$$

Where B_m is the measured peak width at half height and B_s is the standard peak width at half height obtained from a commercial sample. It should be noted that the error of determination is 20-30 % due to the fact that nanoparticles can often form twinned structures.¹¹ For this reason, sizes determined from XRD will differ slightly from electron microscopy size analyses.

In order to produce an XRD pattern, a beam of X-rays are required. These are produced by bombarding a pure metal with high-energy electrons in a vacuum. Usually, copper metal is used for this purpose and the wavelength of the radiation produced is 1.5406 $\text{\AA}$. XRD presents an attractive characterisation technique which causes minimal damage to a material and its surface. The resulting diffraction pattern can be identified by comparison of the peak positions and relative intensities with standard references in the Joint Committee on Powder Diffraction Standards (JCPDS) database.

X-Ray powder diffraction was performed using a Siemens-500 X-Ray diffractometer. Powder samples were deposited on silica glass using silica gel to adhere the sample to the glass surface. Overnight spectra were run for all samples. Diffractograms were then compared to the JCPDS database.

2.3.4 Magnetisation Measurements

The most important properties of magnetic materials are the type, strength and direction of their magnetisation. Generally, magnetic materials can be classified into two broad categories: soft or hard. Soft magnetic materials typically have very small coercivities (<1 Oe), whereas hard magnetic materials which possess high saturation magnetisations and large coercivity values (>10 Oe), which makes them useful in permanent magnet applications.

2.3.4.1 Vibrating Sample Magnetometry (VSM)

Vibrating sample magnetometry is one method of determining the magnetic properties of both bulk and nanomaterials. The characteristics of any magnetic material can be best described by examining their hysteresis loop. To induce magnetisation using VSM, a sample is exposed to an external magnetic field (H), which induces a magnetic moment. Mechanical vibration (*i.e.* sinusoidal motion) causes a magnetic flux which induces a voltage which is proportional to the magnetic moment of the sample. The type of magnetisation that a sample possesses is demonstrated in the form of a characteristic hysteresis loop.⁶ The parameters of this hysteresis loop allow the material to be characterised in terms of its saturation magnetisation (M_s), its remanence (M_r) and its coercivity (H_c) (Figure 2.3). Superparamagnetic materials generally do not demonstrate a hysteresis loop, instead presenting no remanence magnetisation at 0 T and no coercivity at 0 Am²/kg.

Magnetisation measurements were carried out by Dr. Fiona Byrne and Dr. Munuswamy Venkatesan using a vibrating sample magnetometer (VSM) at room temperature with field applied up to 1 T. The dried sample was weighed, wrapped in aluminium foil and placed in a hexagonal PVC holder. The sample was placed within a uniform magnetic field and mechanically vibrated between a series of coils. A changing magnetic flux was generated which induces a voltage in the pick-up coils. The amplitude of the sinusoidal voltage is proportional to the magnetic moment of the sample. The VSM was calibrated using a nickel sample of known mass. Nickel is ferromagnetic and has a magnetic moment $\sigma = 55.4$ Am²/kg at 1 T at room temperature.

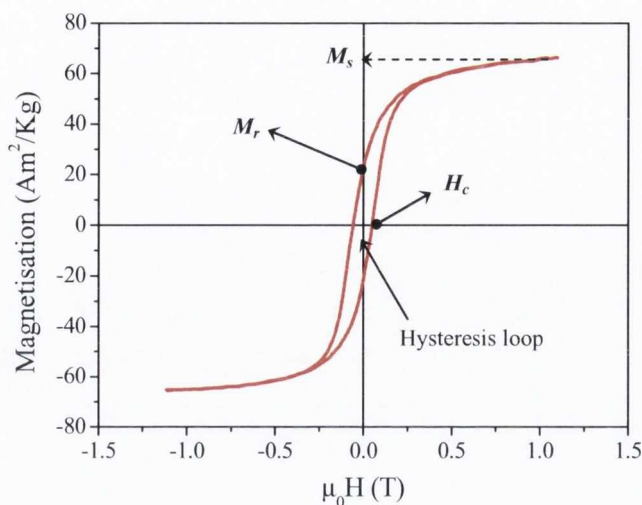


Figure 2.3: Typical magnetisation curve for a sample of ferromagnetic cobalt ferrite nanoparticles.

2.3.4.2 Superconducting Quantum Interference Device (SQUID)

A SQUID magnetometer uses a combination of superconducting materials and Josephson junctions to measure magnetic fields. Josephson junctions are the junctions, or separations, between two superconducting layers which allow the tunnelling of electrons across the separation, causing a superconducting current (termed a Josephson current). The Josephson current is extremely sensitive to magnetic fields. Application of a magnetic field perpendicular to the plane of the SQUID magnetometer causes a phase difference in the electron-pair wave. Monitoring of the current flowing in the SQUID allows the measurement of the magnetic field. SQUID magnetometers are highly sensitive and can be used to measure very weak magnetic fields, in the order of 10^{-9} Tesla or lower.

SQUID measurements were carried out by Dr. Olga Kazakova in the National Physics Laboratory, London, using a MPMS Quantum Design SQUID magnetometer with a ± 7.0 Tesla magnet configuration and a temperature range of 1.9 to 400 K.

2.3.5 Electron Microscopy

Electron microscopy is a useful technique which is widely used across a wide range of scientific disciplines as it can be applied to investigate micro- and nano-materials as well as crystal structures. The resolution of optical microscopes is restricted by the wavelength

of visible light. High energy electrons, however, have much shorter wavelengths, less than 1 Å, which means they have a propensity to provide images with significantly higher resolution.

2.3.5.1 Transmission Electron Microscopy (TEM)

Transmission electron microscopes have similar designs to optical microscopes, except that the source which is used to visualise the sample is a beam of electrons instead of a beam of light. TEM can provide details on the morphology, topography, composition and crystallographic information of a sample.¹² Electrons, focussed into a beam, are accelerated towards the sample, where lenses and apertures focus the beam precisely onto the sample. Upon illumination of the sample with the electron beam, only the electrons which are not blocked by the sample pass through to a phosphor image screen. This generates light which allows the user to view the image. The advantages of TEM include its high magnification capabilities and its ability to provide both image and diffraction information from a single sample.¹¹

The interactions of the electrons with the sample as they pass through it can yield different kinds of information about the chemical and physical properties of a sample. Unscattered transmitted electrons are those which pass through the sample without any interaction. Electrons which undergo elastic scattering have deviated from their original path because of their interaction with the sample. Their interaction causes no loss of energy to the sample and these electrons can give rise to diffraction patterns. Inelastic interactions between the primary electrons and the sample electrons lead to a loss of energy to the surroundings. The magnitude of the energy loss will depend on the element the electrons have interacted with. The energy lost can excite vibrations at the surface of the sample and the resulting energy loss peaks can be observed. This technique is called Electron Energy Loss Spectroscopy (EELS).

Scanning Transmission Electron Microscopy (STEM) differs from conventional TEM by focusing the electron beam into a narrow spot which is scanned over the sample in a raster. STEM microscopes can be equipped with Bright Field (BF) or High Angle Annular Dark Field (HAADF) detectors. BF detectors collect the transmitted electrons and hence the holes in the sample appear bright. On the other hand, HAADF detectors collect

inelastic scattered electrons and exclude transmitted electrons, making the holes in the sample appear dark. HAADF detectors tend to be very sensitive to variations in the atomic number of atoms in a sample, which lead to variations in image contrast.

TEM images were obtained on a Jeol JEM-2100, 200 kV LaB₆ instrument, operated at 120 kV with a beam current of about 65 mA. HAADF-STEM images and EELS measurements were taken using a FEI Titan Electron Microscope operated at 100 kV. Samples for TEM and STEM were prepared by deposition and drying of a drop of the powder dispersed in water or the appropriate liquid sample, onto a carbon-coated 300-mesh copper grid. Diameters were measured using the ImageJ version 1.40 software program; average values were calculated by counting a minimum of 100 particles.

2.3.5.2 Scanning Electron Microscopy (SEM)

In scanning electron microscopy, a focussed beam of electrons is passed over the surface of a material. As the electrons strike the surface of the sample, they interact with it and these interactions result in the emission of electrons and photons, including secondary electrons, backscattered electrons and x-rays. These can be collected and formed into various types of SEM images.¹¹

Secondary electrons occur as a result of primary electrons interacting through inelastic scattering with atomic electrons, transferring its energy to the other electron, causing it to emit from the sample. Backscattered electrons are those which are elastically scattered after an interaction of the primary electron with the atomic nucleus of the sample. They have the about the same energy as the primary electron and the higher the atomic number of the sample material, the more likely it is to have an interaction of the electrons with the nucleus and hence emit backscattered electrons. Finally, the interaction of a primary electron can cause the ejection of a core electron from an atom in the sample. This high energy electron can 'fall' back to its ground state and emit its energy in the form of x-rays with a characteristic wavelength. As a result, SEM can not only provide an image of the topography and morphology of a sample but can additionally be used for characterisation of the chemical composition of the material in a technique called Energy Dispersive X-ray Analysis (EDX).

Scanning electron microscopy (SEM) images of the samples were obtained using a Hitachi S-4300 scanning electron microscope, which was operated at 5.0 kV. Samples were adhered to an aluminium stub and then gold-coated before imaging.

2.3.6 Photon Correlation Spectroscopy (PCS)

Photon correlation spectroscopy (PCS), also known as dynamic light scattering (DLS), is a technique used to measure the size of particles in the sub-micron range. It provides information about the average particle size in suspension and also measures the width of the particle distribution, called the polydispersity index (PDI). Particles which are suspended in a liquid are never stationary. PCS utilises the Brownian motion of particulates undergoing diffusion in a liquid sample to provide a measurement of the hydrodynamic radius of the sample. In this way, it differs from electron microscopy, which shows the primary particle size of a sample which has been dried on a substrate. As such, average diameters according to PCS are often factors of ten larger than those measured using electron microscopy (Figure 2.4).

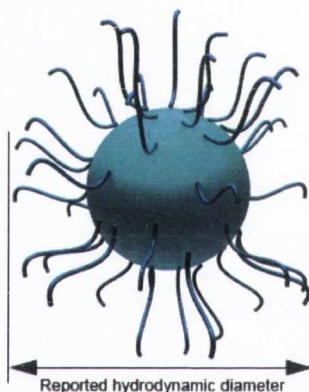


Figure 2.4: Schematic representation of nanoparticle with hydrodynamic radius which is dependent on the core as well as surface structures, as measured by PCS.

An important feature of nanoparticle suspensions is that small particles move more quickly than larger particles and this relationship is defined by the Stokes-Einstein equation (Equation 5).

$$D = kT / 6 \pi r \eta \quad (5)$$

Where D is the diffusion constant, k is the Boltzmann constant, T is the temperature, r is the radius and η = solvent viscosity.

The illumination of randomly moving particles in a liquid with a laser causes scattering of the light. This scattered intensity fluctuates as the particles move under Brownian motion. Mathematical analysis of this fluctuation in the light intensity allows determination of an intensity distribution of the average hydrodynamic radius. This is carried out using a digital correlator within the machine, which serves to measure the degree of similarity between two intensity signals over a period of time. A correlation function is measured for any given sample and the rate of decay of the correlation function can be related to the particle size. The correlation function can then be further manipulated mathematically to provide information about the volume distribution and the PDI. A typical distribution plot showing the average hydrodynamic radius of a sample of stabilised magnetic nanoparticles can be seen in Figure 2.5.

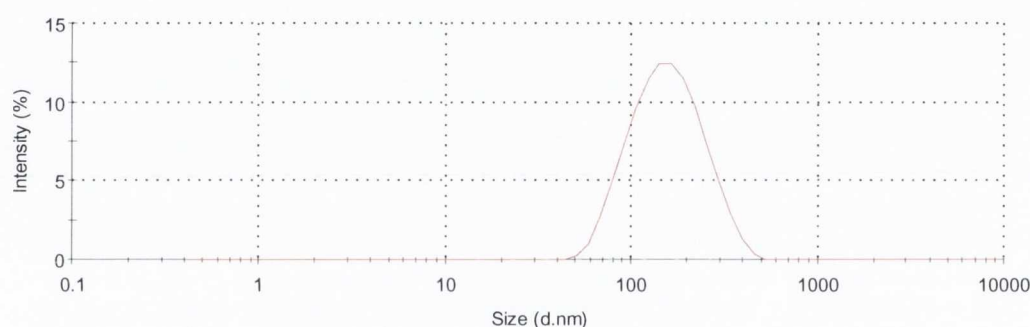


Figure 2.5: Size distribution (by intensity) for a standard sample of stabilised magnetic nanoparticles with a hydrodynamic radius of 144 nm and PDI of 0.182.

Photon correlation spectroscopy measurements were carried out using a Malvern Zetasizer Nano at 25 °C. Liquid samples were placed in disposable cuvettes and loaded into the sample chamber. A 50 mW laser with a wavelength of 632.8 nm was used as the light source and the measurements were recorded at a detection angle of 173 ° (backscatter).

2.3.7 Zeta Potential

Zeta potential is a physical property which is exhibited by any particle in suspension. Investigation of this value provides valuable information about the surface charge of sub-micrometre particles. The zeta potential of any sample is a consequence of the existence of surface charge and can give information about electrical interaction forces

between the dispersed particles. Stability of nanoparticle suspensions is vital for many applications, and several different parameters should be taken into account when investigating stability, the most important of these being the charge of the particles with respect to the liquid in which they are suspended. The balance between these charges can dictate the stability of the suspension over time.

On the surface of a nanoparticle, a net charge can develop which affects the distribution of ions in the surrounding interfacial region. This surface charge causes an increased concentration of counter ions close to the surface of the particle. Thus, an electrical double layer exists around each particle in any given sample. A schematic representation of the nanoparticle can be seen in Figure 2.6.

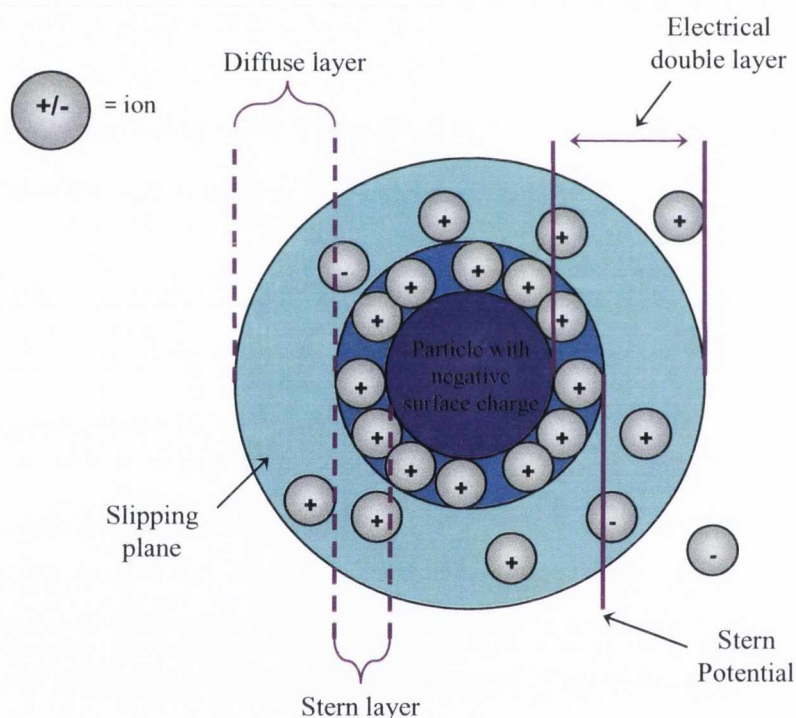


Figure 2.6: Schematic representation of a negatively charged nanoparticle and its interactions with the surrounding liquid.

Within the diffuse outer layer, there is a theoretical boundary. Inside this boundary, the ions and particles form a stable entity. When a particle moves, the ions within the boundary move with it, but any ions which are beyond the boundary do not travel with the particle. Figure 2.7 shows the effect of nanoparticle distance on surrounding ions. The

boundary is called the surface of hydrodynamic shear or the slipping plane. The potential that exists at this boundary is known as the Zeta Potential.

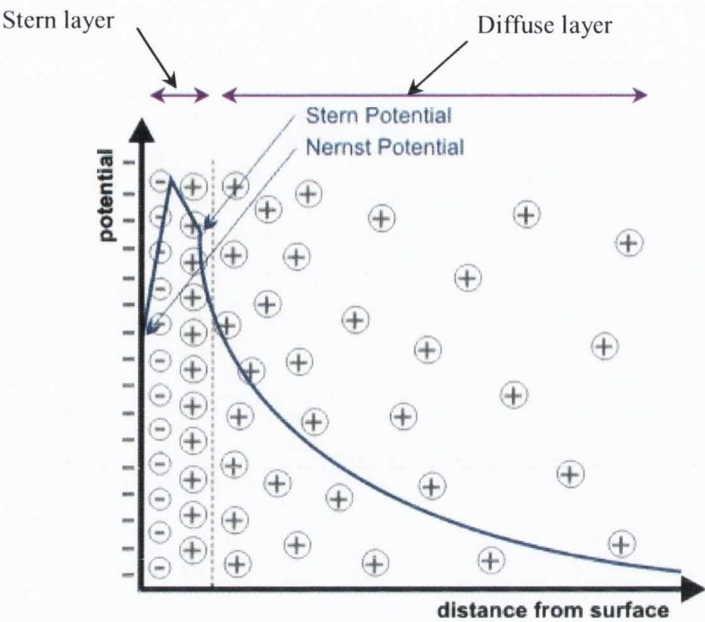


Figure 2.7: Graph showing the effect of distance from the nanoparticle with negative surface charge on the potential of the surrounding ions.

Zeta potential is measured by applying an electrical field across the suspension. Particles which possess a zeta potential will move towards the electrode of opposite charge. The velocity of a particle in an electric field is commonly referred to as its electrophoretic mobility. Zeta potential can be obtained by the application of the Henry equation (Equation 6).

$$U_E = \frac{2 \epsilon \zeta f(\kappa a)}{3 h}$$

(6)

Where U_E is the electrophoretic mobility, ζ is the zeta potential, ϵ is the dielectric constant of the medium, h is the viscosity of the medium, $f(\kappa a)$ is Henry’s function, a is the particle radius and κa is the ratio of particle radius to double layer thickness.

Zeta potential measurements were carried out using a Malvern Zetasizer Nano by injecting ~1 mL of aqueous sample into a disposable zeta capillary cell and carrying out an electrophoresis experiment in air at 25 °C.

2.3.8 Ultraviolet-visible Spectroscopy (UV-vis)

UV-visible spectra arise as a result of the absorption of a beam of incident photons by a sample. The region of the electromagnetic spectrum generally measured for this technique is from 200-900 nm (covering both the UV and the visible range, see Figure 2.1). The Beer-Lambert law (Equation 7) demonstrates that the absorption of light (A) is directly proportional to the path length of the cell used (l) and the concentration (c) of the sample under investigation.

$$A = \epsilon c l \quad (7)$$

Where ϵ is the extinction coefficient of the substance ($M^{-1} \text{ cm}^{-1}$). Bands in UV-vis spectra correspond to electronic transitions, as absorption of the incident light promotes excitation of the valence electrons in a molecule. The frequency (and also the intensity) of the absorbed photon is directly proportional to the energy difference between the ground and excited levels. The wavelength of absorption of radiation is characteristic of the material under investigation.

UV-vis absorption spectra were recorded using a Cary 50 UV-Vis spectrophotometer. A quartz cell with four polished windows and a 3.5 mL volume capacity was employed in all UV-vis spectroscopy measurements.

2.3.9 Photoluminescence Spectroscopy (PL)

Photoluminescence or fluorescence spectroscopy is a type of electromagnetic spectroscopy used for analysing materials which emit radiation upon absorption of light. Absorption of a photon of light, usually ultraviolet light, excites the electrons in molecules of certain compounds from their ground state to a vibrational state within the molecule's excited electronic state. Collisions with other molecules cause the loss of vibrational energy until it reaches the lowest state of its excited form. Emission of a photon of light occurs when the electron falls from this excited state back to the ground state. Electrons which fall to different vibrational levels of the ground state have different energies, which results in the emission of different frequencies of light. Analysis of these frequencies allows the identification of the different vibrational levels within a molecule. The fluorescent lifetime of a molecule refers to the time the molecule stays in its excited state before emitting a photon. Phosphorescence refers to emission of a photon of light from the

triplet excited state of a molecule. This state is lower in energy than the singlet excited state and becomes occupied by an electron if the spin of the excited state is reversed, *via* intersystem crossing. The Jablonski diagram describes the various relaxation mechanisms for excited state molecules (Figure 2.8).

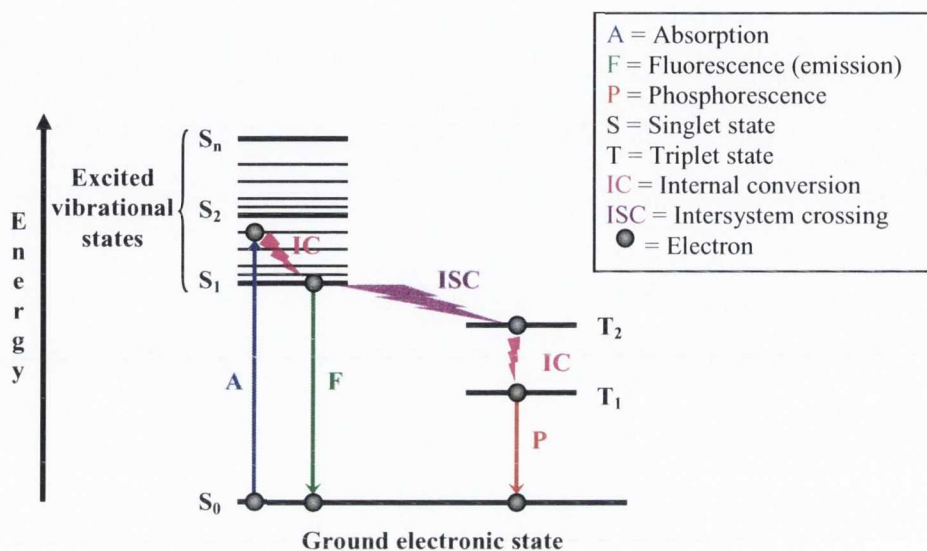


Figure 2.8: Jablonski diagram showing the absorption and relaxation mechanism of radiation within the electronic states of a molecule.

Photoluminescence measurements on liquid samples were performed on a Cary Eclipse spectrophotometer. A quartz cell with four polished windows and a 3.5 mL volume capacity was employed in liquid fluorescence spectroscopy measurements. Fluorescence lifetime decays were measured by Dr. Yury Rakovich using a time-correlated single photon counting machine (Time-Harp, PicoQuant). The samples were excited by 480 nm picosecond pulses generated by a PicoQuant, LDH-480 laser head controlled by a PDL-800B driver. The setup was operated at an overall time resolution of approximately 150 ps. Decays were measured to 3000-5000 counts in the peak and deconvoluted using non-linear least squares analysis (FluoFit, PicoQuant).

2.3.10 Nuclear Magnetic Resonance (NMR)

Nuclear magnetic resonance spectroscopy is a powerful technique which is used to deliver detailed information about molecular structure and bonding. It is dependent on the

magnetic properties of the nucleus. When a nucleus is placed in a magnetic field it may absorb energy (radiofrequency). The energy ($E = h\nu$) of the absorbed radiation is characteristic of the nucleus and its environment. Certain atomic nuclei possess spin angular momentum and this gives rise to different spin states. The number of possible orientations is given by $2I + 1$, where I is the spin quantum number and it is possible to have values of 0, half and whole integers.¹⁵ Nuclei with $I = 0$ do not possess a magnetic moment and therefore do not demonstrate NMR signals; all other nuclei can. Nuclei, such as those with $I = \frac{1}{2}$ like ^1H , have two possible arrangements, either aligned 'with' (α) or 'against' (β) an applied magnetic field (B_0), generating two spin states. These are two different energy states and it is the transition between these that can be monitored and is the origin of the NMR effect. The difference between these two spin states is directly proportional to the magnitude of B_0 . A slight excess of spins aligns with B_0 and this creates a net magnetisation in the sample (M_0). In a static magnetic field, these nuclei precess around the magnetic field at a frequency dependent on the strength of the magnetic field, the Larmor frequency (ω_0) (Equation 8) (Figure 2.9).

$$\omega_0 = \gamma B_0 \quad (8)$$

Where γ is the magnetogyric ratio.

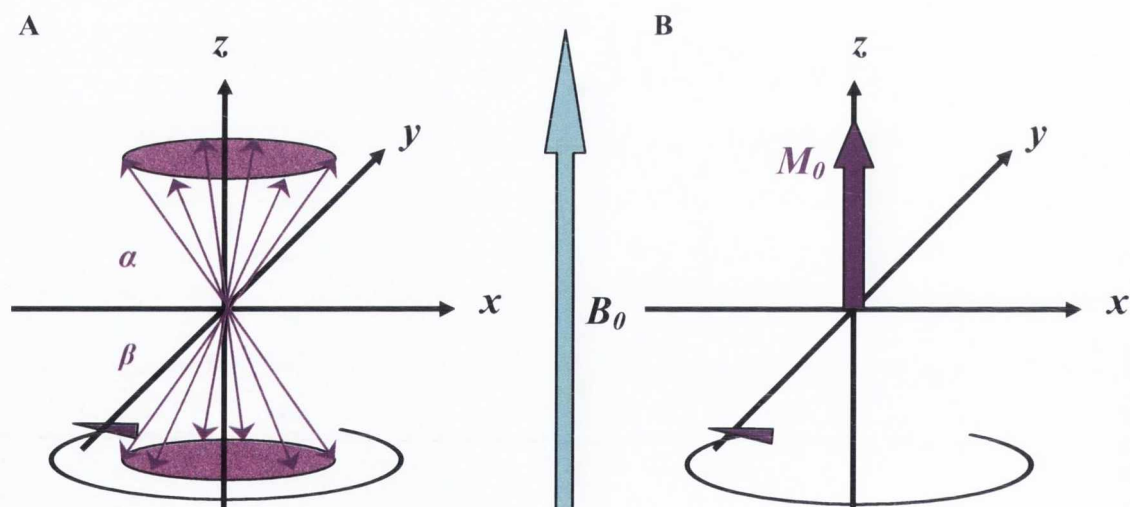


Figure 2.9: A) Schematic representation of the precession of magnetic moments around the z-axis in the presence of a magnetic field, B_0 ; B) Simplified schematic demonstrating the excess spin alignment creating a net magnetisation, M_0 .

Since the external applied magnetic field is much greater than the sample's magnetisation, M_0 , the sample is difficult to detect. Therefore, a second magnetic field is applied perpendicular to the external field by applying a radiofrequency pulse (B_1) along the x-axis. This causes the magnetic moments to move to the x-axis, away from their equilibrium state (Figure 2.10).

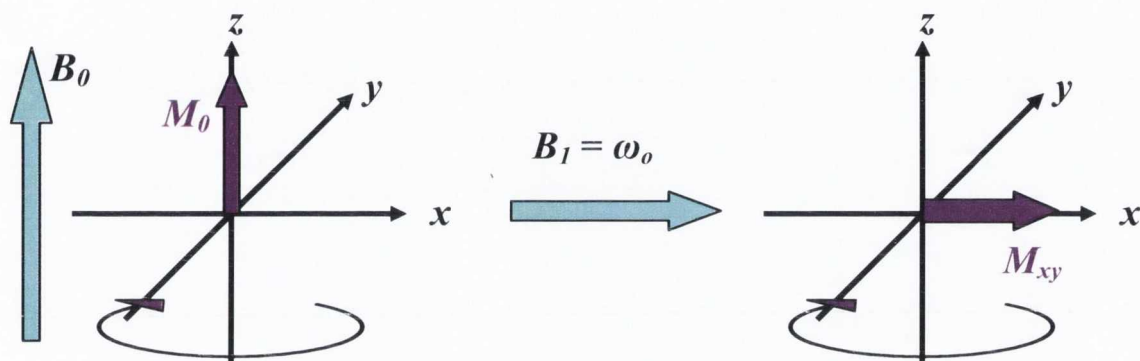


Figure 2.10: Schematic illustration of resonance, the condition where the applied radiofrequency (B_1) equals the Larmor frequency (ω_0) and the net magnetisation changes plane.

Upon the removal of B_1 , the nuclei return to their previous equilibrium. M_{xy} returns to M_0 in a spiralling motion while still rotating at ω_0 . This is referred to as longitudinal relaxation and the time it takes is T_1 . The motion of the magnetic moments generates a current in a receiver coil in the x-axis which is then used to construct a time domain NMR signal. A Fourier transform is then used to generate the typical frequency domain spectrum.

NMR spectra were collected from Bruker 400-Avance-3 (9.4 T), Bruker 600-Avance-2 (14 T) and Bruker Avance-DPX-400 (9.4 T) spectrometers.

2.3.11 Nuclear Magnetic Resonance Dispersion (NMRD)

Nuclear magnetic resonance dispersion is a characterisation technique which allows the investigation of the proton relaxivity of magnetic materials in suspension over a wide range of fields. By investigating the field dependence of the proton relaxation rate, a profile of the colloidal aqueous system can be built up. Fast field cycling NMR (FFC-NMR) is a technique which is used to obtain longitudinal relaxation times (T_1) or

alternatively relaxation rates (R_1). A plot of R_1 as a function of frequency is known as a nuclear magnetic resonance dispersion (NMRD) profile. NMRD profiles provide information about the environment of the molecules and the profiles can be interpreted using different theories that have been developed for different types of systems. In contrast to NMR, FFC-NMR relaxometry involves the rapid switching of magnetic fields throughout the experiment in order to measure T_1 over a wide range (several orders of magnitude) of low magnetic field strengths.

Relaxation of nuclei of a molecule which has been stimulated by an applied field can occur by non-radiative release of its energy to either its surroundings (spin-lattice relaxation time, T_1) or to other nuclear spins (spin-spin relaxation time, T_2). The spin-lattice relaxivity, r_1 , is related to the observed spin-lattice relaxation time, $T_{1(obs)}$ (Equation 9).

$$\begin{aligned} R_{1(obs)} &= \frac{1}{T_{1(obs)}} = \frac{1}{T_{1(diam)}} + \frac{1}{T_{1(para)}} \\ &= \frac{1}{T_{1(diam)}} + r_1[Fe] \end{aligned} \quad (9)$$

Where $T_{1(diam)}$ is the native relaxation time of the supporting fluid (water), $T_{1(para)}$ is the relaxation time of the agent in suspension and r_1 is the relaxivity of the agent.

The coupling of proton spins with materials of larger magnetic moments can enhance the relaxation of water, which makes such materials useful as contrast agents in magnetic resonance imaging. The relaxation process occurs due to interactions between water protons and the magnetic entity. There are two theories which help to explain such interactions: inner- and outer-sphere relaxations.^{13,14} Inner sphere relaxation deals with the direct exchange which may occur between coordinated water molecules and the bulk water surrounding the sample. For superparamagnetic particles, the inner sphere contribution to the relaxation is minor and more often completely negligible as compared to the dominant outer sphere contribution. This relaxation is due to the movement of the water protons near the local magnetic field gradients generated by the magnetic ion. The relaxation process for magnetic nanoparticles is governed by the diffusion of water molecules around the iron core.

In order to calculate the relaxivity of the colloidal samples investigated by this technique, it was necessary to determine the metal concentration of the sample using inductively coupled plasma atomic emission spectroscopy (ICP-AES). Careful determination of the metal concentrations was required, as this can significantly distort the resulting relaxivity values in the NMRD profile. ICP-AES is an emission spectrophotometric technique which is a very accurate and sensitive method for determining the concentration of metal ions in samples. A plasma source is used to dissociate a sample into its constituent ions and excite them to a higher energy level. As they return to their ground state, they emit energy at specific wavelengths characteristic of their chemical composition. These can then be compared to standard solutions which allow the determination of a sample of unknown concentration.

All field-cycling relaxometry experiments were performed on a Spinmaster PPC-2000 Fast Field-Cycling NMR Relaxometer (Stelar) using a sample volume of 0.5 – 1 mL. The use of a Spinmaster Variable Temperature Controller allowed sample temperatures to be controlled within about 0.1 °C and a minimum temperature equilibration time of 20 min preceding all measurements. All measurements were carried out at 25 °C over the frequency range 0.01-20 MHz. ICP-AES was carried out using a Varian Liberty 220ICP.

2.3.12 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis is a technique which monitors the temperature-dependant weight loss of a material. It can give information about the behaviour of materials and compounds at different temperatures, the stability and stoichiometry of a reaction, and more commonly, the composition of functionalised materials.¹⁶ It can also demonstrate the oxidation of a material, such as Fe_3O_4 to $\gamma\text{-Fe}_2\text{O}_3$.

The machine operates by combining a microbalance with a temperature-programmable furnace. It provides a curve of percentage weight loss against the temperature range scanned. The signal output from a TGA can be electronically differentiated to provide a derivative thermogravimetric curve (DTG).

Thermogravimetric analysis (TGA) measurements were carried out in air for iron oxide samples and in nitrogen for air-sensitive metallasiloxanes using a Perkin Elmer Pyris 1 TGA with a temperature scan rate of 10 °C min⁻¹ from 30 to 900 °C.

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Chapter 3

Preparation and Optimisation of Silica Nanoparticles

3.1 Introduction

Silica particles have been synthesised in sizes ranging from 5 nm to several microns in diameter. There are several different synthetic techniques which can be used to prepare silica nanoparticles. These include colloidal and surfactant template techniques,^{1,2} water-in-oil microemulsions,^{3,4} stirred bead milling,⁵ synthesis by ‘fumed’ silica nanoparticles,⁶ flame spray pyrolysis,⁷ reverse micelle and sol-gel processing,⁸⁻¹¹ continuous microwave hydrothermal synthesis,¹² and self-assembly in basic solutions of organic and inorganic cations.¹³ These techniques can yield nanoparticles which are small in size and have narrow size distributions. However, many of these methods of preparation are costly and time-consuming. One of the most widely used procedures to prepare silica nanoparticles is the relatively simple Stöber method.^{14,15} The Stöber synthesis involves the hydrolysis and condensation of an alkoxysilane, such as tetraethylorthosilicate (TEOS), in an aqueous alcohol medium, using ammonium hydroxide as the catalyst.^{16,17} The Stöber method works very well for the fabrication of large (hundreds of nanometres or several microns in diameter) silica particles. The resulting particle size and distribution can be affected by several experimental parameters, including reagent concentration, heat and agitation during the preparation procedure.^{18,19} However, this method can give unreliable results in the preparation of small sized (below 50 nm) silica nanoparticles.¹⁴

The preparation of different nanosized silica particles has been intensively studied by several groups.^{14,18-21} Nevertheless, it is often the case that, despite similar experimental methods, the results obtained are contradictory – as emphasised by Rao *et al.*²⁰ Therefore, there is still the need for a reliable, optimised technique for the production of small nanosized silica particles. In addition, previous work has also been carried out in which the types of reagents used have been investigated.^{22,23} However, we have chosen to use a TEOS, ethanol and water system with ammonium hydroxide as the basic catalyst, as this is the most widely used reagent system employed for silica nanoparticle preparation.

Dye-doped fluorescent silica nanoparticles are of particular interest. In general, fluorescent nanoparticles hold great promise in biomedicine due to their small sizes, which allows their infiltration into cells and their luminescent intensity, which allows imaging of cells to be carried out.²⁴ Dye-doped silica nanoparticles show distinct advantages over Quantum Dots (QDs), fluorescent dyes, upconverting phosphors and plasmon resonant particles because of their water dispersity and ease of surface modification with different functional groups for subsequent bioconjugation, due to well-known silica chemistry.²⁵ Fluorescent nanoparticles can be prepared using traditional core-shell dye-doping methods.²¹

Manipulation of the structure and morphology of materials on the nanoscale is of great interest as it could allow precise control over the local environment of materials. Indeed, hollow nanostructures may find immediate applications in fields such as catalysis and drug delivery as well as being highly useful as anti-reflective coatings on surfaces.^{26,27} One well-known approach for preparing hollow silica nanostructures is by the use of a template, often a surfactant or core material, which is subsequently removed by chemical extraction or calcination.^{26,28-30} The preparation of such materials without the need for an internal stabiliser and its consequent removal is an attractive prospect.

The Kirkendall theory describes the diffusion of components in a system across a concentration gradient and the effect this has on mechanical and chemical processes; this can be applicable to both solids and liquids.^{31,32} Recently, this effect has been utilised to prepare nanomaterials by controlling the difference in diffusion rates between two components in a reaction to prepare alloyed or hollow materials. Yin and co-workers have prepared hollow cobalt oxide nanocrystals from cobalt particles by relying on the diffusion of atoms to the surface to undergo controlled oxidation and the formation of voids in the centre of the particles.³³

3.2 Aims

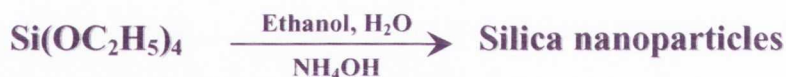
The main aim of the work presented in this chapter is the optimisation of the preparation of silica nanoparticles. The well-documented Stöber technique for preparing silica nanoparticles will be used; we plan to modify the Stöber synthesis to optimise the preparation of silica nanoparticles of small sizes and narrow standard deviation. We plan to

prepare silica nanoparticles with narrow size distribution by the hydrolysis and condensation of tetraethylorthosilicate in water and ethanol in the presence of ammonium hydroxide. Statistical analyses (in the form of a factorial design investigating the variation of reagent concentrations) will be used to optimise the preparation of small sized silica nanoparticles with small standard deviation.³⁴ Statistical analyses will show whether there is a significant correlation between reagent concentrations, which have an impact on the resultant particle size. Various agitation methods employed in nanoparticle preparation will be investigated. This part of the work will also involve synthesis of luminescent silica nanoparticles. In addition, we plan to develop new approaches for the preparation hollow silica nanoparticles where an organic dye can be encapsulated within the nanoshells.

3.3 Preparation and Characterisation of Silica Nanoparticles

3.3.1 Preparation of Silica Nanoparticles – Initial Investigation

Silica nanoparticles were prepared using the well-documented Stöber method¹⁴ and our modifications of this method. The Stöber synthesis involves a hydrolysis reaction of tetraethylorthosilicate (TEOS) with water, followed by a condensation reaction using a basic catalyst in water (Scheme 3.1).



Scheme 3.1: Schematic presentation of the preparation of silica nanoparticles using the Stöber method – a hydrolysis and condensation reaction.

Alteration of reagent concentration and of the method of agitation proffered nanoparticles of varying size, shape and size distribution. Initial investigation of parameter variation causing nanoparticle size deviation was carried out by Stöber and colleagues.¹⁴ The Stöber method of preparation uses an ultrasonic bath at ice-cold temperatures. This method allows production of particles which are normally between 100 nm and 1 micron in diameter and this paved the way for many more investigations into particle size optimisation. A more recent useful investigation of optimisation was carried out by Rao *et al.*,²⁰ who used a different method of agitation and reagent addition. This involved a semi-

batch method with mechanical stirring and external heat application using a water bath. Their results yielded nanoparticles which were between 10 and 240 nm in diameter. This is much closer to the size range that we are interested in for this project. However, there is a great deal of contradiction between results present in the literature, particularly with regard to the particles yielded through control reported by variation of parameters. For this reason, we decided to attempt to reproduce some of these results and vary the main parameter which affects particle size – the concentration of ammonium hydroxide catalyst. Table 3.1 presents the results obtained when mechanical stirring with variation of ammonium hydroxide concentration only was used.

Table 3.1: Reagent ratios, resulting particle size and standard deviation of experiments carried out.

Sample	Ammonium hydroxide conc. (mM)	Molar ratio of TEOS:H ₂ O :Ethanol	d _{TEM} ^[a] (nm)	d _{hyd} ^[b] (nm)	PDI
A	1.5	0.05:0.2:0.4	15 ± 3	36.2	0.215
B	2	0.05:0.2:0.4	16 ± 3	32.7	0.110
C	3	0.05:0.2:0.4	21 ± 4	38.7	0.187
D	4.5	0.05:0.2:0.4	26 ± 5	39.1	0.057
E	7	0.05:0.2:0.4	43 ± 16	73.6	0.056
F	15	0.05:0.2:0.4	160 ± 21	255	0.358
G	30	0.05:0.2:0.4	206 ± 17	313	0.172
H	45	0.05:0.2:0.4	237 ± 16	440	0.303
I	70	0.05:0.2:0.4	270 ± 18	278	0.048

[a] d_{TEM} refers to the average diameter of particles calculated from >100 nanoparticles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions.

3.3.2 Characterisation of Silica Nanoparticles

Aqueous suspensions of the nanoparticles were characterised using Transmission Electron Microscopy (TEM) and Photon Correlation Spectroscopy (PCS); solid samples of the nanoparticles were characterised by Fourier-Transform Infrared (FTIR) spectroscopy.

3.3.2.1 Transmission Electron Microscopy

TEM images were taken of the washings of nanoparticles which were stable solutions in Millipore water. The TEM images (Figure 3.1) show nanoparticles which vary in size and size distribution. According to the TEM images, particle sizes increase with an increase in the concentration of ammonium hydroxide added during the synthesis (Figure 3.2). At low ammonium hydroxide concentrations, the nanoparticles prepared proved to be small in size with narrow standard deviations (15 ± 3 nm). This information allowed us to optimise the ammonium hydroxide concentration for the preparation of silica nanoparticles, producing small particles with narrow size distributions. Histograms showing the size and size distribution amongst the samples prepared can be seen in Figure 3.3.

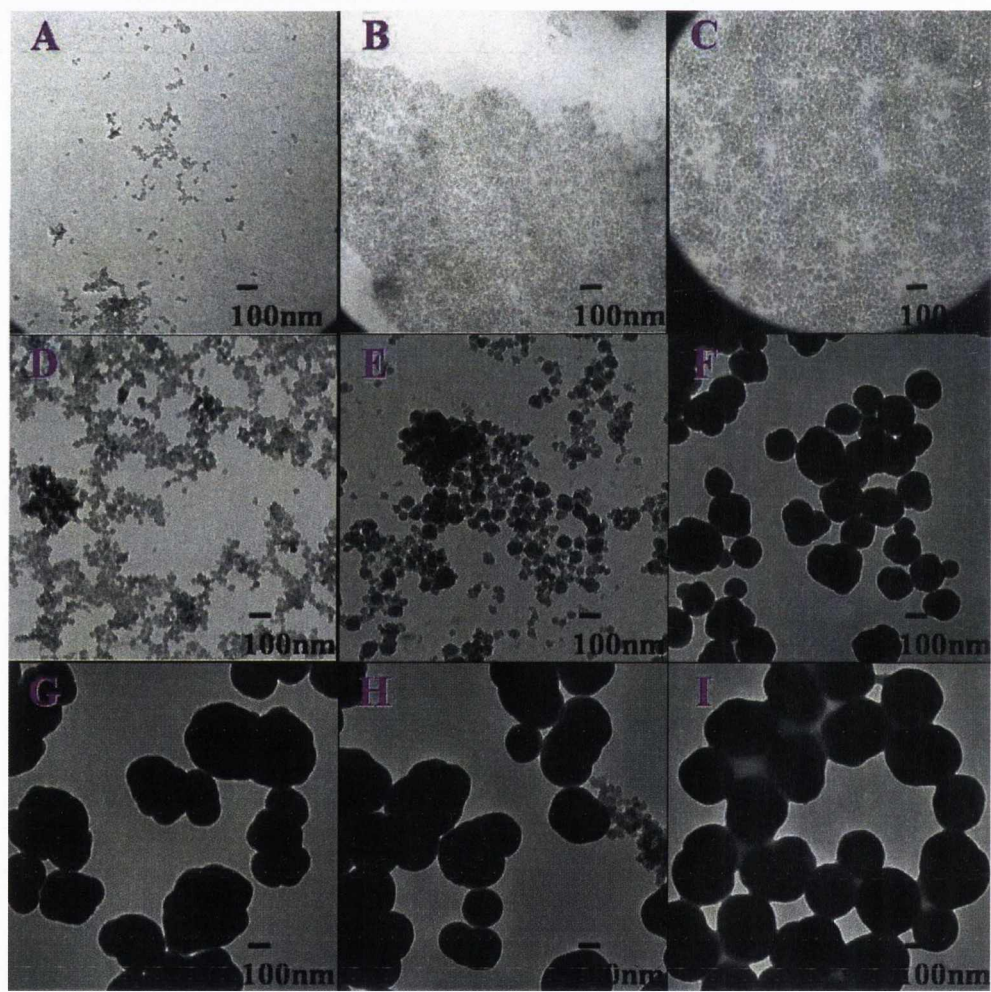


Figure 3.1: TEM images of silica nanoparticles prepared according to Table 3.1 as labelled. Samples shown at x20,000 magnification; scale bar 100 nm.

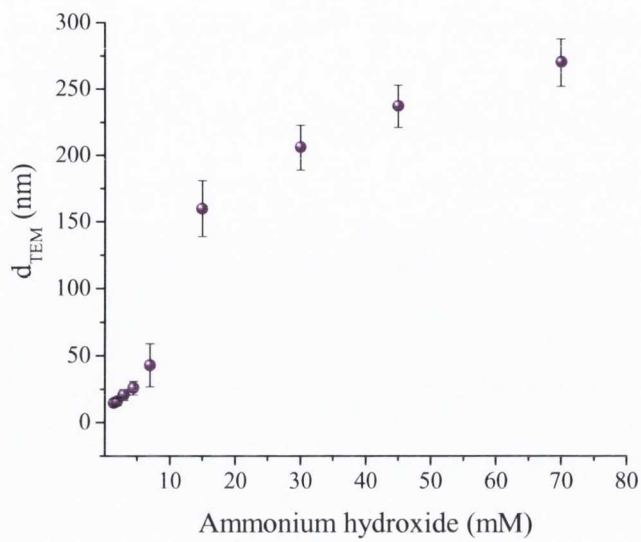


Figure 3.2: Graph showing increasing nanoparticle size with increasing ammonium hydroxide concentration.

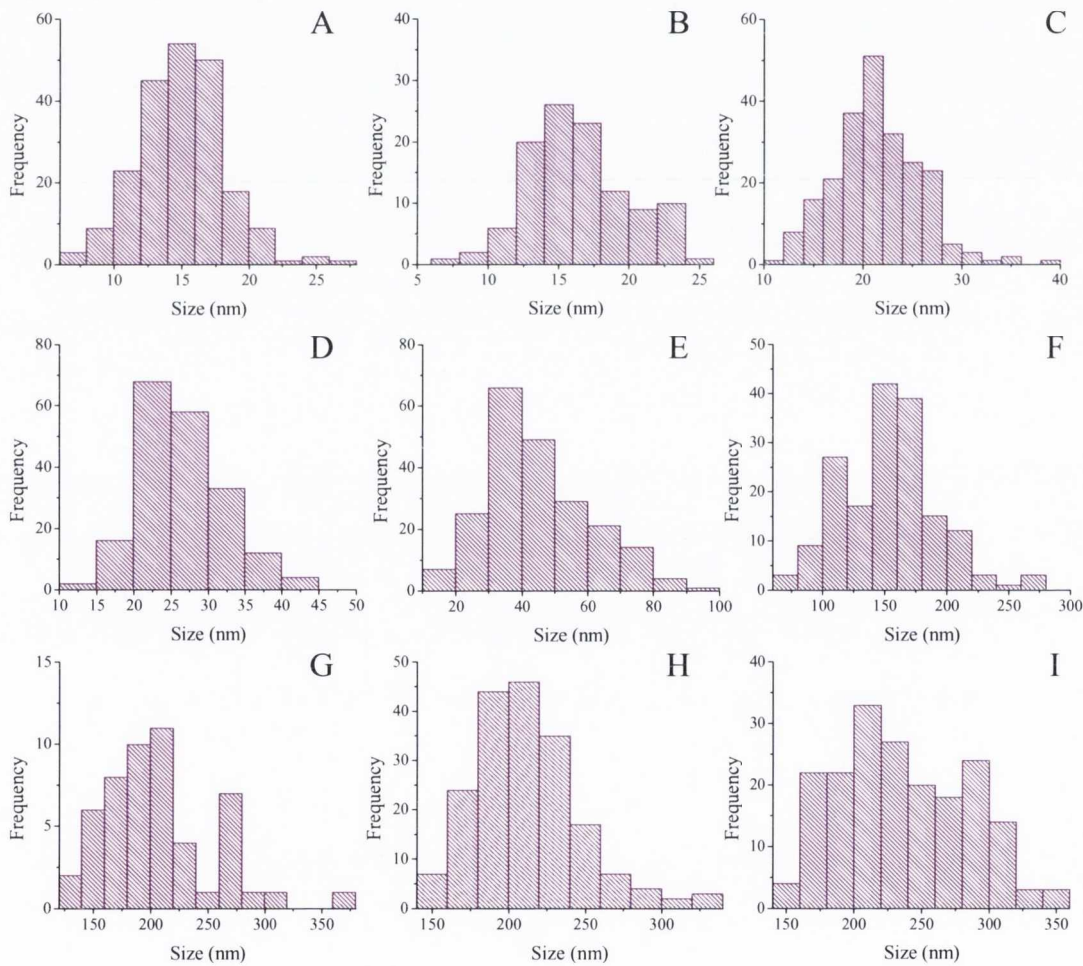


Figure 3.3: Histograms showing size distribution of nanoparticles prepared according to Table 3.1.

3.3.2.2 Photon Correlation Spectroscopy

Photon Correlation Spectroscopy (PCS) measurements were carried out on the washings of the samples in water (Table 3.1). As can be seen, the results deviate somewhat from the sizes calculated from the TEM images. This is due to differences between the measurement techniques. In TEM, images are taken of nanoparticles after they have dried onto a surface; PCS, on the other hand, is carried out on samples in suspension. This takes into account Brownian motion effects, as well as any hydrogen bonding and van der Waals interactions between the particles and surrounding solvent molecules which may contribute to the overall particle size. Due to these effects, the PCS results measure the hydrodynamic radius of the particles in liquid and hence show a larger value for the nanoparticles' diameter. The PCS data also allows us to check the behaviour of the particles and their distribution in suspension, using the polydispersity index (PDI). In Table 3.1, the PDI values can be seen to be well below 1 which indicates the monodispersity of the nanoparticle suspensions.

3.3.2.3 Infrared Spectroscopy

FTIR spectroscopy (*Figure A1.1, Appendix 1*) of silica nanoparticles agrees with reported spectra.^{35,36} The most intense peak, centred at 1110 cm^{-1} , represents the Si-O-Si bond. This peak and the shoulder associated with it can be assigned to asymmetric stretching vibrations of the three-dimensional Si-O-Si network. A weaker peak at about 790 cm^{-1} corresponds to symmetric stretching vibrations of Si-O-Si. Another weak peak at approx. 950 cm^{-1} can be associated with stretches of Si-OH or Si-O⁻ groups.³⁶ The broad peak at $3440\text{--}3460\text{ cm}^{-1}$ represents water and OH⁻ groups on the surface of the nanoparticle. The other peaks which are present may be assigned to various organic species present in the sample.

3.4 Optimisation of the Preparation of Silica Nanoparticles

3.4.1 Statistical Study

We have chosen to carry out a 2^2 statistical analysis, which is a multi-factorial study where two factors are each investigated at two levels. The two parameters varied in the first statistical study were the quantities of TEOS and ammonium hydroxide solution. The

two parameters varied in the second statistical study were the amounts of water and ethanol. The response measured was the nanoparticle average diameter in nanometres. The levels at which the concentrations were varied can be seen in the table accompanying the descriptions of the designs (Tables 3.2 and 3.3). More than two concentration levels have been used to complete the study and allow a response surface graph to be plotted. Statistical significance calculations were carried out on the results obtained from *Minitab 14* programme using Student's t-test. In these calculations, the parameters varied were assumed to be independent of each other. If the results appeared to be statistically significant (*i.e.* having a P-value of less than 0.05), then an interaction between the parameters involved is implied. These calculations take into account chance variation of results. Each data point in the factorial design was repeated experimentally a minimum of three times and the experiments were carried out in a random order each time to eliminate trends due to chance variation.³⁷

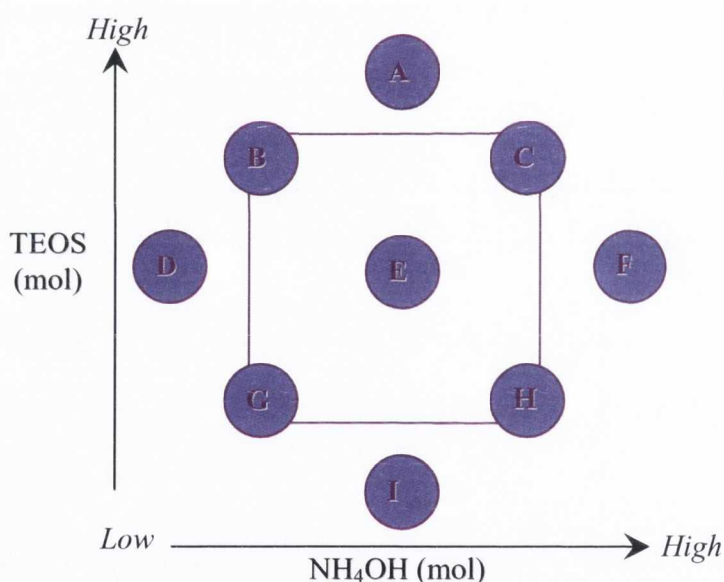
3.4.2 Statistical Design

One of the main aims of our work was to optimise the synthesis of small sized silica nanoparticles. We previously investigated the effect of altering the concentration of ammonium hydroxide on the size of the resultant nanoparticles. However, the variation of only one parameter does not take into account interactions between other conditions in the system and how these might affect particle growth. For this reason, a statistical analysis of the preparation of silica nanoparticles was carried out in order to optimise the other conditions for the production of small sized silica nanoparticles by the traditional Stöber method. For potential biomedical applications, nanoparticles of a small size (<50 nm) are required. The most important parameters involved in the production of these particles are the quantities of the reagents – TEOS, ethanol, water and ammonium hydroxide solution. Varying each of these parameters one at a time would be inefficient and time consuming. Also, by varying one at a time, nothing can be deduced about the interactions between these factors. It is better to design an experiment where the factors can be changed simultaneously in a systematic way (Scheme 3.2). This allows an estimation of the effects of the variables and their interactions. This type of experiment is a factorial design. Here, the factorial experiment is employed in the form of a response surface model (Figure 3.8).

The results can be presented graphically to represent the area of the optimum result. This allows us to check when we are approaching the maximum conditions, when we reach the maximum and when we have gone beyond it. Two statistical studies have been carried out: the first investigates the potential interaction between the quantities of TEOS and ammonium hydroxide; the second examines the possible interactions between the amounts of ethanol and water solvents.

3.4.3 Results and Characterisation of Statistical Study 1

This statistical design investigates the potential interaction between the quantities of TEOS and ammonium hydroxide. The study can be represented schematically as in Scheme 3.2. The concentrations of the solutions were varied according to Table 3.2. Solutions were prepared using magnetic stirring and gentle heating at 40-50°C. Reactions were carried out in a random order.



Scheme 3.2: Presentation of the first statistical design of optimisation model for the preparation of small sized silica nanoparticles by the classical Stöber method.

All nanoparticles were characterised using TEM, PCS and FTIR spectroscopy. Size studies of nanoparticles from TEM images were carried out on all samples, in order to identify optimal concentrations of reagents to yield smallest particle size. The results of

this can be seen in Table 3.2. Statistical analyses were presented as 3-D response surface models (Figure 3.8).

Table 3.2: Relative amounts of reagents in reaction and resulting nanoparticle sizes – statistical study 1.

Sample	TEOS (mmol)	Ammonium hydroxide (mmol)	Ethanol (mol)	Water (mol)	d _{TEM} ^[a] (nm)	d _{hyd} ^[b] (nm)	PDI
A	70	3	0.4	0.2	5 ± 1	57	0.122
B	60	2	0.4	0.2	21 ± 7	49	0.136
C	60	4.5	0.4	0.2	30 ± 6	71	0.141
D	50	1.5	0.4	0.2	18 ± 4	40	0.132
E	50	3	0.4	0.2	23 ± 5	45	0.102
F	50	7	0.4	0.2	28 ± 8	91	0.113
G	40	2	0.4	0.2	18 ± 5	35	0.105
H	40	4.5	0.4	0.2	18 ± 4	41	0.072
I	40	3	0.4	0.2	15 ± 4	32	0.103

[a] d_{TEM} refers to the average diameter of particles calculated from >100 nanoparticles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions.

3.4.3.1 Transmission Electron Microscopy

TEM images were taken of all the washings of nanoparticles which were stable solutions in Millipore water. The TEM images (Figure 3.4) show nanoparticles which vary in size and size distribution. Details of the resultant nanoparticle sizes for statistical study 1 can be seen in Table 3.2.

To schematically represent these results, the size distributions for an average size of a minimum of 100 particles of each sample have been plotted. The particle histograms for each sample can be seen in Figure 3.5. These results are also represented in the form of a three-dimensional surface contour model (Figure 3.8).

The TEM images show that the particles are consistently small in size, with narrow size distributions (Figure 3.5). The smallest particles were observed in sample A (5 nm ± 1). Therefore, the conditions which provide the smallest sized nanoparticles are high levels of TEOS combined with low levels of ammonium hydroxide solution.

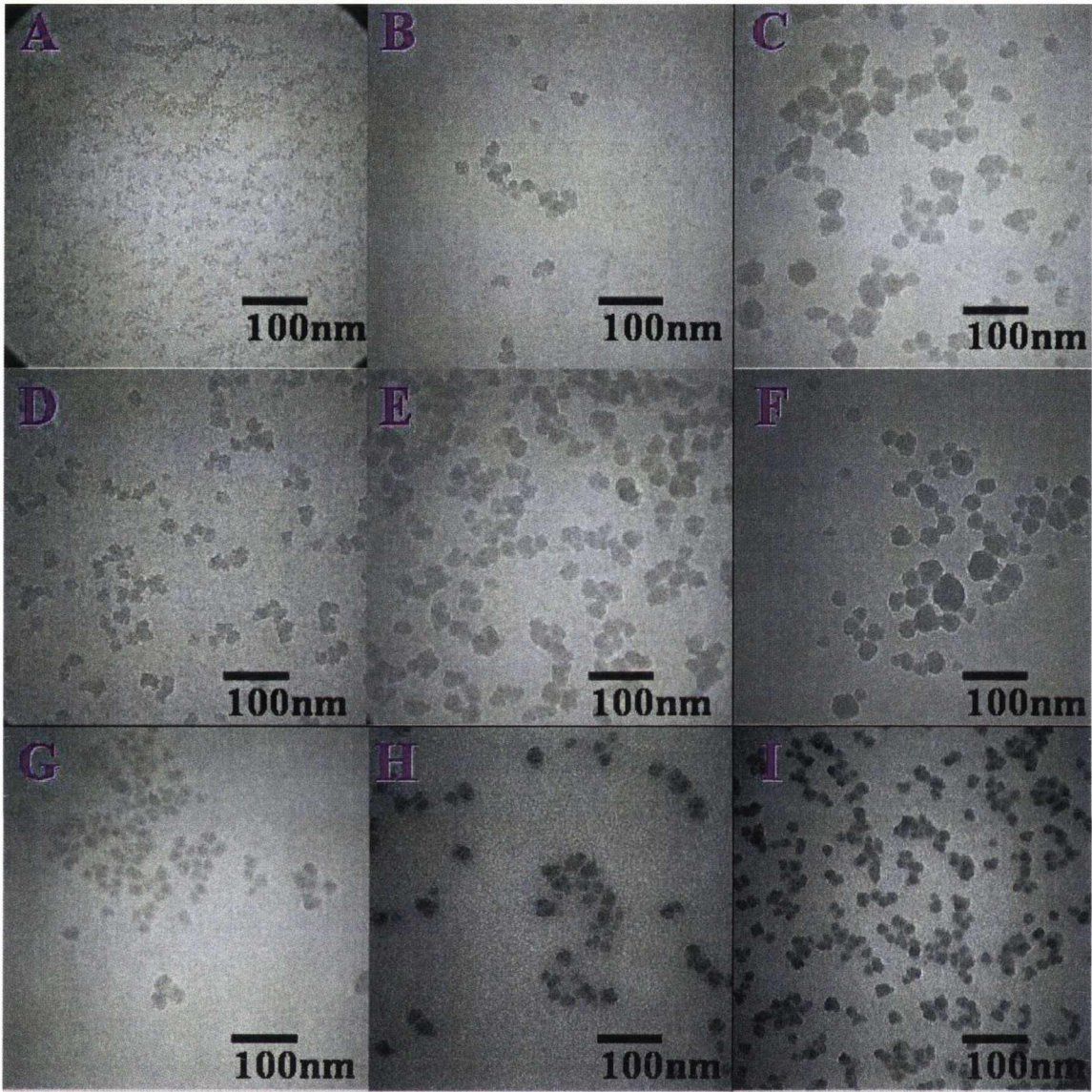


Figure 3.4: TEM images of samples prepared according the statistical study 1, shown at x50,000 magnification; scale bar 100 nm.

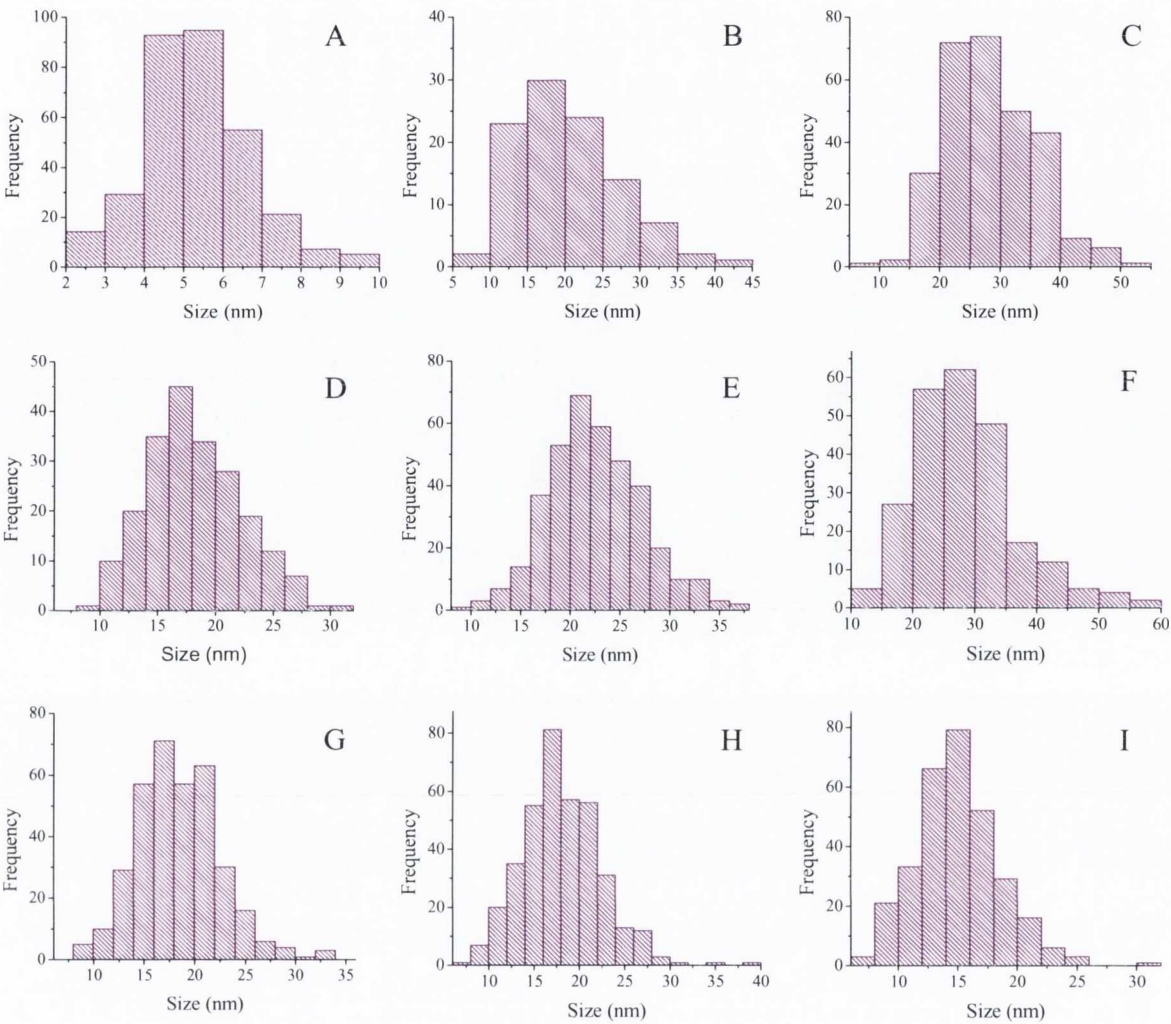


Figure 3.5: Histograms showing size distribution of nanoparticles prepared according to statistical study 1.

3.4.3.2 Photon Correlation Spectroscopy

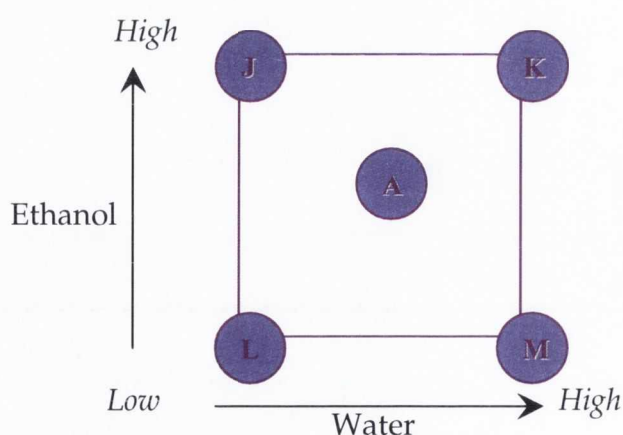
PCS measurements show that the nanoparticles are larger when compared to the results calculated by TEM (Table 3.2). This is due to the higher hydrodynamic radius of the particles in suspension and can be further explained by clustering of particles, which takes place in solution, where hydrogen bonding, electrostatic and van der Waals forces can come into play. The PDI values show a low polydispersity for the nanoparticle samples.

3.4.3.3 Infrared Spectroscopy

FTIR spectroscopy (Figure A1.2) of silica nanoparticles agrees with reported spectra.^{35,36} As previously, the most intense peak, centred at 1050 cm^{-1} and the shoulder associated with it can be assigned to the asymmetric stretching vibrations of the Si-O-Si bonds. Weak peaks at about 790 cm^{-1} and 950 cm^{-1} correspond to symmetric stretching vibrations of Si-O-Si and stretches of Si-OH or Si-O⁻ groups respectively.³⁶ The broad peak at $3440\text{--}3460\text{ cm}^{-1}$ represents water and OH⁻ groups on the surface of the nanoparticle. The other peaks which are present may be assigned to various organic species present in the sample.

3.4.4 Results and Characterisation of Statistical Study 2

This statistical design investigated the potential interaction between the quantities of ethanol and water. The study can be represented schematically as can be seen in Scheme 3.3. The concentrations of the solutions were varied according to Table 3.3. Solutions were prepared using magnetic stirring and gentle heating at $40\text{--}50^\circ\text{C}$. Reactions were carried out in a random order. Size studies of nanoparticles from TEM images (Figure 3.6) were carried out on all samples, in order to identify optimal concentrations of reagents to yield smallest particle size. The results of this can be seen in Table 3.3. The particle histograms for each sample can be seen in Figure 3.7. Statistical analyses were presented as 3-D response surface models (Figure 3.8).



Scheme 3.3: Presentation of the second statistical design of optimisation model for the preparation of small sized silica nanoparticles by the classical Stöber method.

Table 3.3: Relative amounts of reagents in reaction and resulting nanoparticle sizes – statistical study 2.

Sample	TEOS (mmol)	Ammonium hydroxide (mmol)	Ethanol (mol)	Water (mol)	d _{TEM} ^[a] (nm)	d _{hyd} ^[b] (nm)	PDI
A	70	3	0.4	0.2	5 ± 1	57	0.122
J	70	3	0.6	0.1	16 ± 4	61	0.160
K	70	3	0.6	0.4	21 ± 5	36	0.111
L	70	3	0.2	0.1	34 ± 27	140	0.122
M	70	3	0.2	0.4	21 ± 8	262	0.206

[a] d_{TEM} refers to the average diameter of particles calculated from >100 nanoparticles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions.

3.4.4.1 Transmission Electron Microscopy

TEM images were taken of the washings of nanoparticles which were stable solutions in Millipore water. The TEM images (Figure 3.6) show nanoparticles which vary in size and size distribution: Details of the resultant nanoparticle sizes for statistical study 2 can be seen in Table 3.3 and the particle histograms for each sample are shown in Figure 3.7. These results are also represented in the form of a three-dimensional surface contour model (Figure 3.8).

TEM images once again show that particles are consistently small in size with narrow size distributions. Overall, the smallest particles were those observed previously in sample A (5 nm ± 1).

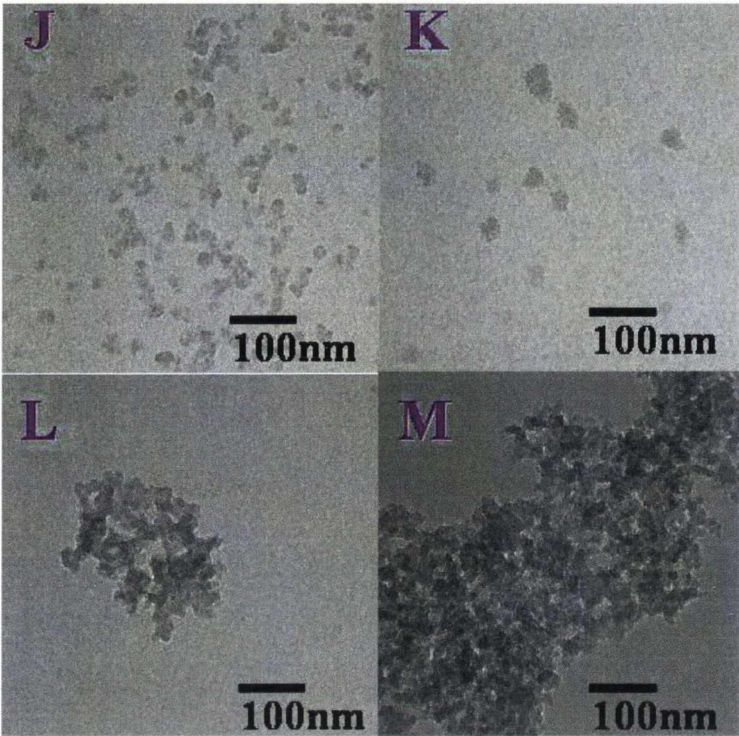


Figure 3.6: TEM images of samples prepared according to the statistical study 2, shown at x50,000 magnification; scale bar 100 nm.

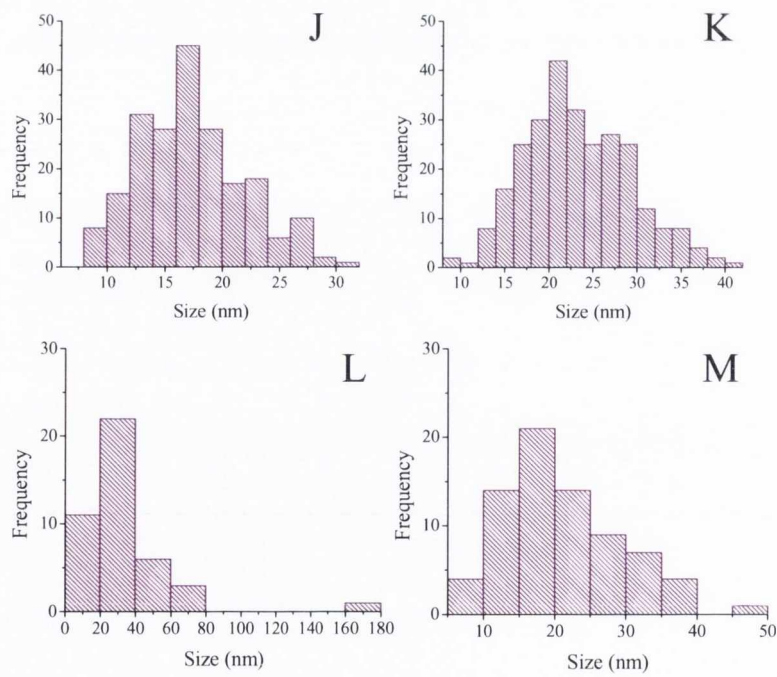


Figure 3.7: Histograms showing size distribution of nanoparticles prepared according to statistical study 2.

3.4.4.2 Photon Correlation Spectroscopy

PCS measurements show that the nanoparticles are larger when compared to the results calculated by TEM (Table 3.3). This is due to the higher hydrodynamic radius of the particles in suspension and can be further explained by clustering of particles, which takes place in solution, where hydrogen bonding, electrostatic and van der Waals forces can come into play. The PDI values show a low polydispersity for the nanoparticle samples.

3.4.4.3 Infrared Spectroscopy

FTIR spectroscopy (*Figure A1.3*) of silica nanoparticles display peaks in identical regions to the particles prepared previously, see Section 3.4.3.3

3.4.5 Findings of Statistical Designs

These factorial designs can be represented in the form of three-dimensional surface contour graphs (*Figure 3.8*). The contours represent the response of the system – in this case the resultant nanoparticle size. Blue areas show the smallest particles while red areas show the largest particles. This allows us to easily choose the parameter concentrations which provide optimised size nanoparticles.

Statistical calculations were carried out to investigate the potential for interaction between different factors. Analysis of variance of the two-way interaction gave a P-value of 0.448 for the first statistical study and 0.667 for the second statistical study. These values indicate that the results are not statistically significant and hence, the amounts of TEOS and ammonium hydroxide solution are not influenced by one another. Similarly the quantities of ethanol and water are not influenced by one another.

We can conclude that the optimal numbers of moles of reagents are 70 mmol of TEOS, 3 mmol of ammonium hydroxide, 0.2 mol of water and 0.4 mol of ethanol for the synthesis of small sized nanoparticles. This combination of amounts of reagents provides us with very small sized nanoparticles with a narrow size distribution ($5\text{ nm} \pm 1$).

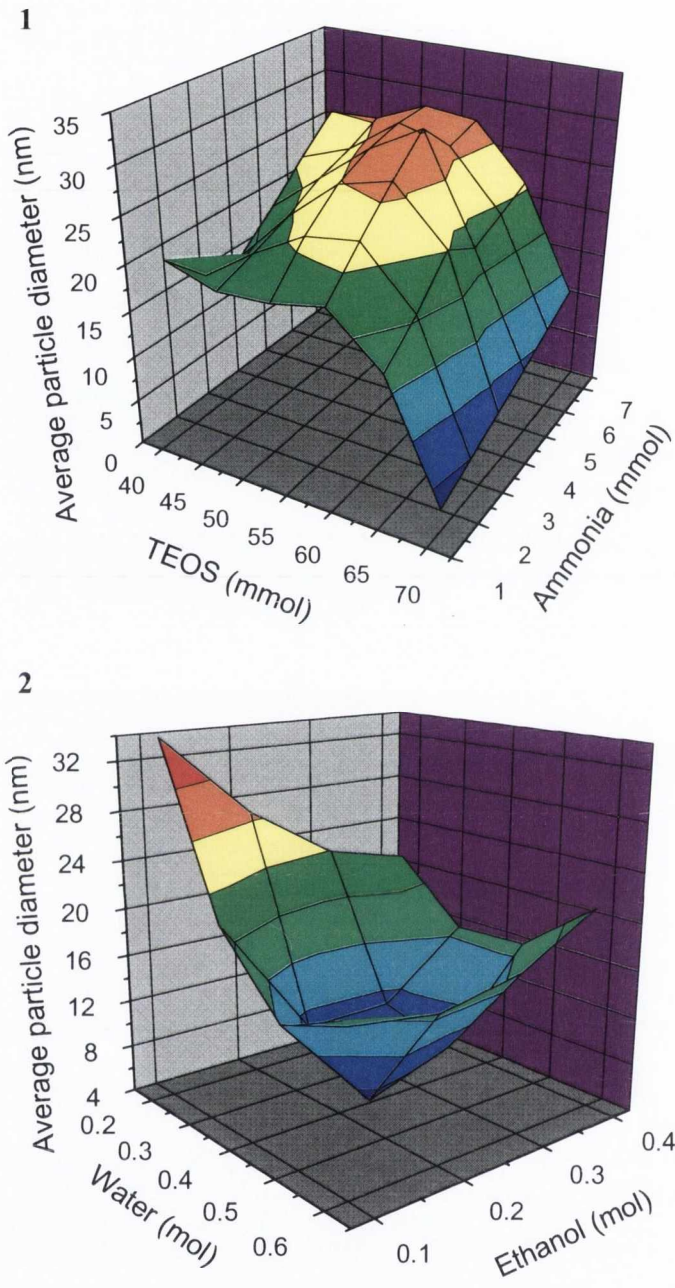


Figure 3.8: 3-D surface contour models of the first (1) and second (2) statistical studies where reagent concentrations were chosen as factors to be varied.

Low amounts of ammonium hydroxide solution yield smaller sized nanoparticles since silica particle nucleation proceeds by aggregation of siloxane substructures which is strongly influenced by the surface potential of silica particles and by the ionic strength of

the reaction medium. Thus, small nanoparticles are usually formed due to the low ionic strength of the solution at low concentrations of ammonium hydroxide.¹⁷ The amount of water and ethanol play a role in the hydrolysis step of the mechanism. An aspect of particle formation and growth previously considered by van Blaaderen *et al.* involves the amount of water present.^{16,17} According to this research, particle growth relies on monomer addition, with the growth rate being controlled by the rate of alkoxide hydrolysis. Further work investigating the mechanism of particle growth by Osseo-Assare and Arriagada agrees with this hypothesis regarding the growth rate dependency on TEOS hydrolysis, but argues that a different mechanism is rate-determining in the later stages of growth.¹⁶ Our optimised reagent results are in good agreement with these previous publications.

3.5 Investigations of Various Agitation Methods

In colloidal science, agitation can frequently perform two opposite roles in the flocculation of colloidal particles. For example, mechanical shear can break up aggregated particulates and keep particles well dispersed in liquids. It has also been postulated that mechanical stirring could induce colloidal coagulation, enhancing both the intensity and probability of mutual collisions of particles.¹⁸

The preparation of silica nanoparticles thus far has involved agitation *via* mechanical stirring and external heat application. As documented by Stöber, ultrasonic treatment in an ultrasonic bath can be a useful method of agitating the system. This method, however, does hold limitations. The most concerning factor is the degree of local heat generated by the ultrasonic vibrations which can result in high temperatures. This in turn causes the production of larger sized particles which ripen faster during the Ostwald process due to this heat. The possibility of using such a system has been investigated by Stöber in his original 1968 publication.¹⁴ However, a detailed study into the use of other agitation methods while controlling temperature has not previously been reported. In this part of the work, we investigate and compare the use of ultrasonic treatment (in the form of ultrasonic bath and ultrasonic tapered tip equipment) and microwave treatment to prepare silica nanoparticles. The optimised concentrations of reagents, as found from the previous statistical experiments, have been used throughout (70 mmol TEOS, 3 mmol ammonium

hydroxide solution, 0.4 mol ethanol, 0.2 mol water). All other experimental conditions were kept as stable as possible.

3.5.1 Preparation and Characterisation of Samples Prepared Using Different Agitation Methods

The introduction of energy into the system was investigated by attempting various agitation methods while keeping all reagent concentrations at their optimal level, as established by the previous set of experiments. The different methods used gave widely different results in terms of the sizes of the nanoparticles produced, as can be seen in Figures 3.9, 3.10 and 3.12.

Initially, ultrasonic bath treatment was used to prepare silica nanoparticles. The results demonstrated that small sized nanoparticles could be prepared; however the reliability of this method was questionable, as repetition of experiments resulted in particles which varied in their size distribution. This can be seen in Figure 3.9 which shows TEM images of two samples prepared with identical conditions, where image (b) shows the presence of two populations of differently sized nanoparticles. Variation of the time spent in the bath did not affect the sizes of the resulting nanoparticles. It is thought that the nature of the ultrasonic vibrations and the large size of the bath (5 L capacity) caused the ultrasonic waves to distribute unevenly throughout the sample, causing this variation in the resulting nanoparticle size.

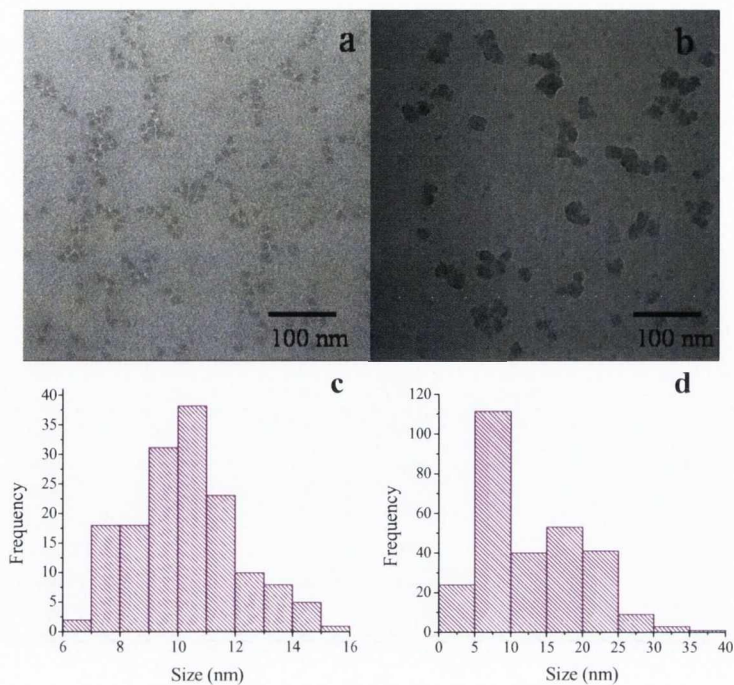


Figure 3.9: TEM images of (a) sample 1 (10 ± 2 nm) and (b) sample 2 (13 ± 7 nm); Histograms of (c) sample 1 and (d) sample 2. Samples were prepared using identical conditions using the ultrasonic bath.

More intensive ultrasonic treatment was employed by using an ultrasonic tapered tip. It was expected that the ultrasonic tip would cause larger amounts of energy to be delivered to the samples and would cause a decrease in the time needed to prepare the nanoparticles. The time spent under the ultrasonic tip was varied and the temperature was controlled by using an ice bath (Table 3.4). The pulsed setting allows ultrasonic vibration to cycle between on and off over one second. TEM images and their accompanying histogram profiles (Figure 3.10) show the nanoparticles that were prepared using the ultrasonic tapered tip.

The TEM images of these samples (Figure 3.10) and their sizes as calculated from the images (Table 3.4) show a slight variation between the resulting sizes of the nanoparticle samples A, B, C and D with the standard deviations remaining relatively small. Surprisingly, the longer time spent under continuous sonication does not cause significantly larger particles to be formed. The introduction of pulsing vibrations does not appear to have a major effect on either particle size or standard deviation. The introduction of ice into the system caused the most noticeable difference in the resulting particles – with

smaller sized nanoparticles being formed in sample E. This is due to the ice cooling the overall system, lowering the heating effect of the sonic vibrations.

Table 3.4: Conditions used to prepare samples using ultrasonic tapered tip and resulting nanoparticle sizes.

Sample	Reaction time (mins)	Conditions	$d_{\text{TEM}}^{[a]}$ (nm)	$d_{\text{hyd}}^{[b]}$ (nm)	PDI
A	2	No ice; continuous sonication	20 ± 4	48	0.127
B	8	No ice; continuous sonication	18 ± 3	110	0.295
C	8	Ice; continuous sonication	17 ± 5	87	0.218
D	8	No ice; pulsed sonication	16 ± 4	51	0.173
E	8	Ice; pulsed sonication	6 ± 2	126	0.178

[a] d_{TEM} refers to the average diameter of particles calculated from >100 nanoparticles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions.

The PCS average diameters shown in Table 3.4 are, in general, larger than the TEM average diameter results. These results are similar to previous findings and can be explained by the aggregation of particles in water as a result of hydrogen bonding and van der Waals interactions. Some samples demonstrate significantly larger sizes in PCS compared to one another (*e.g.* samples B and E). As can be seen in TEM, these samples tend to aggregate more, leading the machine to record a higher hydrodynamic radius.

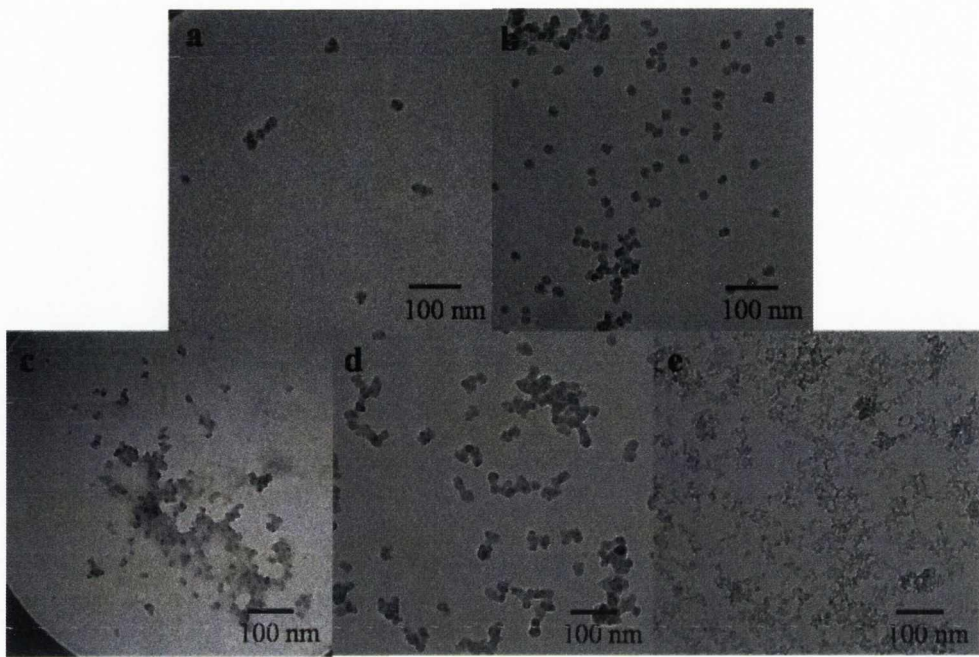


Figure 3.10: TEM images of samples corresponding to samples A-E in Table 3.4, scale bar 100 nm.

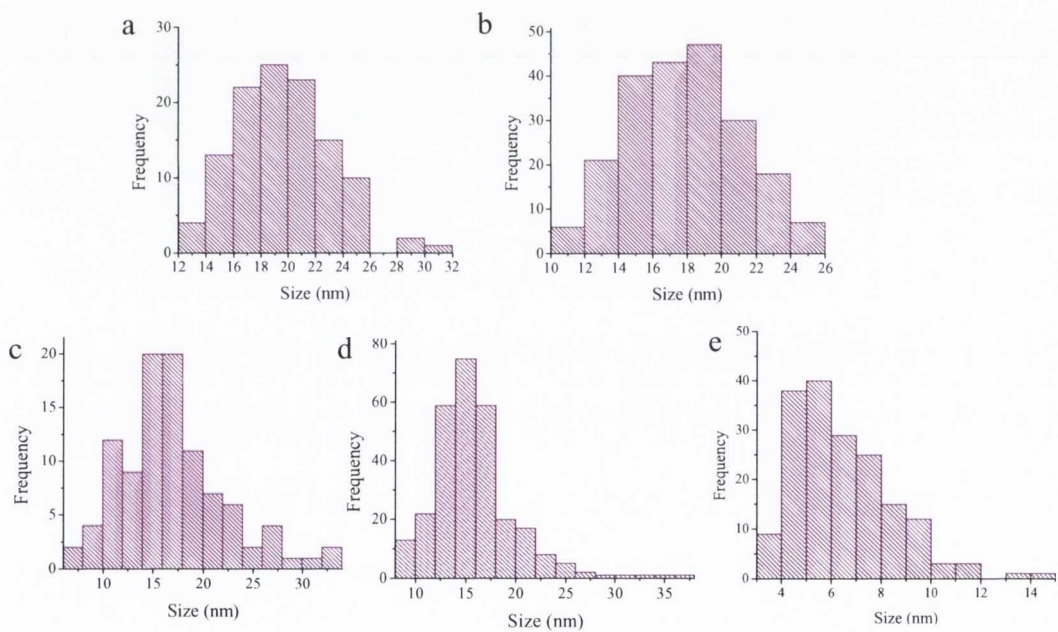


Figure 3.11: Histograms of size distribution of samples A-E according to Table 3.4.

Microwave treatment was also attempted as a method of introducing energy to the system. The length of time of microwave treatment was varied and an ice bath was used in an attempt to control the temperature. This method proved to be very unreliable and

reproducible results were difficult to obtain. The solutions tended to boil very easily and neither the use of an ice bath nor scaling up rectified this problem. Some particles proved to be very small in size with narrow size distribution (Sample 1; 20 ± 5 nm), whereas others provided much larger sized nanoparticles with large size distributions (Sample 2; 33 ± 26 nm), even under the same reaction conditions. TEM images and histograms of typical samples prepared using microwaving are shown in Figure 3.12. These images show the variation in the sizes of the resulting nanoparticles – with some small particles present as well as larger aggregates.

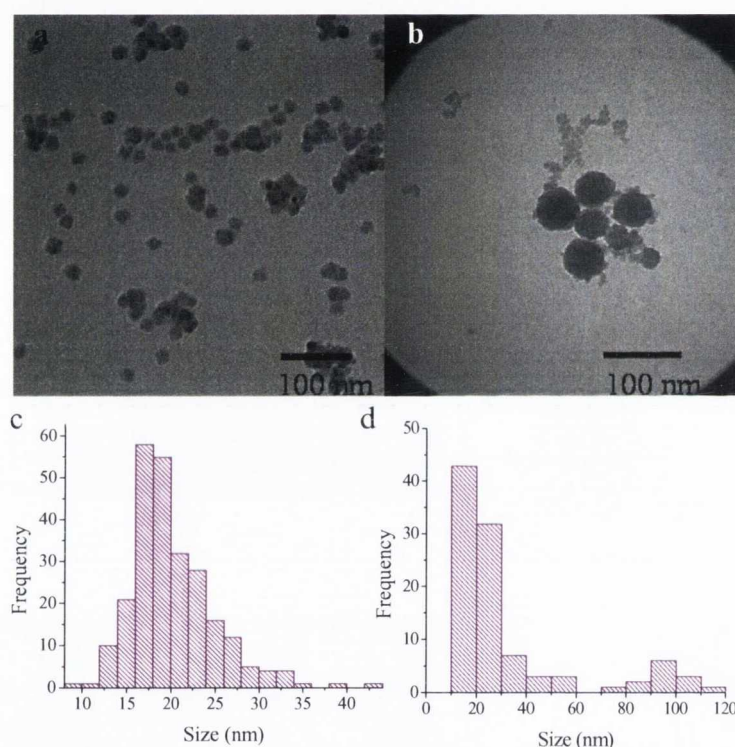


Figure 3.12: TEM images of (a) sample 1 (20 ± 5 nm) and (b) sample 2 (33 ± 26 nm); Histograms of (c) sample 1 and (d) sample 2. Samples were prepared using identical conditions using the microwave.

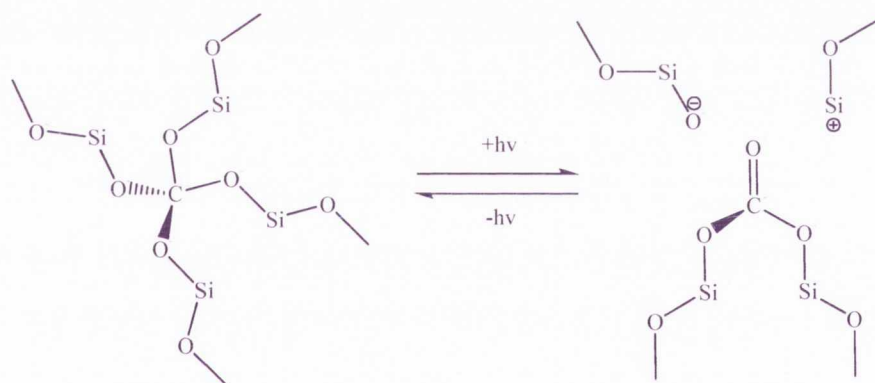
The most successful method of introducing energy during the synthesis of silica nanoparticles is by using ultrasound in the form of the ultrasonic tapered tip. Using this method, we have successfully reduced the preparation time of silica nanoparticles to less than 10 minutes, a significant reduction when compared the traditional aqueous preparations of 2 hours or more. Careful control of the reaction temperature using ice

during the reaction procedure prevents the growth of the nanoparticles to larger sizes by Ostwald ripening.

3.5.2 Silica Nanoparticles with White Emission

Small sized luminescent silica nanoparticles which demonstrate strong broad white emission have been prepared using our modified Stöber technique, without the incorporation of traditional organic dyes or metallorganic dopants.

Previously, Green *et al.* have reported highly luminescent silica sol-gels.³⁸ These sol-gels are produced at very high temperatures (400-500° C) and it has been proposed that heat may cause the decomposition of organic species during the reaction process to create carbon substitutional defects for Si, which are thought to be the luminescent species in the lattice (Scheme 3.4). Luminescence in silica gels has also been attributed to carbonyl substitution by contamination due to ageing in ambient conditions.³⁹ We aimed to use this information to formulate a new method of preparing silica nanoparticles which demonstrate similar luminescence in an attempt to produce luminescent silica particles.



Scheme 3.4: The possible luminescent emission originating from carbon substitutional defects in silica sol-gels, reproduced from³⁸.

Unfortunately there are significant constraints within the traditional Stöber method used to prepare silica nanoparticles, which requires low boiling point solvents and low temperatures, since high temperatures lead to increased particle size and their aggregation. Hence, we were unable to directly apply Green *et al.*'s preparative technique to the production of nanoparticles. Therefore, we faced an extremely challenging task to generate

similar substitutional carbon defects in the silica matrix without using traditional heating methods. This was achieved by investigating the method of agitation as the technique of introducing energy to the system during the synthesis, *in lieu* of the high temperatures adopted by Green *et al.* We attempted to use intensive mechanical stirring, ultrasound or microwave radiation and kept all reagent concentrations at an optimum level as found in previous experiments.³⁴ These methods gave widely different results in terms of the sizes of nanoparticles produced, as has been discussed in Section 3.5.1 previously. In addition, the luminescent emission recorded from the samples prepared using these different methods varied.

After these experiments, it was decided that the very high intensity energy of the ultrasonic tapered tip can be used to generate interstitial carbon defects within the silica matrix. The localised energy of the ultrasound, focused by the tapered tip, causes local ‘hot spots’ which provide high energy and temperature to the system and mimic the high heat sintering method used by Green *et al.* in their sol-gel synthesis. This approach was very successful and resulted in highly luminescent samples.

3.5.2.1 Solid State Photoluminescence

Solid state photoluminescence measurements were carried out on samples dried in air for 48 hours (excitation wavelength was 457 nm). The spectra are presented in Figure 3.13 below. These spectra show broad white emission from solid samples of nanoparticles. The highest intensity peak is for the sample prepared using the ultrasonic tapered tip, with its peak centred at ~588 nm. Green *et al.* present similar data for silica gels prepared from tetramethoxysilane (TMOS) at high temperatures, attributing these impressive emission properties to the decomposition of alkyl groups which may create a carbon substitutional defect for Si.³⁸ This high intensity broad emission is a result which has not been seen for nanostructures of silica to date. The peaks representing the samples prepared using microwave treatment and mechanical stirring are similar in shape to the sample made using the ultrasonic tapered tip; however, they are significantly lower in intensity. This is due to the agitation method used. Indeed, these latter techniques provide substantially lower energy input into the synthetic system.

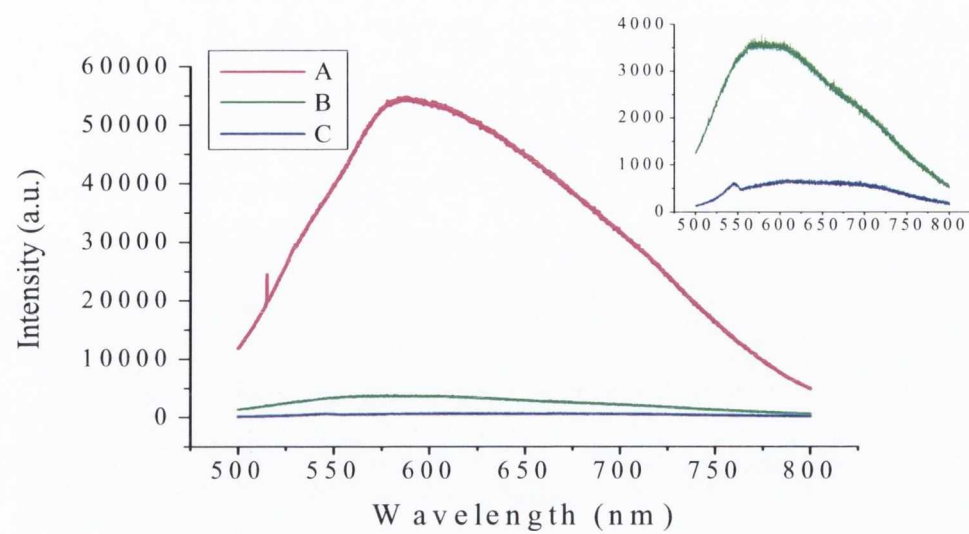


Figure 3.13: Solid state photoluminescence spectra of samples prepared by ultrasonic tapered tip (A), microwave (B) and stirring (C); inset shows close-up of samples B and C, $\lambda_{ex} = 457$ nm.

3.5.2.2 Fluorescent Lifetime Measurements

Lifetime measurements were carried out on the sample prepared using the ultrasonic tapered tip (Figure 3.14). Fluorescence lifetime decays were measured using a time-correlated single photon counting machine. The samples were excited by 480 nm picosecond pulses. The PL decay curves have been successfully simulated using a biexponential function with a shorter lifetime equal to 0.84 ns and a longer one equal to 10.5 ns. The value of the longer lifetime of 10.5 ns is close to one documented by Green *et al.*³⁸ This biexponential fit could indicate the possible presence of multiple defects in the sample.

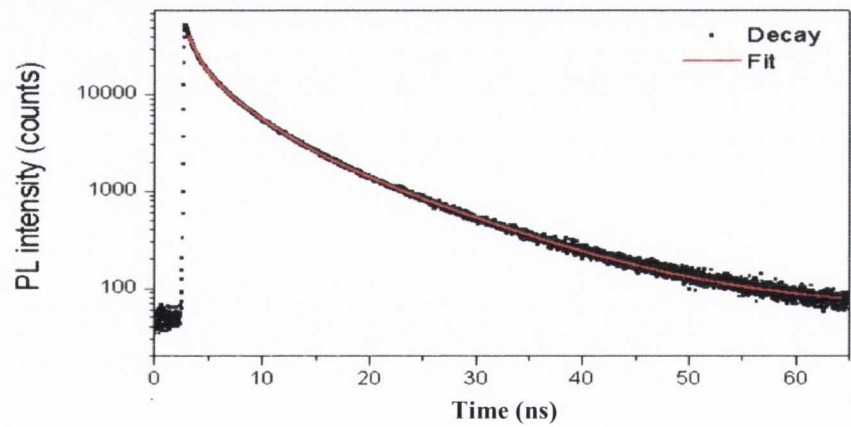


Figure 3.14: Lifetime measurement of sample A, prepared using the ultrasonic tapered tip; $t_1 = 0.84$ ns; $t_2 = 10.5$ ns.

3.5.2.3 Electron Microscopy

TEM and STEM images in Figure 3.15 show the amorphous nature of the nanoparticles and their mesoporosity. SEM confirms the nanoparticulate nature of the sample when dried to the solid state, demonstrating that this unusual emission is originating from the nanoparticles themselves and not some amorphous xerogel-like structure formed during the drying process. Fluorescence microscope images clearly show broad white emission upon illumination (Figure 3.15).

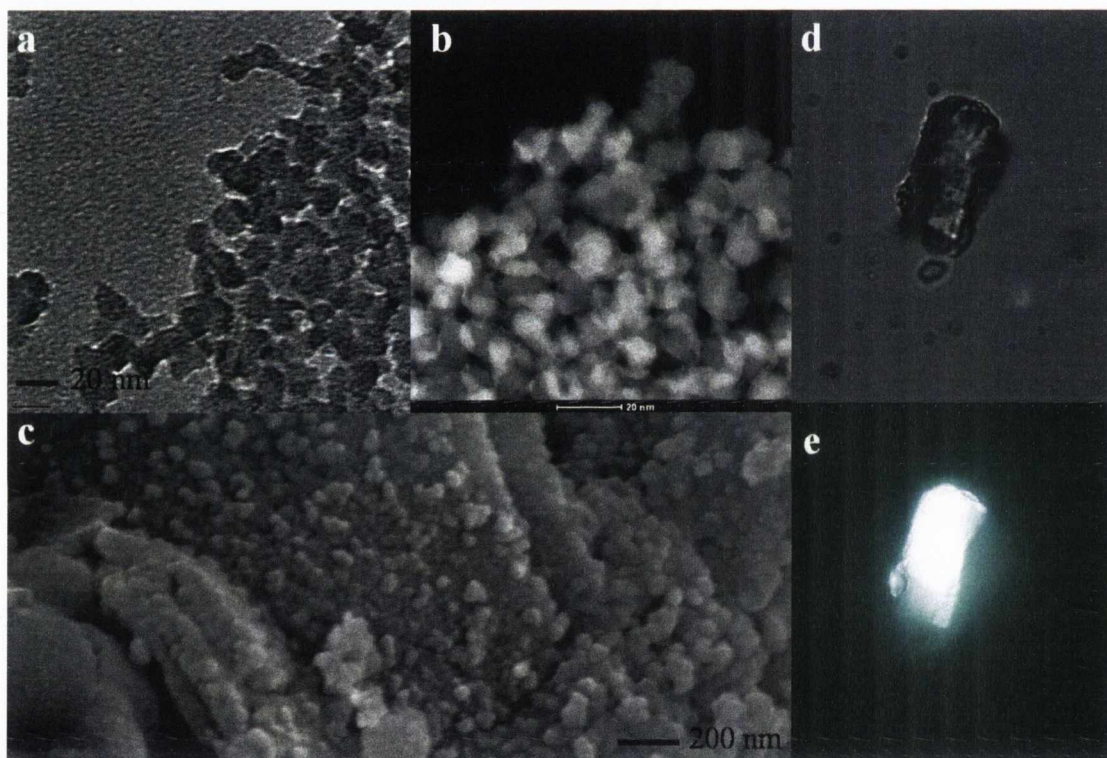


Figure 3.15: Sample prepared using ultrasonic tapered tip (a) TEM image; (b) HAADF STEM image; (c) SEM image showing the nanoparticulate nature of the particles when dried to the solid state; (d) Light microscope image; (e) Bright white emission can be seen when illuminated with light (λ_{ex} 510 nm).

3.5.3 Investigation of Dependence of White Emission on Reaction Conditions

In order to determine the nature of the luminescence, several samples of silica nanoparticles were prepared using the ultrasonic tapered tip with varying treatment time and ammonium hydroxide catalyst. It was found that there was no correlation between the sizes of the nanoparticles and their luminescent intensity, or peak position (Table 3.5;

Figure 3.16), indicating that the luminescence is not intrinsic, but highly likely to be due to defects, as previously postulated. One noticeable difference between the spectra in Figure 3.16 was the presence of a second peak or shoulder in many of the samples which seemed to vary in its intensity. It is thought that this second peak could be due to the presence of another type of defect in the silica matrix. Indeed, increasing the time spent under ultrasonic irradiation has no effect on the resulting size of the nanoparticles but appears to cause the intensity of the luminescence of the second peak or shoulder to decrease. This could be due to the defect species being burnt out of the silica matrix due to the longer time spent undergoing treatment. This second type of defect could be a silicon carbide species.

Table 3.5: Samples prepared using ultrasonic tapered tip and resulting nanoparticle sizes.

Sample	Conditions	d_{TEM} ^[a] (nm)
A	1.5 mmol NH ₄ OH; 20 mins	14 ± 3
B	1.5 mmol NH ₄ OH; 40 mins	14 ± 4
C	3 mmol NH ₄ OH; 20 mins	17 ± 6
D	3 mmol NH ₄ OH; 40 mins	17 ± 5

[a] d_{TEM} refers to the average diameter of particles calculated from >100 nanoparticles according to TEM measurements; NH₄OH is ammonium hydroxide solution.

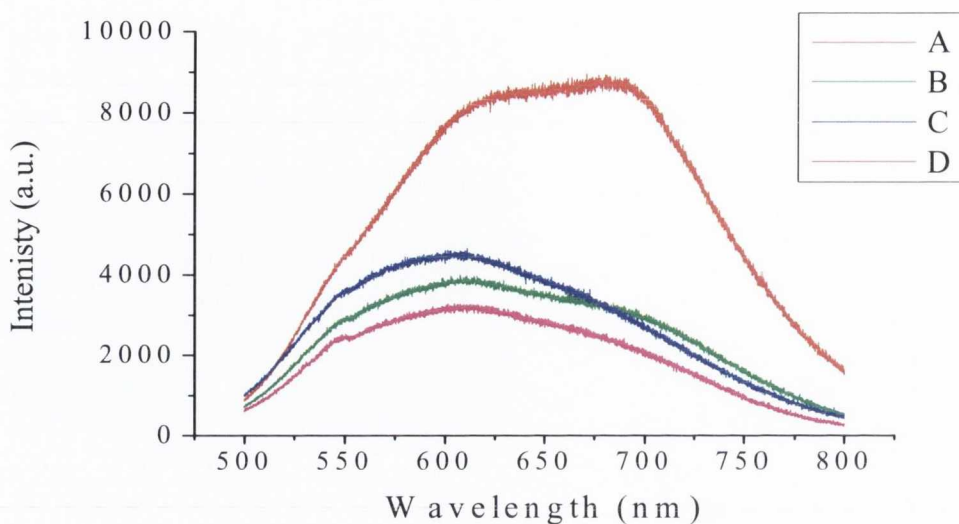


Figure 3.16: Solid state photoluminescence spectra of samples A-D prepared using the ultrasonic tapered tip according to Table 3.5, $\lambda_{ex} = 457$ nm.

The luminescence of the nanoparticles is quenched upon addition of water. This is thought to occur due to the mesoporosity of the silica nanoparticles, as can be seen in the STEM image in Figure 3.15b. Attempts to protect the luminescence by coating with materials such as APTES and gelatine were unsuccessful.

The quenching of the luminescent emission in the particles was found to be completely reversible. After water or any alcohol solvent was introduced to the nanoparticles, they demonstrated no photoluminescent signal using aqueous detection techniques. Drying the samples again over 48 hours at $\sim 40^{\circ}\text{C}$ to a white powder yielded solid state photoluminescence signals once again (Figure 3.17). This property could allow these particles to be used as moisture sensors. The apparent lowering in intensity seen in Figure 3.17 is due to the intensity of the laser and beam focus during the solid state measurement.

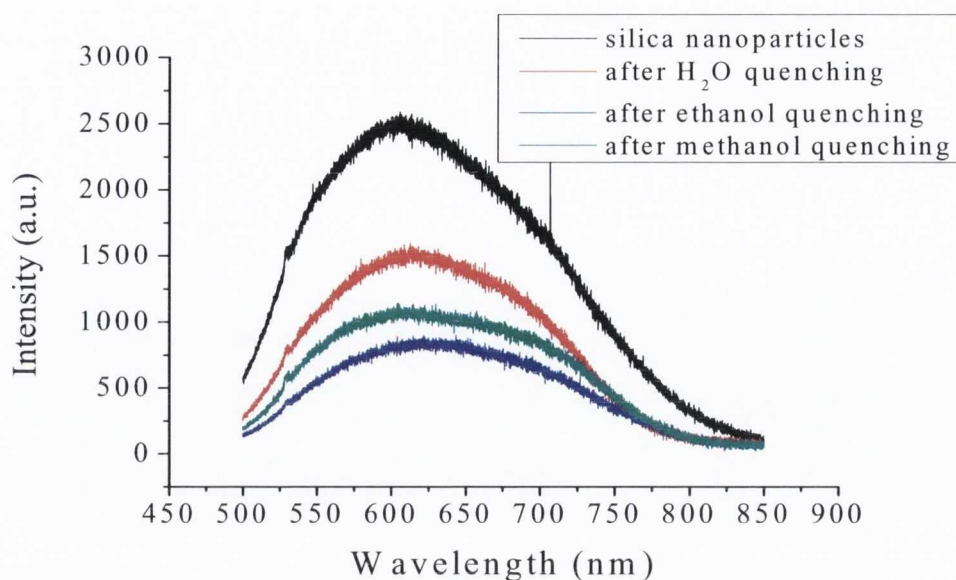


Figure 3.17: Solid state photoluminescence spectra showing luminescence of nanoparticles after reversible quenching with various solvents, $\lambda_{ex}=457$ nm.

3.5.3.1 Infrared Spectroscopy

FTIR spectroscopy gave characteristic peaks which were in close correlation with literature as well as with Green *et al.*'s results (Figure A1.4).³⁸ There are strong bands associated with Si-O stretching and bending vibrations apparent at $1090, 800\text{ cm}^{-1}$. The regions between $3000\text{--}2700\text{ cm}^{-1}$ and $1700\text{--}1400\text{ cm}^{-1}$ indicate the presence of hydrocarbon and carbonyl impurities, as expected.

3.5.3.2 Raman Spectroscopy

Raman spectroscopy was carried out in order to elucidate the possible identity of the defect causing the broad white emission observed in samples prepared using the ultrasonic tapered tip. These spectra can be seen in Figure 3.18, where they are compared to the spectrum of glass. The peak at 980 cm^{-1} is due to Si-OH vibrations.⁴⁰ The peak which can be seen at 800 cm^{-1} is assigned to the stretching vibration of Si-O-Si. Traditionally, two peaks at 480 and 600 cm^{-1} are named D₁ and D₂ lines respectively. They were initially described as “defect bands” but are now known to be assigned to symmetric oxygen breathing vibrations of 4- and 3-membered rings.^{41,42} The D₂ peak is very low intensity in our samples. The peak at approx. 365 cm^{-1} , referred to as the R-line, can be seen in all

samples as well as the glass sample (where it is centred at 355 cm^{-1}), and can be assigned to the O-bending motion of connected SiO_4 tetrahedra in the silica matrix. The spectra have not been normalised due to the amorphous nature of the samples and therefore they have not been discussed in terms of their intensities. It should be noted that Vaccaro *et al.* have reported the connection between the broad luminescence of their high temperature treated fumed silica nanoparticles to Raman stretches.⁴¹ They postulate that the defects which are responsible for the particles' emission are localised on the outer shell of the particles and hence are particle surface specific. They track this using Raman spectroscopy by monitoring the R-line. Our samples appear to follow a similar size trend, where shifting in the R-line according to the particle size occurs. The smaller sized particles, samples A and B (14 nm) have their R-lines centred at 365 cm^{-1} , whereas the larger particles, samples C and D (17 nm) have their R-lines centred at 361 cm^{-1} . This shifting of the R-line to lower frequencies is thought to correspond to a decreasing surface signal due to the lower surface area to volume ratio of the larger particles. Unfortunately, identification of any defect responsible for this emission is difficult due to the strong signals arising from the SiO_2 matrix of the samples.

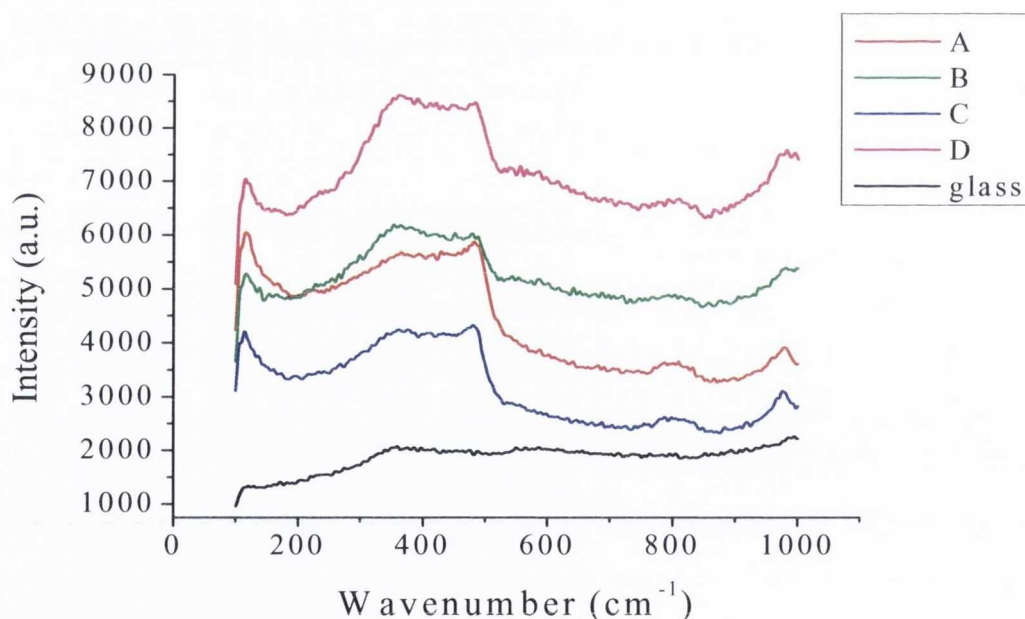


Figure 3.18: Raman spectra of samples A-D prepared according to Table 3.5 compared with glass, $\lambda_{\text{ex}} = 785\text{ nm}$.

3.6 Hollow Silica Nanoparticles

3.6.1 Preparation of Hollow Silica Nanoparticles

Hollow silica nanoparticles were prepared using a modified Stöber technique and utilising the Kirkendall effect, where the diffusion of the components within a system can affect the chemistry involved. This was carried out by controlled injection of an aqueous solution containing the ammonium hydroxide catalyst into an organic solution containing the silica source (TEOS) (Figure 3.19). Aqueous droplets of ammonium hydroxide were injected into the organic phase, creating an emulsion. The interaction of TEOS with the surface of the water droplet causes the formation of a silica shell, yielding a void inside. Any aqueous material, such as a luminescent moiety or drug molecule, may be encapsulated inside this void. This was demonstrated by incorporating an organic dye, rhodamine B, inside the shell of the silica nanostructure. The dye was dissolved into the aqueous layer prior to injection into the organic layer, causing the entrapment of the dye molecules within the silica shell.

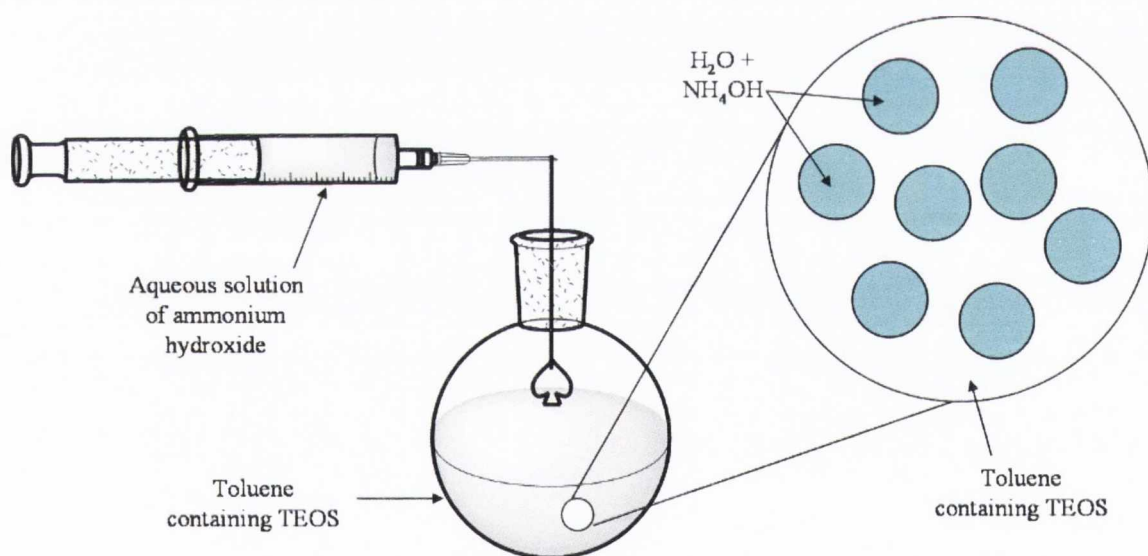


Figure 3.19: Schematic representation of injection apparatus used to prepare hollow silica spheres; blue circles represent aqueous ammonium hydroxide droplets as an emulsion in the organic phase containing TEOS.

3.6.2 Characterisation of Hollow Silica Nanoparticles

Silica nanoparticles with unusual hollow structures were prepared using the method outlined above. These particles were washed using centrifugation with water before characterisation by TEM, FTIR, UV-vis and luminescence spectroscopy.

3.6.2.1 Transmission Electron Microscopy

TEM images were taken of the particles prepared (Figure 3.20). These images demonstrate silica nanoparticles of various sizes including interesting onion-like structures which appear to have multiple layered shells (Figure 3.20b). These structures are thought to form due to the porosity or cracks in the thin silica shell which is deposited upon injection of the aqueous droplets into the organic layer. As TEOS reacts with the water droplets within the emulsion, forming a silica shell, their porosity or cracks allows TEOS to diffuse into the particle towards more water molecules within the sphere, providing further sites for the hydrolysis and condensation of silica. This process continues until all of the water molecules have been used up and results in a multiple-layered onion-like silica nanostructure. The particles prepared were 23 ± 6 nm in diameter.

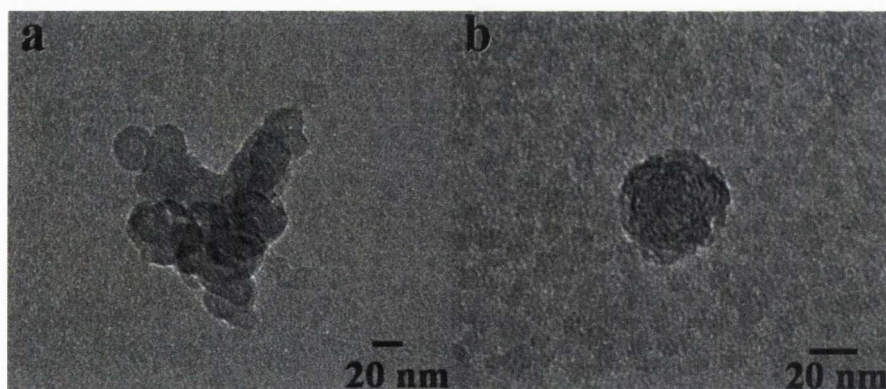


Figure 3.20: (a) and (b) TEM images of hollow silica nanoparticles prepared using injection technique.

Despite these multi-layered structures being formed *in lieu* of the hollow nanocapsules originally envisaged, it is still possible to incorporate materials within the silica layers. This was demonstrated by incorporating rhodamine B dye into the aqueous phase. Two different concentrations of dye solution were tested; sample A contains a low

concentration and sample B contains a high concentration of dye (see experimental section for more details). According to TEM, Sample A was 24 ± 5 nm in diameter and sample B was 29 ± 6 nm in diameter. The particles prepared can be seen in Figure 3.21, which display multi-layered hollow structures.

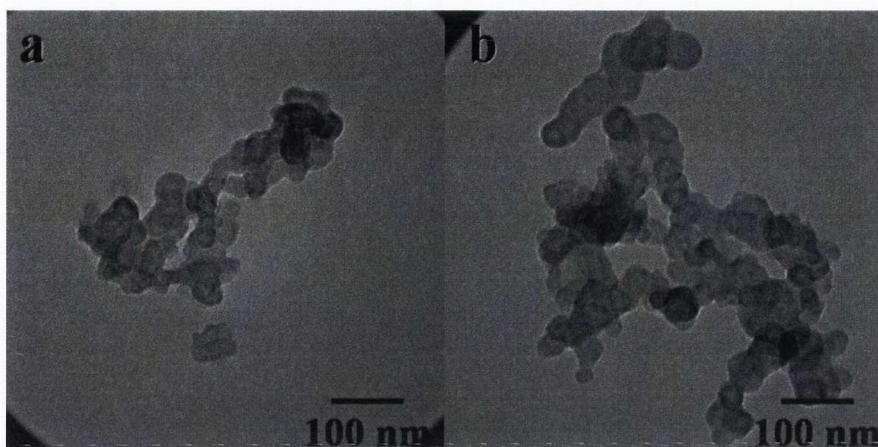


Figure 3.21: TEM images of hollow silica nanoparticles prepared using injection technique with the incorporation of rhodamine B dye; (a) Sample A and (b) Sample B.

3.6.2.2 UV-vis and PL Spectroscopy

UV-visible spectroscopy was carried out on the two samples of silica nanoparticles with encapsulated rhodamine B (Figure 3.22). The spectra show the peaks as expected at 525 and 360 nm, representative of the dye encapsulated within the particles. The stronger absorbance of sample B is due to the higher concentration of dye used in their preparation, leading to more molecules of the dye being encapsulated within the layers of the silica nanoshells.

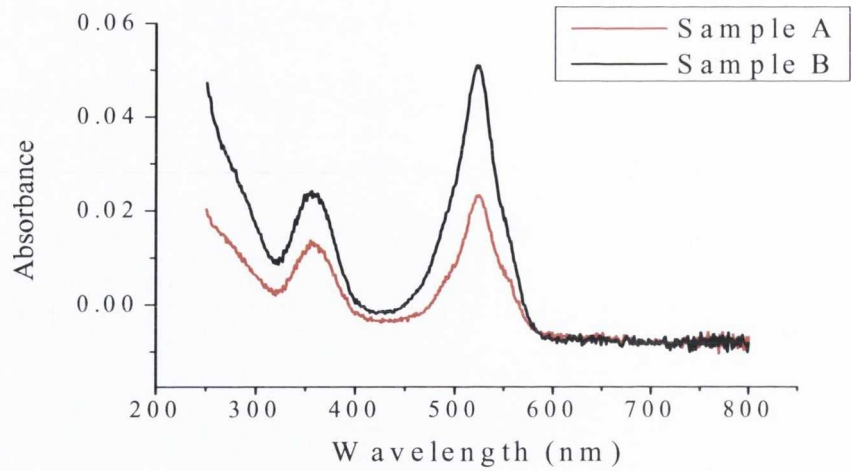


Figure 3.22: UV-visible spectra showing the absorption of silica nanoparticles prepared with a low concentration (Sample A – red) and a high concentration (Sample B – black) of rhodamine B dye.

Photoluminescence spectra of the samples in water were recorded (Figure 3.23). Excitation of the samples with 520 nm light caused emission centred at 550 nm. Once again, the higher intensity of sample B is due to the higher concentration of rhodamine B used.

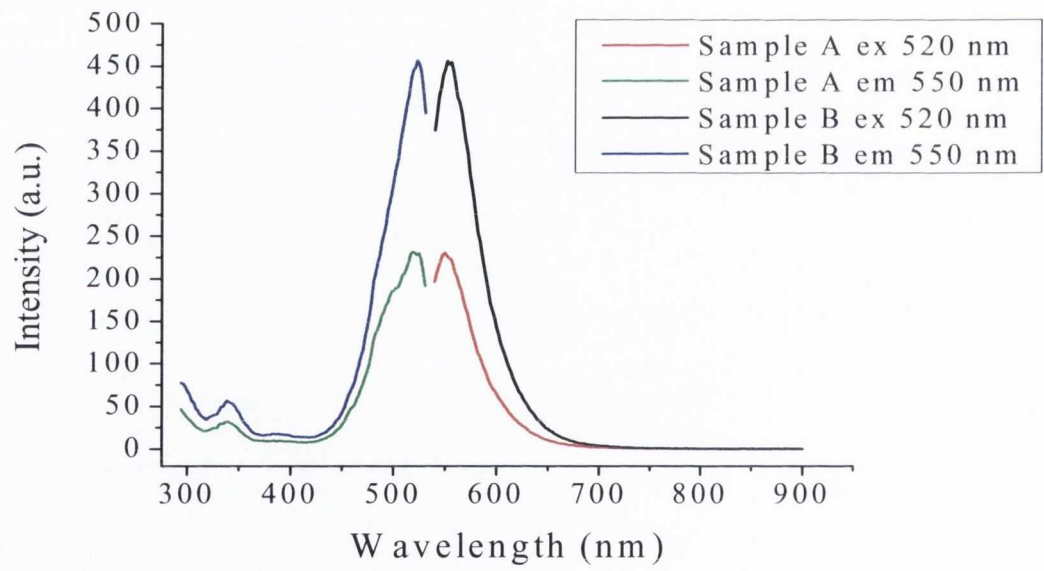


Figure 3.23: Emission and excitation spectra of silica nanoparticles prepared with a low concentration (Sample A) and a high concentration (Sample B) of rhodamine B dye, λ_{ex} = 520 nm, λ_{em} = 550 nm.

3.7 Conclusions

We have prepared a range of silica nanoparticles using an optimised Stöber technique. It was found that the alteration of reagent concentrations and of the method of agitation proffered nanoparticles of varying size, shape and size distribution. The smallest size nanoparticles (5 ± 1 nm) were obtained at high levels of TEOS (70 mmol), low levels of ammonium hydroxide (3 mmol) and medium levels of ethanol and water (0.2-0.4 mmol) in solution. The statistical analysis based on the factorial design experiment was employed in the form of a response surface model, where the parameters can be represented graphically to identify the area of optimum result. The use of statistical analyses provided a new approach for the optimisation of silica nanoparticle sizes by varying reagent quantities. This allowed us to find the optimum conditions for the preparation of silica nanoparticles of a certain size. Our results highlight the benefit of utilising statistical designs in the preparation of nanoparticles. The designs demonstrate the correlation between the concentrations of various parameters and how these interactions affect the properties of the resulting nanoparticles. We believe that this statistical approach could be used for optimisation of the preparation of various types of nanoparticles (not only for silica). This should open up new opportunities in the reproducible fabrication of nanoparticles with controlled size and narrow size distribution.

We have demonstrated that agitation plays a significant role in this synthesis, as well as the temperature during the preparation procedure. Our modifications of the agitation method during experiments have led to the dramatic reduction of the reaction time of the preparation of silica nanoparticles while maintaining their desirable small sizes and narrow size distributions.

We have successfully prepared novel silica nanoparticles which demonstrated strong white luminescence without the introduction of any traditional organic or metallorganic dyes. The strong broad emission of the nanoparticles in the solid state is attributed to substitutional carbon defects within the silicon dioxide matrix of the nanoparticles. It was also found that this defect luminescence is easily quenched by water and some other species. To the best of our knowledge, this is the first time this luminescence has been reported in nanoparticulate silica. This material was prepared by a low cost preparative technique and should be very useful for further development of new

silica based nanomaterials. This work could also prove invaluable for biological, photonics and sensing applications using silica nanoparticles.

Nanostructures of silica particles with a multi-layered structure have been prepared using an injection technique which yields small sized nanoparticles with interesting onion-like or hollow morphologies. The formation of these ‘nanoshells’ relies on the diffusion of an alkoxysilane, residing in an organic phase, to an aqueous phase. We have demonstrated the feasibility of incorporating materials within these ‘nanoshell’ structures by encapsulation of an organic dye. This method could be used to prepare a variety of nanomaterials with a broad range of potential applications.

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Chapter 4

Rare Earth Metallasiloxanes as Precursors for Luminescent Silica Nanoparticles

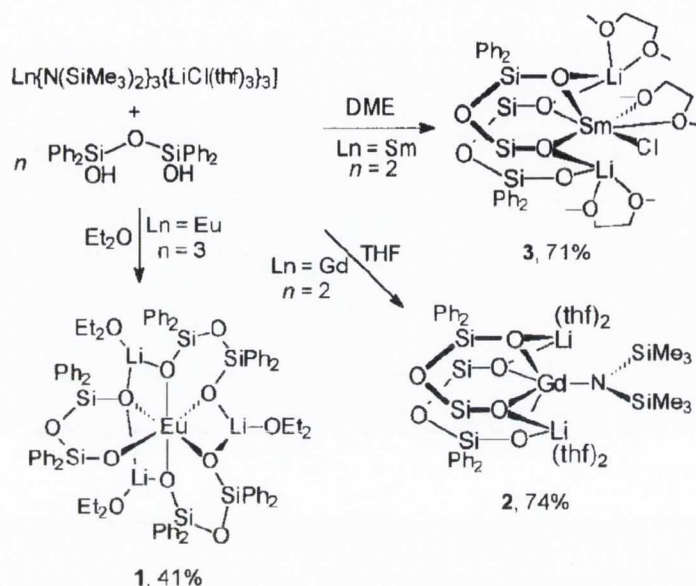
4.1 Introduction

Luminescent silica nanoparticles hold great promise as biomarker tools in the emerging field of nanomedicine. Whilst organic dyes and quantum dot-based materials possess useful properties, their downsides are numerous. The ease with which organic dyes photobleach makes them difficult to use within many biological applications. Quantum dots, which have very strong emission characteristics, are regarded as highly toxic and hence unattractive for use in medical diagnostics. Rare earth (RE) metals may offer advantages over these luminescent materials, due to their superior luminescence properties, including very long decay times, greater resistance to photobleaching and sharp emission profiles.¹ The incorporation of RE ions into silicates is of interest for a wide variety of applications, including optics, catalysis and biomedicine.^{2,3} In fact, RE-based silica nanoparticles have proven to be useful in techniques such as multiplexed immunoassay measurements, where they have demonstrated advantages over conventional fluorescent dyes.⁴

Siloxanes and silsesquioxanes can be used as ligands in the formation of a wide variety of metallorganic complexes, since they have reactive Si-OH functionalities which allow them to be exploited to form main group, transition metal and rare earth metal compounds.⁵ Metallasiloxanes and metallasilsesquioxanes contain the functional group Si-O-M, where M can be a main group metal, d-transition metal or f-group element. In general, the preparation of metallasiloxanes is well documented; several types of them have been prepared and they have been utilised as heterogeneous catalysts in industry.⁵⁻⁷ However, this is still a very challenging area of chemistry, due to difficulties with crystallisation, characterisation and manipulation of selected metals, including rare earth metals.

Lanthanide-based metallasiloxane complexes are very interesting materials, which can serve as molecular models of rare earth containing silica supported heterogeneous

catalysts. These complexes have been investigated by Edelman and co-workers, who use the so-called ‘silylamide’ route to prepare lanthanide disiloxanediolates, reported in several publications (Scheme 4.1).^{3,8,9}



Scheme 4.1: Synthesis of lanthanide disiloxanediolates via the ‘silylamide’ route.⁹

Incompletely condensed trisilanol ligands (Figure 4.1) are particularly useful in the preparation of metallasilsesquioxanes. The unique coordinating ability of this sterically demanding tridentate ligand prevents linear Si-O-M bonding angles and severely limits the extent of aggregation.

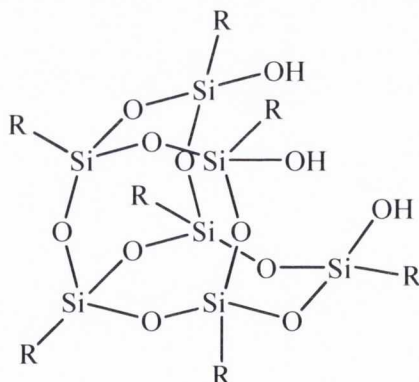


Figure 4.1: Structure of incompletely condensed trisilanol ligand $[\text{R}_7\text{Si}_7\text{O}_9(\text{OH})_3]$, where $\text{R} = n\text{-C}_6\text{H}_{11}$ (Ligand A).

Metallasilsesquioxane complexes can be prepared with a variety of metals at their centres – including alkali, transition and RE metals.^{3,5,6,10} Fully metallated silsesquioxane derivatives are versatile building blocks and are often used for the construction of bimetallic species and complexes containing functional groups.^{3,10} Previous work has incorporated multiple metal ions into these ligand cages (Figure 4.2).³

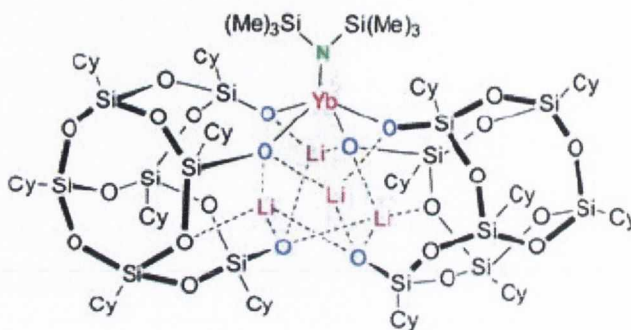


Figure 4.2: The structure of lithium-ytterbium metallasilsesquioxane derivative (Cy = cyclohexyl).³

Metallasilsesquioxane materials could prove highly useful as model compounds which can help to provide insight into the processes that occur on metal-modified silica surfaces, such as heterogeneous catalysts.^{3,5-8,11} Indeed, it is thought that metal compounds derived from polyfunctional silanols, such as silanetriols or incompletely condensed silsesquioxanes, are realistic models for this scenario, since they exhibit structural similarities with modified silica surfaces.⁸ On this basis, it is expected that such materials could also prove to be ideal as ‘dopants’ or precursor materials for the preparation of luminescent silica nanoparticles.

Silica-based fluorescent europium nanoparticles have great potential as fluorescence probes for biological systems, due to their small sizes, strong emission properties and silanol surface which can enable further modification with ease.¹² In fact, the incorporation of luminescent lanthanide ions, particularly Eu^{3+} , into silica matrices has become more prevalent in recent years.¹³⁻¹⁷ In addition, dual-luminophore silica nanoparticles could provide nanoprobe with enhanced fluorescence.¹⁸

The incorporation of rare earth ions into silica nanoparticles is traditionally carried out using one of two methods. The first is a solution chemistry technique which involves

the incorporation of rare earth ions through the addition of the appropriate rare earth salt to an acid catalysed sol-gel reaction. This yields nanoparticles which are typically 500 nm to micrometres in diameter. Er^{3+} -doped SiO_2 particles were prepared by this approach by de Dood *et al.*¹⁷ However the particles have a wide size distribution and aging in aqueous solutions leads to large aggregates of particles, which is thought to occur due to the influence of the charged RE ions. Luminescence only originates from their particles after high temperature annealing to remove quenching O-H groups. More recently, Eu^{3+} -doped SiO_2 nanoparticles have been prepared by different groups using a modified Stöber technique, yielding smaller sized nanoparticles with strong characteristic Eu^{3+} emission.^{13,16} Another solution chemistry approach to lanthanide-doped silica nanoparticles is the use of a water-in-oil (W/O) reverse microemulsion technique, which yields nanoparticles of less than 100 nm diameter.^{14,15,19} The second, non-solution approach involves ion implantation of lanthanide ions using a sputtering technique which allows strict control over the lanthanide concentration.²⁰

Thermolysis is a well-known technique for immobilising materials on silica or alumina surfaces.^{21,22} In the past, this has been carried out by thermal decomposition of the material in the presence of the silica or alumina support. The idea of reacting solid inorganic precursors through solventless synthesis is not a new one, it has been well-used in solid state reactions for many years.²³ It presents a promising technique which could be developed as a method of preparing nanostructured materials. Over the past few years, a number of reports have demonstrated the formation of nanostructures from the thermolysis of inorganic molecules and clusters, including MnO nanoparticles and Cu_2S nanorods.²⁴⁻²⁶ This method has proven to be a successful one since interparticle collisions rarely occur in a solventless reaction environment and particle growth can proceed primarily by monomer addition to the particle surface leading to monodisperse size and shape distributions.²⁵ However, in order to optimise this for any system, the choice of the correct precursors is vital. In metallasiloxane and metallasilsesquioxane complexes, the existing siloxane ligand network which surrounds the metal firstly provides protection of the RE metal centre, preventing the formation of RE-O-RE clusters which facilitate quenching by non-radiative recombination through energy dissipation and cross relaxation. It also provides a silicate

shell which could allow sites for further binding and growth of nanostructures. In addition, the luminescence from RE ions is often improved by thermal treatment.¹⁷

4.2 Aims

The main aim of this part of the work is to prepare metallasiloxane and metallasilsesquioxane materials based on rare earth metals. These materials will be used as precursors in the preparation of luminescent rare earth metal doped silica nanoparticles.

The RE metals we have chosen to investigate in this part of the work include Eu and Yb. This is due to their inherent usefulness in a variety of fields. For example, Eu^{3+} materials display excitation and emission in the UV-visible range of the spectrum, making them an excellent choice as fluorophores for luminescent probes in biomedicine.¹² Yb^{3+} ions, in combination with Eu^{3+} ions, can serve as upconverting phosphors and offer advantages in optical biological imaging.¹⁸

We plan to prepare the metallasiloxane and metallasilsesquioxane derivatives using traditional inorganic synthetic chemistry from siloxane precursors. Once the derivatives have been made, they will be used to prepare luminescent silica nanoparticles using a thermal decomposition approach and their emission properties will be investigated. This work is expected to contribute to the development of luminescent silica nanoparticles based on rare earth metals which have sharp emission profiles, long decay times and large Stokes shift. They are expected to provide alternative materials to silica nanoparticles which are doped with organic dyes.

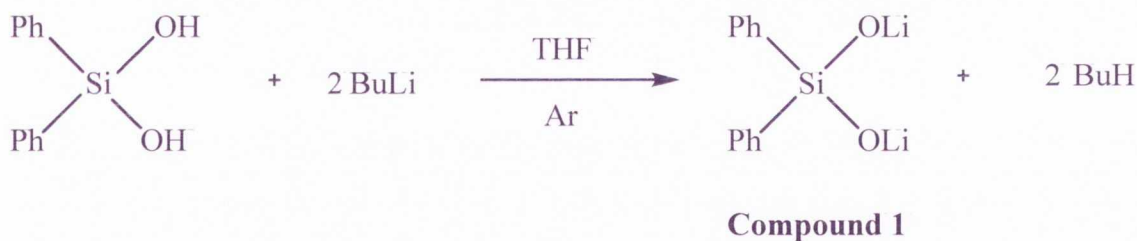
4.3 Preparation and Characterisation of Rare Earth Precursor Materials

Most rare earth metallasiloxane complexes are moisture sensitive therefore their synthesis was carried out using standard Schlenk techniques under argon gas, with all solvents dried prior to use. It is important to note that due to their 4f ground state electronic configuration, most lanthanide complexes in the 3+ oxidation state are paramagnetic, except for La^{3+} and Lu^{3+} . Complexes of many lanthanides have NMR signals which are broadened and paramagnetically shifted, which often makes their NMR spectroscopic

studies difficult. The sensitive nature of many of the lanthanide complexes used in this part of the work makes crystal growth challenging.

4.3.1 Preparation and Characterisation of $[\text{Ph}_2\text{Si}(\text{OLi})_2]$

$[\text{Ph}_2\text{Si}(\text{OLi})_2]$ (**Compound 1**) was prepared by reacting diphenylsilanediol with butyllithium using a previously reported method (Scheme 4.2).²⁷ The product was a white solid which was characterised using Nuclear Magnetic Resonance (NMR) and Fourier Transform Infrared (FTIR) spectroscopy. ^{29}Si NMR of **Compound 1** is difficult to obtain due to solubility issues. However, a ^7Li NMR of **Compound 1** (Figure A2.1, Appendix 2) shows peaks at -0.20 and 1.56 ppm in an approximate ratio of 1:5. This would normally indicate the presence of two lithium species in the complex, which is unexpected due to the symmetry of this compound. This could be due to solvent (*e.g.* THF) coordinated to one of the Li atoms or due to the partial hydrolysis of the compound in the NMR tube. ^1H NMR spectroscopy of **Compound 1** displays the presence of the phenyl substituents and a distinct lack of peaks which would be representative of the diol functionality of its diphenylsilanediol precursor, indicating the reaction has proceeded to completion as expected, with no precursor remaining.



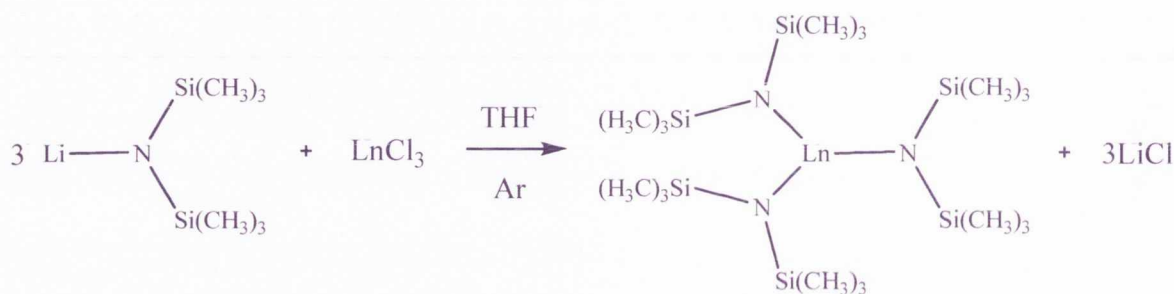
Scheme 4.2: Schematic presentation of the preparation of **Compound 1** $[\text{Ph}_2\text{Si}(\text{OLi})_2]$.

FTIR spectroscopy of $\text{Ph}_2\text{Si}(\text{OH})_2$ (Figure A2.2) shows a broad peak between 2900 and 3400 cm^{-1} which can be readily assigned to OH^- groups on the compound. The strong peak at approximately 1100 cm^{-1} is representative of Si-O bonds. Peaks from 600-800 cm^{-1} and those in the fingerprint region are most likely describing the cyclohexyl substituents in the compound. The FTIR spectrum of **Compound 1** (Figure A2.2) reveals an absence of

the band between 3000 and 3400 cm^{-1} representing the OH^- groups. From this, we can conclude that the deprotonation of silanol groups has occurred.

4.3.2 Preparation and Characterisation of $[\text{Ln}(\text{N}(\text{SiMe}_3)_2)_3]$

Lanthanide silylamide $[\text{Ln}(\text{N}(\text{SiMe}_3)_2)_3]$ compounds where $\text{Ln} = \text{Eu}$ or Yb were prepared using a well-documented method (Scheme 4.3).²⁸ The complexes produced included $[\text{Eu}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 2**) and $[\text{Yb}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 3**). These compounds were prepared with a view to utilising them as precursors for the synthesis of metallasilsesquioxanes *via* the ‘silylamide’ route.



Scheme 4.3: Schematic presentation showing the preparation of $[\text{Ln}(\text{N}(\text{SiMe}_3)_2)_3]$, where $\text{Ln} = \text{Eu}$ (**Compound 2**) and Yb (**Compound 3**).

The products were characterised by NMR and IR spectroscopy. The ^{29}Si NMR of $[\text{Eu}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 2**) is displayed in Figure 4.3 below. There is one peak at 54.8 ppm, representing the single silicon environment in the compound, due to symmetry of the compound. The ^{29}Si NMR of $\text{Yb}(\text{N}(\text{SiMe}_3)_2)_3$ (**Compound 3**) shows one peak at 2.1 ppm. The silicon peak for **Compound 3** is shifted compared to the peak for **Compound 2** due to the paramagnetic nature of the Yb^{3+} ions. ^7Li NMR of all these compounds displayed no peaks and confirms the complete reaction of the reagents.

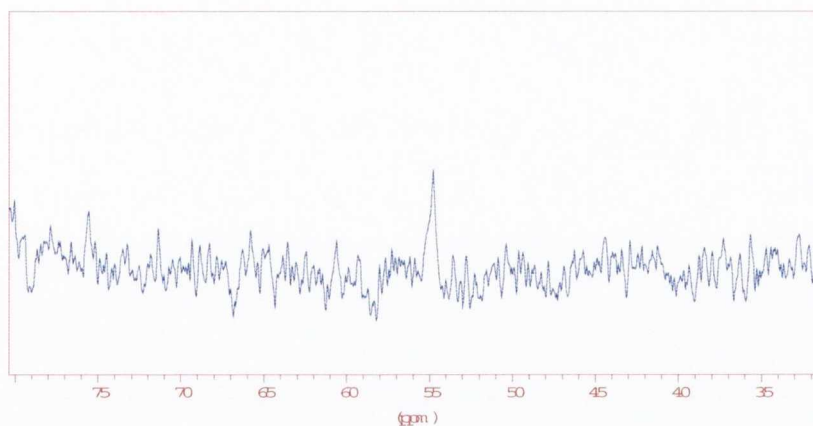


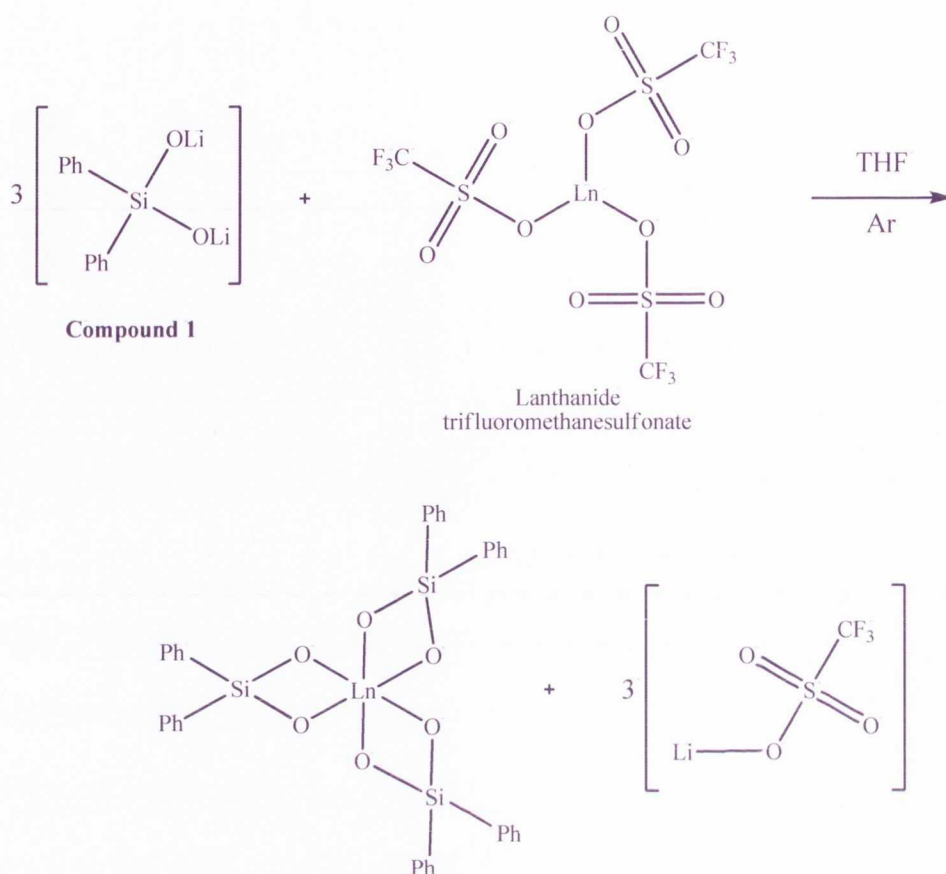
Figure 4.3: ^{29}Si NMR of $[\text{Eu}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 2**) showing one peak at 54.78 ppm.

FTIR spectra were recorded for these samples (*Figure A2.3*), which again show a clear absence of a broad peak for OH^- groups. The strong peak at approximately 1100 cm^{-1} is representative of Si-O bonds. Peaks between 800 and 1300 cm^{-1} are characteristic of methyl groups. Peaks between 840 and 940 cm^{-1} can be assigned to Si-N bonding vibrations.²⁹

4.4 Preparation and Characterisation of Metallasiloxanes

4.4.1 Preparation and Characterisation of $[\text{Ln}(\text{O}_2\text{SiPh}_2)_3]$

The preparation of the metallasiloxane $[\text{Ln}(\text{O}_2\text{SiPh}_2)_3]$, where $\text{Ln} = \text{Eu}$ or Yb , was carried out by reacting three molar equivalents of $[\text{Ph}_2\text{Si}(\text{OLi})_2]$ (**Compound 1**) with one molar equivalent of lanthanide trifluoromethane sulfonate $[\text{Ln}(\text{OSO}_2\text{CF}_3)_3]$ under argon using standard Schlenk techniques (Scheme 4.4).



Scheme 4.4: Schematic presentation of the reaction between **Compound 1** and $\text{Ln}(\text{OSO}_2\text{CF}_3)_3$, where Ln = Eu or Yb, forming $[\text{Eu}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 4**) and $[\text{Yb}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 5**) in two separate experiments.

The products were characterised by NMR and FTIR spectroscopy. As expected, ^{29}Si NMR spectra show a single silicon peak as dictated by the symmetry of the suspected structure of the compounds. ^{29}Si NMR of **Compound 5** $[\text{Yb}(\text{O}_2\text{SiPh}_2)_3]$ (Figure 4.4) shows a single peak, as expected, at -19 ppm. ^{29}Si NMR of **Compound 4** $[\text{Eu}(\text{O}_2\text{SiPh}_2)_3]$ shows the main peak at -18 ppm and a smaller peak at -42 ppm. The peak at -18 ppm corresponds to our target structure, while the weaker peak at -42 ppm may be due to the compound being partially hydrolysed over time in the NMR tube. ^7Li NMR of all the compounds displayed no peaks, confirming the reaction has proceeded and there are no starting materials or by-products remaining.

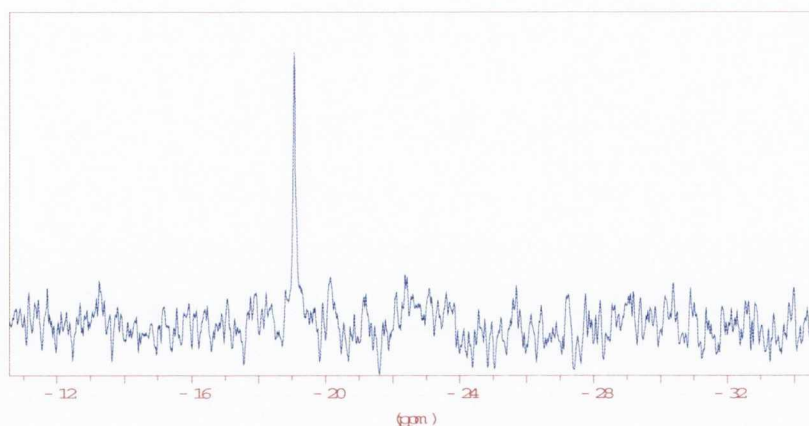


Figure 4.4: ^{29}Si NMR of $[\text{Yb}(\text{O}_2\text{SiPh}_2)_3]$ (**Compound 5**) showing a peak at -19 ppm.

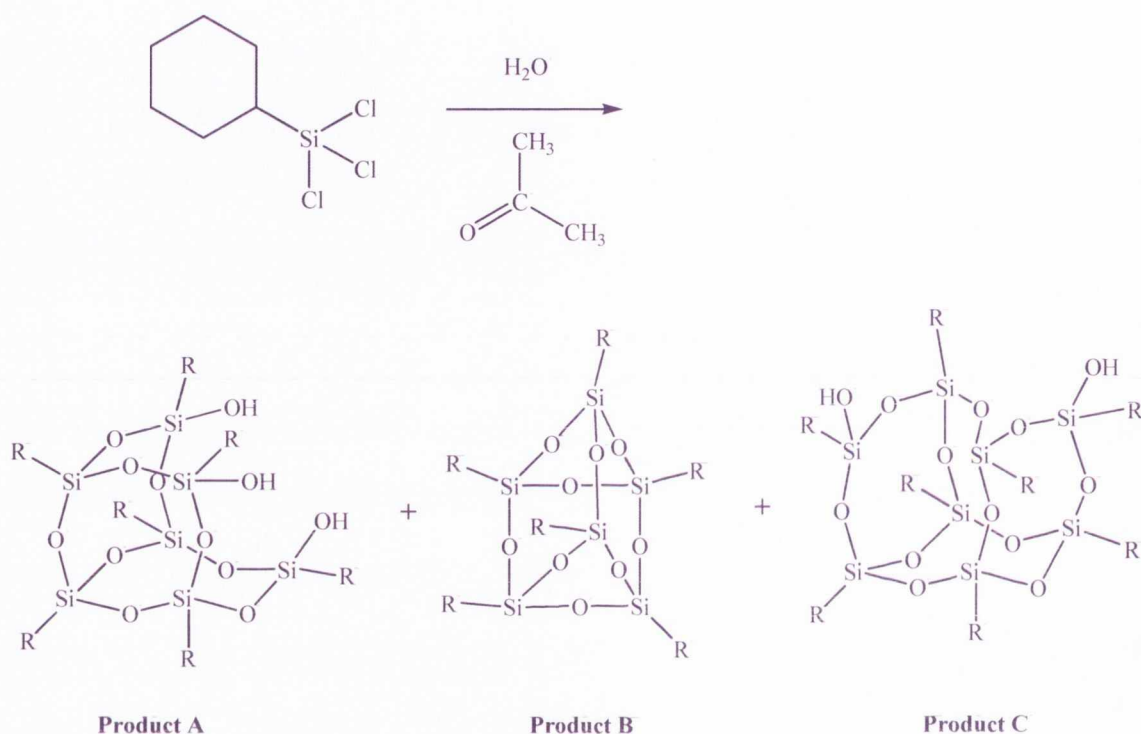
FTIR spectra for these compounds (*Figure A2.4*) show an absence of a broad peak for OH^- groups. The peaks in the fingerprint region and between 600 and 800 cm^{-1} can be assigned to the cyclohexyl groups in the compound. The sharp peak at around 1100 cm^{-1} is due to the Si-O bonds.

4.5 Development of Metallasilsesquioxane Complexes

4.5.1 Preparation and Characterisation of Incompletely Condensed Trisilanol Ligand

The trisilanol derivative $(c\text{-C}_6\text{H}_{11})_7\text{Si}_7(\text{OH})_3$ (Scheme 4.5, **Product A**) was first prepared by Brown and Vogt^{30,31} and was investigated in further detail by Feher.⁵ An improved synthetic route developed by the latter research group involves kinetically controlled hydrolysis of trichlorocyclohexylsilane (Scheme 4.5). As can be seen, by-products produced include a fully-condensed silsesquioxane (Scheme 4.5, **Product B**) and a disilanol (Scheme 4.5, **Product C**). These can be separated using an extraction procedure, which yields **Product A**. The main drawback of this synthetic procedure is that the kinetically controlled hydrolytic polycondensation takes up to three years to complete. However, synthetically useful quantities of the incompletely condensed trisilanol ligand can be isolated from the reaction after several months.

In this project, we prepared the incompletely condensed trisilanol (*c*-C₆H₁₁)₇Si₇(OH)₃, referred to as **Ligand A** throughout. This trisilanol ligand has been used to prepare corresponding metallasilsesquioxane complexes.



Scheme 4.5: Schematic presentation of the synthesis of **A**: trisilanol ligand (R = *c*-C₆H₁₁); and **B** and **C**: its by-products.

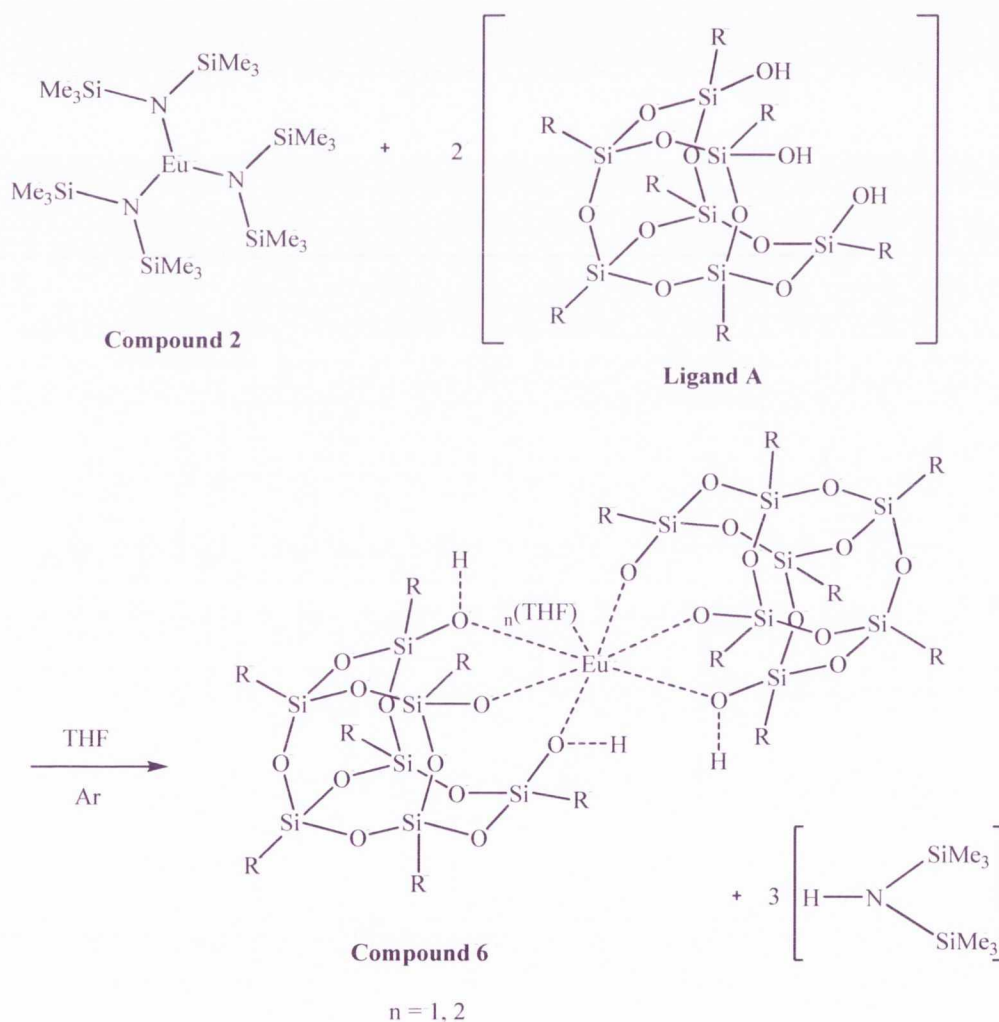
The ²⁹Si NMR of (*c*-C₆H₁₁)₇Si₇(OH)₃ (**Ligand A**) shows three characteristic peaks, at -69.76, -68.23 and -60.34 ppm in a ratio of 3:1:3. These peaks represent the three environments of silica in the ligand due to the symmetry of the complex. The ¹H and ¹³C NMR spectra displayed a series of complex multiplets which were difficult to completely assign, but could be attributed to the cyclohexyl groups and OH⁻ groups. These were in agreement with previously published literature.^{6,32}

Elemental analysis revealed that there was 51.91% carbon and 8.29% hydrogen which was expected according to calculations based on the structure of the compound. FTIR spectroscopy (Figure A2.5) contained peaks between 2900 and 3400 cm⁻¹ indicative of OH⁻ groups, a strong sharp peak at around 1100 cm⁻¹ representing Si-O-Si bonds and

peaks in the fingerprint region for the cyclohexyl functionalities on the corners of the cage structure.

4.5.2 Preparation and Characterisation of Metallasilsesquioxanes

The preparation of these metallasilsesquioxane complexes was carried out using standard Schlenk techniques to prevent hydrolysis of the precursor materials or products. Following a silylamide route, the trisilanol **Ligand A** was reacted with a europium metal precursor [**Compound 2**] in a molar ratio of 2:1 (Scheme 4.6). The complex, **Compound 6** was characterised using NMR and FTIR spectroscopy and elemental analysis.



Scheme 4.6: Preparation of **Compound 6** (suggested structure), using trisilanol **Ligand A**, where $R = c\text{-C}_6\text{H}_{11}$, $n = 1, 2$.

The ^{29}Si NMR of **Compound 6** displays a series of peaks (Figure 4.5). The peak at 11.39 ppm is characteristic of the presence of a small amount of vacuum grease in the sample. The peak at -21.67 ppm corresponds to a by-product of the reaction, such as $\text{H}[\text{N}(\text{SiMe}_3)_2]$. The insets display the peaks which are most likely to be attributed to the structure of the complex of interest. These peaks, at -69.5, -69.2, -67.9, -67.21, -67.15, -67.0, -66.7, -60.0, -58.4, -57.3, -55.6 ppm, are in an approximate ratio of 1:2:1:1:1:1:1:1:2:1:1. The two peaks which are near to one another and appear similar to a doublet signal (at -67.21 and -67.15 ppm) are close in proximity possibly due to a very fast transfer of a proton between two of the OH^- groups in the structure. The presence of coordinated THF molecules to the Eu-metal in the complex can cause a distortion of the shape and symmetry of the molecule. The 11 peaks present in the ^{29}Si NMR are all associated with the suggested structure in Scheme 4.6 due to this lack of symmetry and are in agreement with similar structures which are reported in the literature.³ At this stage, due to the lack of crystallographic data, we cannot identify definitively the final structure or symmetry of **Compound 6**.

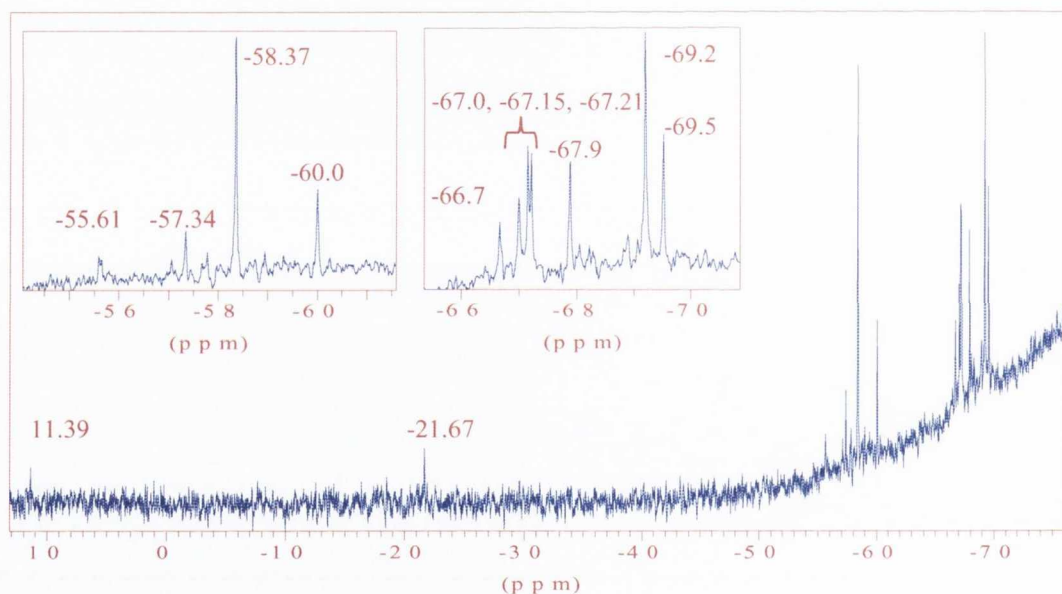


Figure 4.5: ^{29}Si NMR of **Compound 6**, showing peaks at -69.5, -69.2, -67.9, -67.21, -67.15, -67.0, -66.7, -60.0, -58.4, -57.3, -55.6, -21.67, 11.39 ppm, insets show close-up of the peaks representing the structure of **Compound 6**.

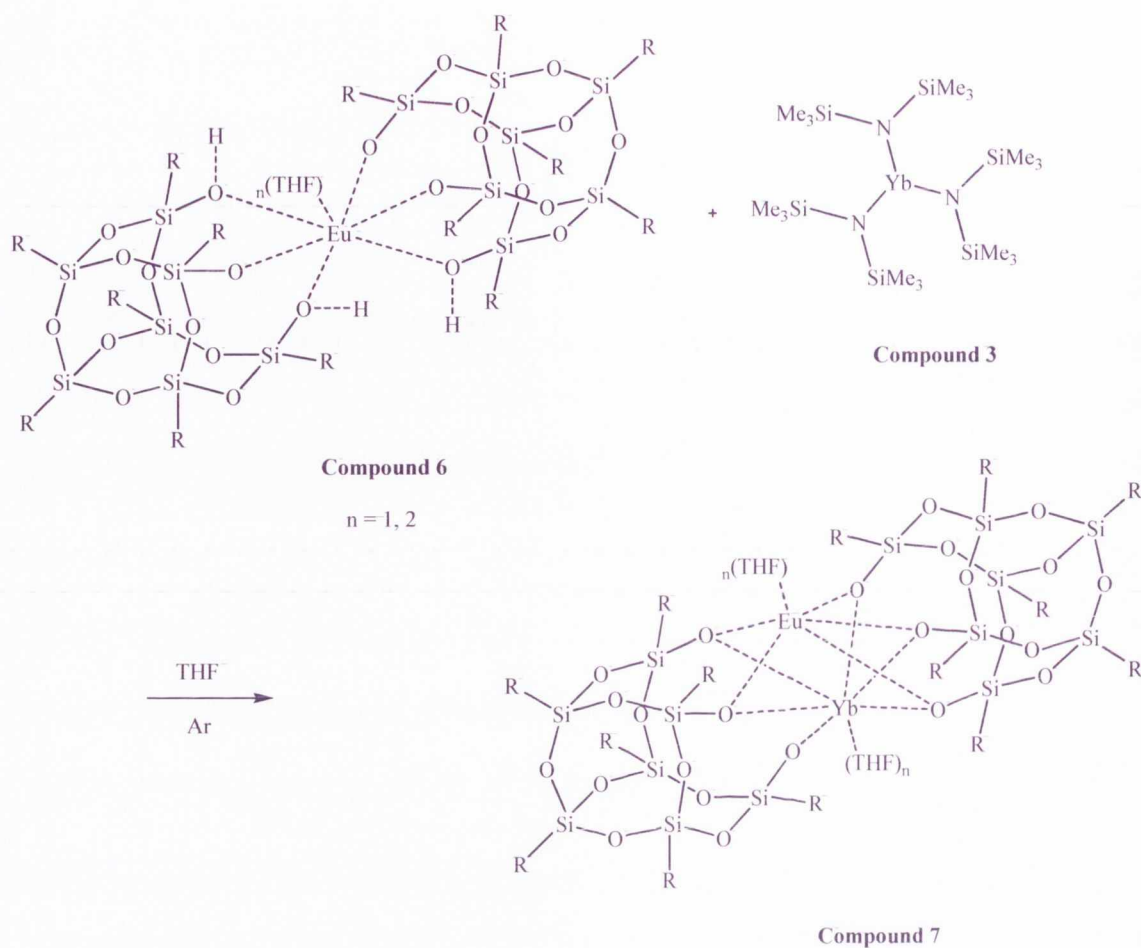
The ^1H and ^{13}C NMR spectra (*Figures A2.6 and A2.7* respectively) show a series of complex multiplets which were difficult to completely assign, but could be attributed to the cyclohexyl groups, OH^- groups and methyl groups of unreacted reagent material.

Elemental analysis of **Compound 6** indicated that there was 43.18% carbon and 7.66% hydrogen. No nitrogen was found, therefore we can be confident that all the reagents were used up during the reaction procedure. These elemental percentages agree with our theoretical calculations, with a small degree of error which may be due to partial hydrolysis of the product with water during the analysis.

The FTIR spectrum of **Compound 6** (*Figure A2.8*) shows a noticeable absence of OH^- groups when compared with the spectrum for the trisilanol **Ligand A** (*Figure A2.5*). This is in agreement with our proposed structure, due to the coordination of these groups to the RE metal (bridging mode), the OH^- groups will no longer appear in the area corresponding to terminal OH^- groups in the FTIR spectrum.

In order to produce a bimetallic metallasilsesquioxane compound, incorporation of ytterbium (Yb) metal into the cage structure was carried out by the addition of one equivalent of $[\text{Yb}(\text{N}(\text{SiMe}_3)_2)_3]$ (**Compound 3**) to **Compound 6** (Scheme 4.7).

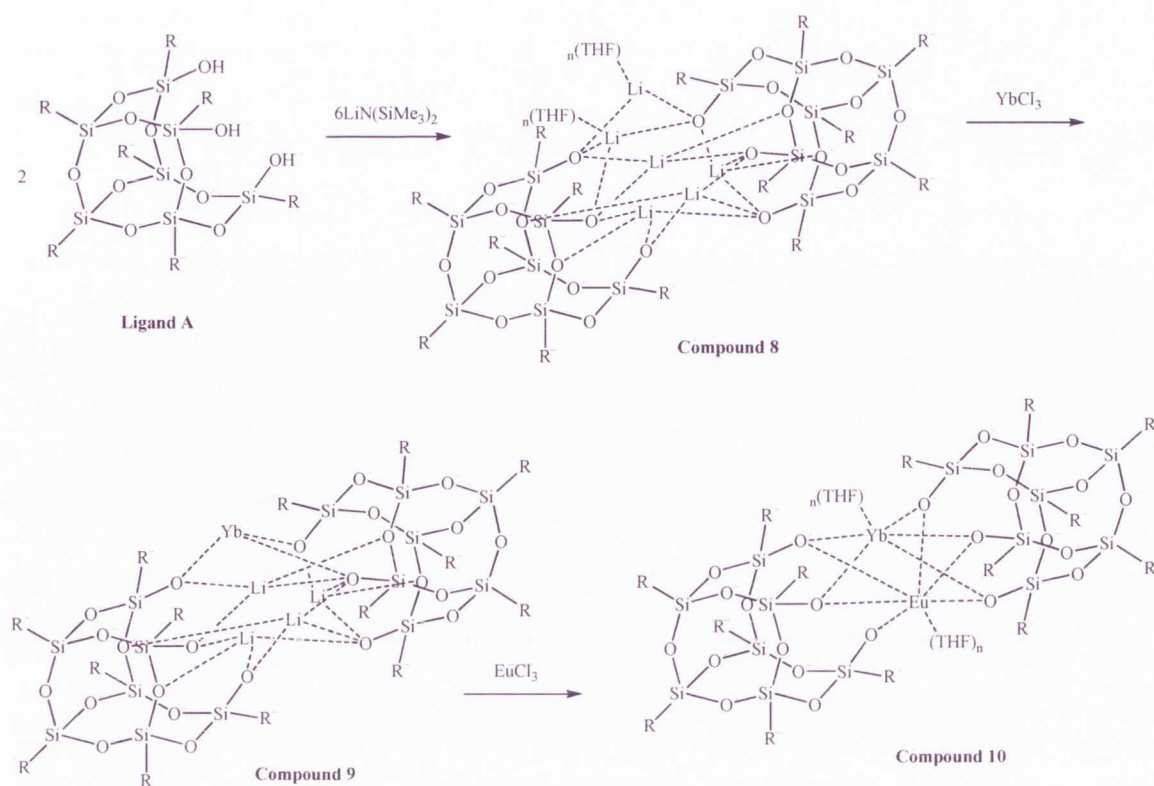
^{29}Si NMR was carried out on **Compound 7**. However, due to paramagnetic shift caused by the presence of the Yb metal in the structure, there were no visible peaks which were useful for elucidation of the proposed structure, as they were most likely masked by the large broad peak present due to the glass of NMR tube. As a result, we cannot definitively conclude that the structure shown in Scheme 4.7 is the true structure of our compound. In order to do this, we require X-ray crystallography, solid state NMR or ^{171}Yb NMR, which is currently under investigation.



Scheme 4.7: Preparation of **Compound 7**, a suspected bimetallic cage structure, using **Compound 6** and **Compound 3**, where $R = c\text{-C}_6\text{H}_{11}$, $n = 1, 2$.

Another route was attempted to prepare metallasilsesquioxanes, using corresponding metal halides and a lithium derivative of the **Ligand A** reported in the literature.³ Again, following the silylamide route, the trisilanol **Ligand A** was reacted with a lithium-silylamide to form a complex lithium-coordinated silsesquioxane cage structure (**Compound 8**) (Scheme 4.8).

²⁹Si NMR of **Compound 8** displays three peaks at -67.11, -66.98 and -58.18 ppm, which matches well with literature (Figure 4.6).³ It was previously found that the structure exists with a box-shaped Li_6O_6 polyhedron at its centre, with two lithium ions coordinated to THF ligands and the others interacting with the framework oxygen atoms in the silsesquioxane cages.



Scheme 4.8: Preparation of lithiated silsesquioxane structure (**Compound 8**), Yb-silsesquioxane complex (**Compound 9**) and Yb-Eu-silsesquioxane cage structure (**Compound 10**), where R = cyclohexyl.

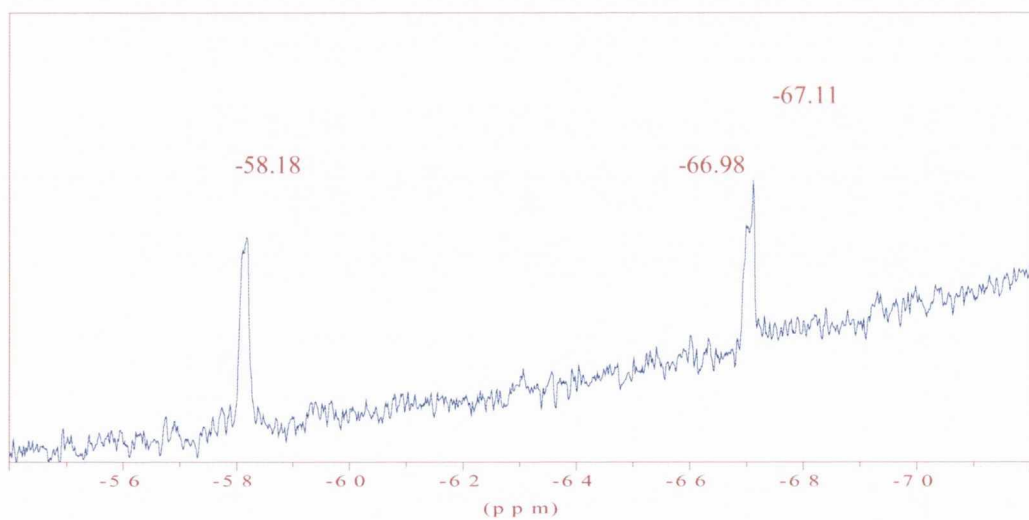


Figure 4.6: ^{29}Si NMR of **Compound 8**, displaying peaks at -67.11, -66.98 and -58.18 ppm.

This lithiated silsesquioxane was then used to prepare rare earth metallated silsesquioxanes (Scheme 4.8). The reaction of **Compound 8** with one equivalent of anhydrous YbCl_3 yielded **Compound 9**. Its ^{29}Si NMR showed one weak peak at -66.69 ppm, which could be indicative of the compound, however, due to the presence of the paramagnetic Yb^{3+} metal, it is likely to be shifted and masked by the large peak due to the silicon glass of the NMR tube. Addition of an equivalent of anhydrous EuCl_3 to **Compound 9** produced the **Compound 10**, with suggested structure according to Scheme 4.8.

The ^{29}Si NMR of **Compound 10** displays peaks at -73.77, -70.08, -69.23, -65.56, -64.75, -61.11, -58.77 and -50.35 ppm (Figure 4.7). These 8 peaks are representative of the coordination of the silsesquioxane ligands around the two metal centres resulting in an unusual structural symmetry. The broad nature of the peak at -50.35 ppm is likely to be due to the paramagnetic broadening due to the presence of the Yb^{3+} metal centre. ^7Li NMR displayed no signal, confirming the removal of all the lithium centres during the reaction. Again, final identification of the structure of **Compound 10** was not possible due to the absence of crystals suitable for X-ray crystallography. It is well-known that the crystallisation of rare earth metallasilsesquioxanes is extremely challenging and many of these compounds frequently have amorphous structures.

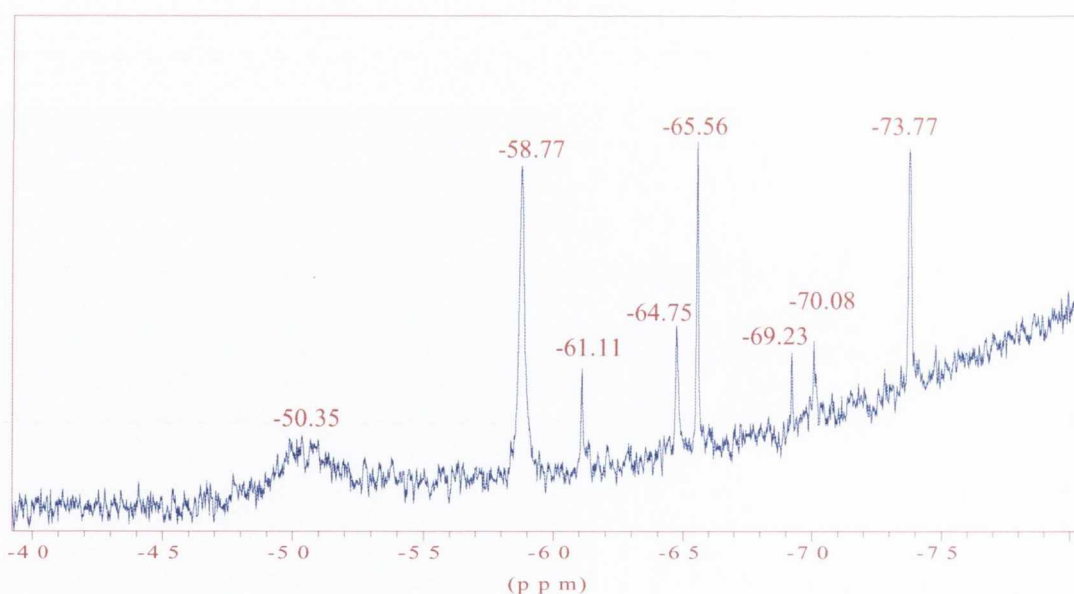


Figure 4.7: ^{29}Si NMR of **Compound 10**, showing peaks at -73.77, -70.08, -69.23, -65.56, -64.75, -61.11, -58.77 and -50.35 ppm.

FTIR spectra of the **Compounds 8, 9 and 10** display peaks at 1100 cm^{-1} representing Si-O-Si bonds and in the fingerprint region representing the cyclohexyl functionalities on the corners of the cage structures (*Figure A2.9*).

4.6 Preparation of RE-Silica Nanocomposites

Rare earth containing metallasiloxanes and metallasilsesquioxanes were used as precursors in the preparation of luminescent silica nanoparticles by thermal decomposition. Thermolysis experiments were carried out on selected samples of metallasiloxanes and metallasilsesquioxanes using a Perkin Elmer Pyris 1 TGA with a burn rate of $10\text{ }^{\circ}\text{C}/\text{min}$ under a nitrogen atmosphere. Their decomposition graphs were analysed and the final products were recovered from the machine after heating for further examination.

4.6.1 Using Metallasiloxanes to Prepare Rare Earth Doped Silica Nanoparticles

The europium-based metallasiloxane, **Compound 4** [$\text{Eu}(\text{O}_2\text{SiPh}_2)_3$], was used to prepare luminescent silica nanoparticles due to the characteristic strong signal emitted by Eu^{3+} in the visible range of the spectrum, allowing ease of examination.

Thermolysis of **Compound 4** was carried out to a temperature of $900\text{ }^{\circ}\text{C}$ (*Figure 4.8*). After this, $\sim 10\%$ of the sample was remaining as a black, non-luminescent solid. It was found that $\sim 16.7\%$ of the sample mass burned off between 35 and $140\text{ }^{\circ}\text{C}$. This was due to coordinated THF solvent molecules and hydroxyl groups which may have resulted from partial hydrolysis of the compound during transfer to the machine. Between 380 and $525\text{ }^{\circ}\text{C}$, $\sim 59\%$ of the sample mass was lost; this corresponds closely to the mass contribution of the hydrocarbon groups calculated to be present on the suspected structure. It was noted that $\sim 76\%$ of the sample remained at $\sim 300\text{ }^{\circ}\text{C}$ and so, thermal treatment was repeated on **Compound 4** to a maximum temperature of $300\text{ }^{\circ}\text{C}$. This resulted in a white solid powder, which was collected and analysed by TEM and photoluminescence spectroscopy.

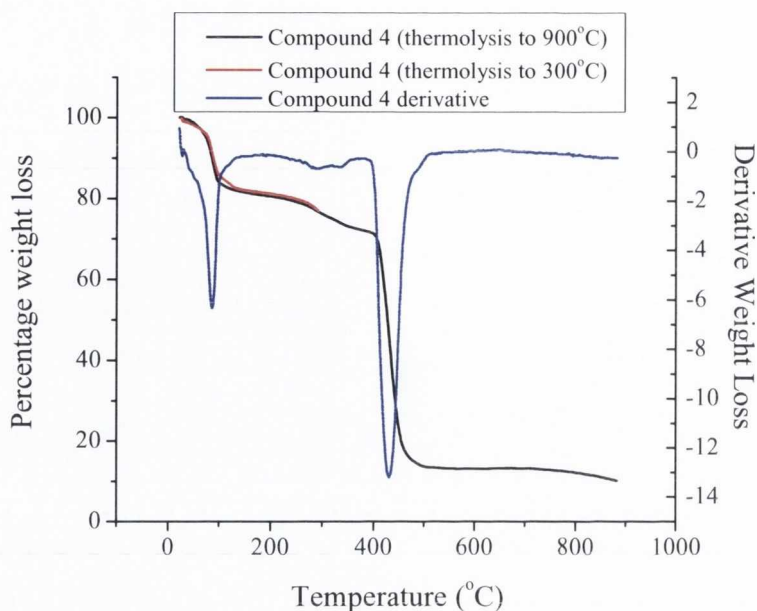


Figure 4.8: Thermal decomposition graph showing the weight loss and derivative curve of **Compound 4** after thermal treatment to 900 °C and 300 °C.

The white powder solid of **Compound 4** post-thermal treatment to 300 °C was suspended into a water solution and characterised by TEM (Figure 4.9). The TEM images collected demonstrated the presence of quasi-spherical nanoparticles which were 28 ± 8 nm in diameter. The particles appeared to be present as small aggregates. The histogram in Figure 4.10 displays the size distribution of the particles.

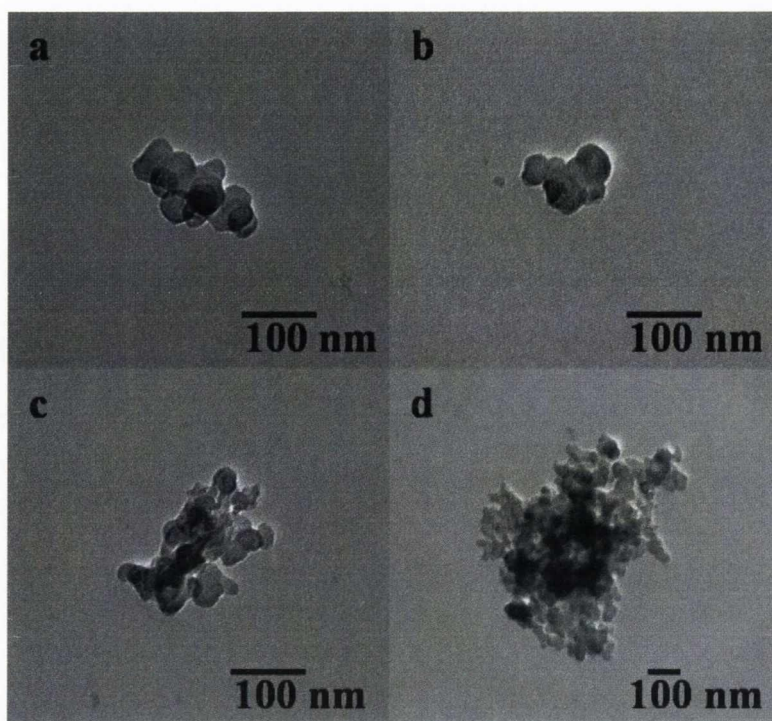


Figure 4.9: TEM images of **Compound 4** after 300 °C thermal treatment; a), b) and c) at x50,000 magnification; d) at x25,000 magnification.

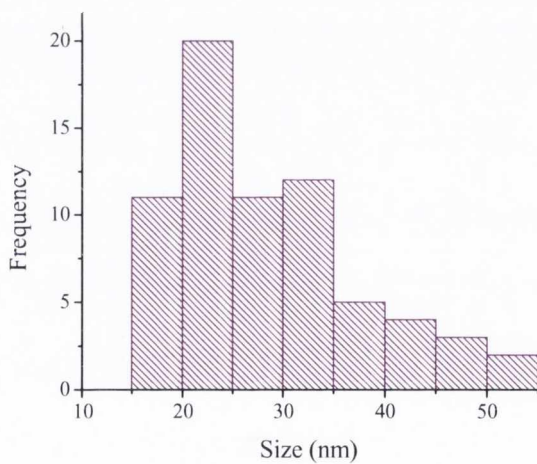


Figure 4.10: Histogram showing size distribution of nanoparticles formed by thermolysis of **Compound 4** to 300 °C.

Solid state photoluminescence spectra demonstrate the characteristic peaks as expected from the Eu^{3+} ions present in the compound (Figure 4.11). Peaks at 578, 591, 617, 650, 700 nm correspond to the Eu^{3+} transitions: $^5\text{D}_0 \rightarrow ^7\text{F}_j$ ($j = 0, 1, 2, 3, 4$). The broad

underlying emission of the sample after thermolysis is due to the presence of carbon defects generated by the high heat treatment of the sample. This phenomenon is comparable to the results described in Section 3.5.2, Chapter 3. Suspension of the sample in aqueous solvents caused quenching of this luminescence, which is indicative of the highly porous nature of the particles formed and the possibility of the presence of the Eu^{3+} ions near to the surface of the structure, allowing them to be easily quenched by the water molecules.

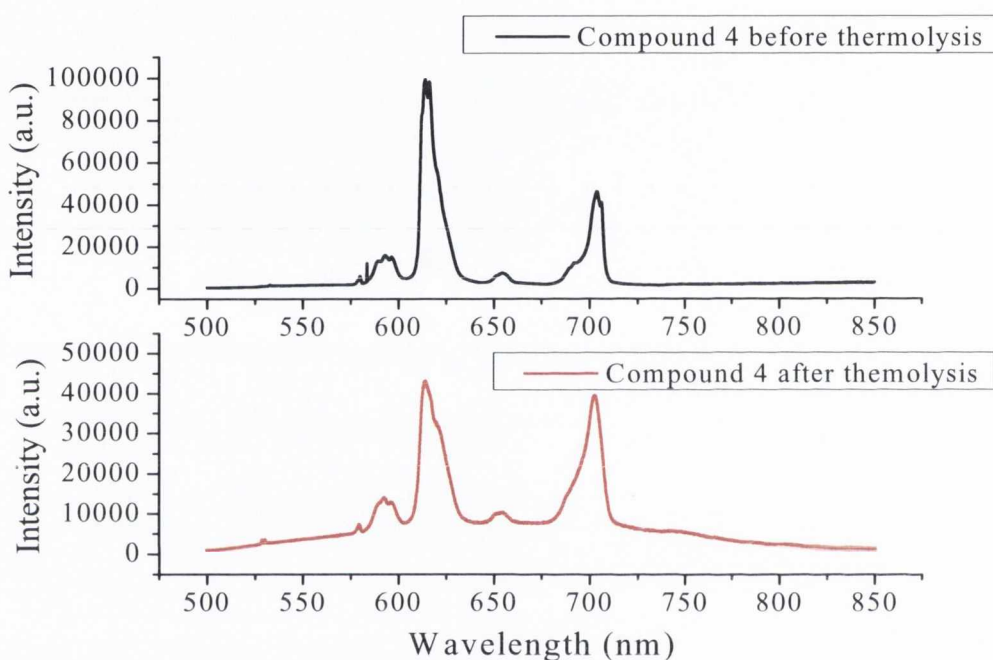


Figure 4.11: Solid state photoluminescence spectra of **Compound 4** before (black) and after (red) thermolysis treatment to 300 °C, $\lambda_{\text{ex}} = 457$ nm.

4.6.2 Using Metallasilsesquioxanes to Prepare Rare Earth Doped Silica Nanoparticles

Thermolysis of **Compound 6** was carried out to a temperature of 900 °C (Figure 4.12). After this, ~35 % of the sample was remaining as a black, non-luminescent solid. The thermal decomposition graph of **Compound 6** is significantly different to that for the trisilanol **Ligand A** from which **Compound 6** was prepared (Figure A2.10), due to the complexation of the compound to the Eu metal centre. The decomposition graph shows a weight loss of ~2.5 % between 150 and 235 °C for **Compound 6**, a loss which is attributed

to the removal of the hydroxyl groups in the structure. A weight loss of $\sim 11\%$ between $250\text{ }^{\circ}\text{C}$ and $350\text{ }^{\circ}\text{C}$ is due to partial degradation of the siloxane groups coordinated to the metal centre. The largest loss of mass, of $\sim 46\%$ occurs between 350 and $600\text{ }^{\circ}\text{C}$, due to the loss of the hydrocarbon groups from the cyclohexyl substituents on the compound.

It was noted that $\sim 85\%$ of the original mass remained after heating to $350\text{ }^{\circ}\text{C}$, therefore thermal treatment on **Compound 6** was repeated, with heating ceased at $350\text{ }^{\circ}\text{C}$. This resulted in a yellow solid which was retained and characterised by TEM and photoluminescence spectroscopy.

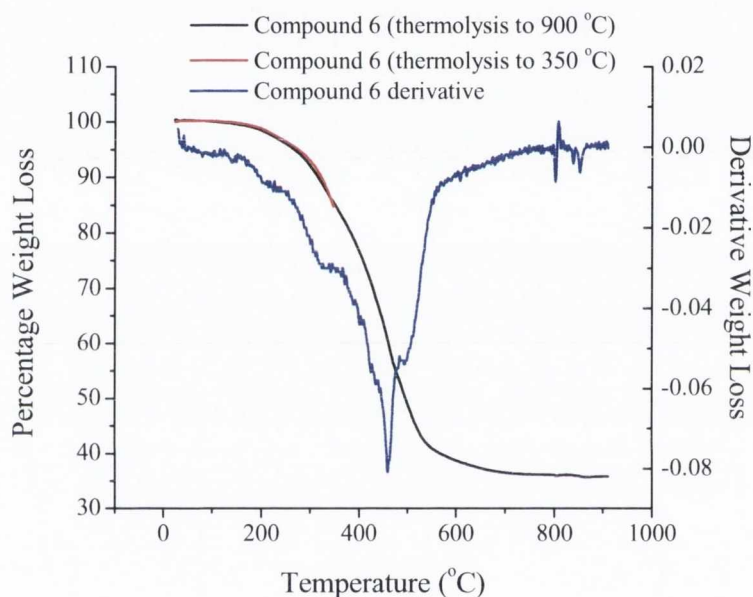


Figure 4.12: Thermal decomposition graph showing the weight loss and derivative curve of **Compound 6** after thermal treatment to $900\text{ }^{\circ}\text{C}$ and $350\text{ }^{\circ}\text{C}$.

The yellow powder of **Compound 6** after thermal treatment to $350\text{ }^{\circ}\text{C}$ was suspended into a water solution and characterised by TEM (Figure 4.13). The TEM images collected demonstrated the presence of aggregates of quasi-spherical nanoparticles which were $13.5 \pm 4\text{ nm}$ in diameter. The histogram in Figure 4.14 displays the size distribution of the particles.

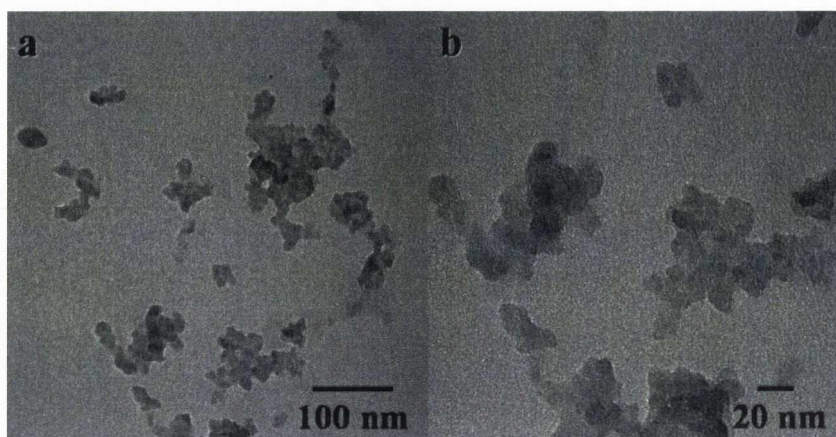


Figure 4.13: TEM images of **Compound 6** after 350 °C thermal treatment; a) and b) at different magnifications.

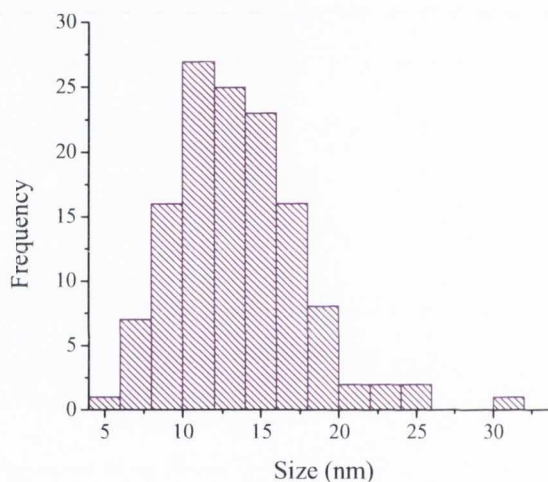


Figure 4.14: Histogram showing size distribution of nanoparticles formed by thermolysis of **Compound 6** to 350 °C.

As with the previous sample, **Compound 6** displays solid state photoluminescence spectra characteristic of Eu^{3+} (Figure 4.15). Broad underlying emission between 500 and 850 nm can be seen for the sample both pre- and post-thermal treatment; however, this is significantly more prominent after thermolysis, where the broad emission masks many of the characteristic Eu^{3+} spectral lines. Once again, this prominent broad spectrum can be attributed to defect emission.

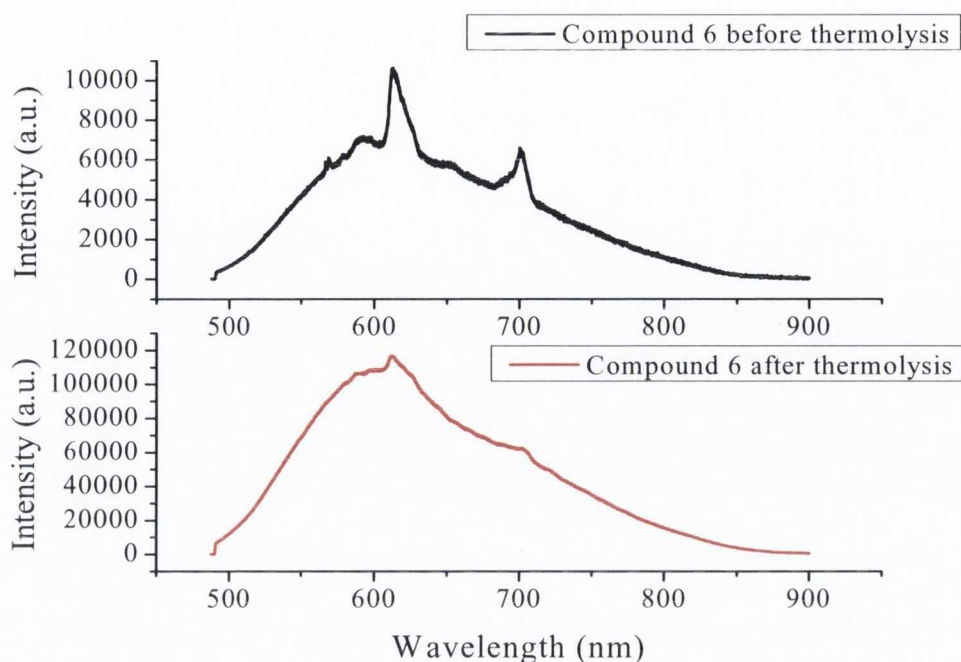


Figure 4.15: Solid state photoluminescence spectra of **Compound 6** before (black) and after (red) thermolysis treatment to 350 °C, λ_{ex} = 488 nm.

Thermolysis of **Compound 7** was carried out to a temperature of 900 °C (Figure 4.16). After this, ~31 % of the sample was remaining as a black, non-luminescent solid. The decomposition graph shows a weight loss of ~5 % between 70 and 175 °C for **Compound 7**, attributed to the removal of the hydroxyl groups and coordinated solvent molecules in the structure. A weight loss of ~17 % between 175 °C and 300 °C is due to partial degradation of the siloxane groups coordinated to the metal centre. The largest loss of mass, of ~46 % occurs between 300 and 600 °C, due to the loss of the hydrocarbon groups from the cyclohexyl substituents on the compound.

It was noted that ~78 % of the original mass remained after heating to 300 °C, so thermal treatment on **Compound 7** was repeated, with heating ceased at 300 °C. This resulted in a white solid which was retained and characterised by TEM and photoluminescence spectroscopy.

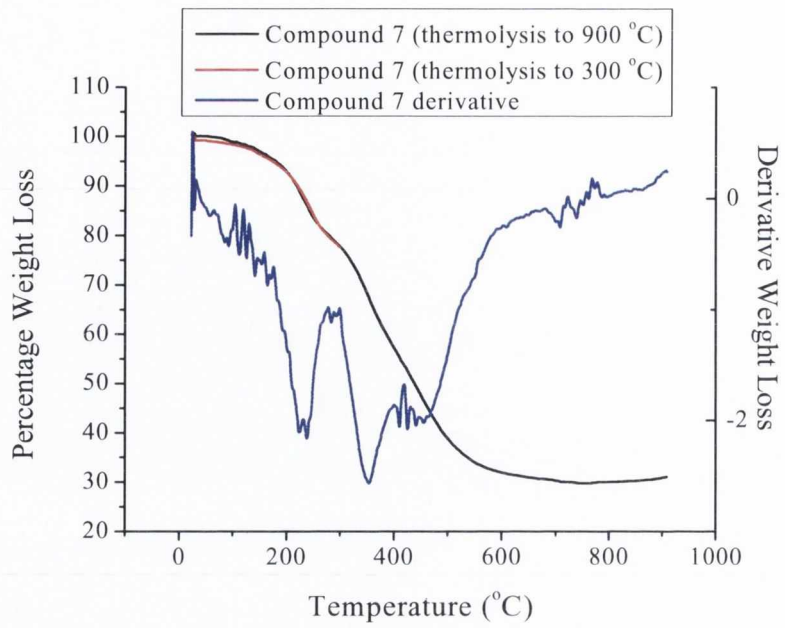


Figure 4.16: Thermal decomposition graph showing the weight loss and derivative curve of **Compound 7** after thermal treatment to 900 °C and 300 °C.

The white powder of **Compound 7** after thermal treatment to 300 °C was suspended into a water solution and characterised by TEM (Figure 4.17). The TEM images collected demonstrated the presence of aggregates of quasi-spherical nanoparticles which were 15.8 ± 5 nm in diameter. The histogram in Figure 4.18 displays the size distribution of the particles.

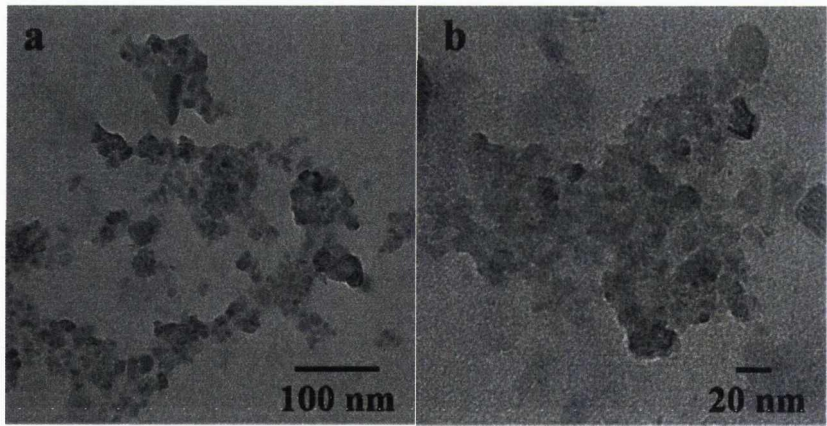


Figure 4.17: TEM images of **Compound 7** after 300 °C thermal treatment; a) and b) at different magnifications.

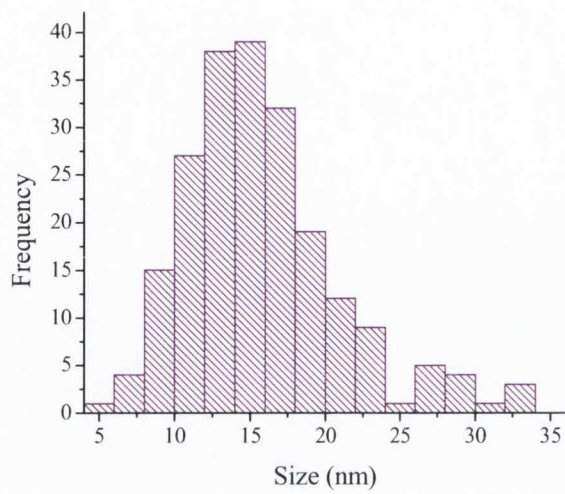


Figure 4.18: Histogram showing size distribution of nanoparticles formed by thermolysis of **Compound 7** to 300 °C.

The photoluminescence spectra of **Compound 7** (Figure 4.19) before and after thermal treatment display a broad emission between 500 and 850 nm. There is a lack of the characteristic peaks expected for the lanthanide ion emission. This is thought to be due to a transfer of energy between Yb^{3+} and Eu^{3+} , causing a quenching of the characteristic Eu^{3+} peaks. The strong broad signal is likely to be due to defect emission, which is not quenched by this energy transfer.

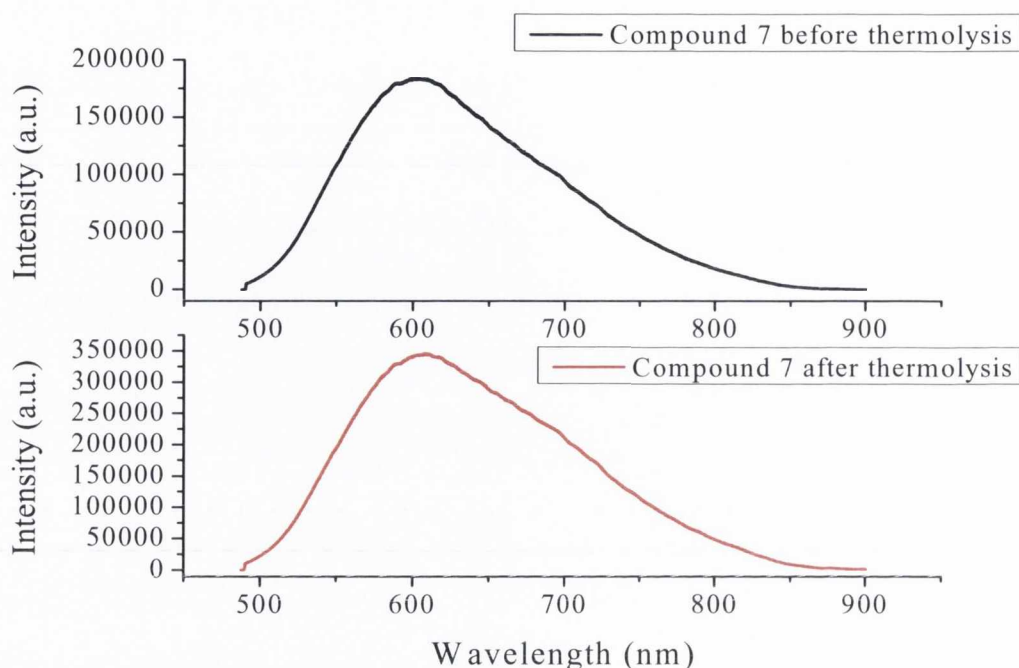


Figure 4.19: Solid state photoluminescence spectra of **Compound 7** before (black) and after (red) thermolysis treatment to 300 °C, $\lambda_{ex} = 488$ nm.

FTIR and Raman spectroscopy confirm that thermal treatment of metallasiloxane and metallasilsesquioxane compounds results in SiO₂-based nanostructured composite materials (*Figures A2.11-2.16*).

4.7 Conclusions

A series of new rare earth metal based siloxane and silsesquioxane materials were prepared using documented procedures and modifications of these methods to provide new structures. These materials were characterised using NMR and FTIR spectroscopy. Full structural characterisation was challenging for the complexes, due to their air-sensitive nature and difficulties encountered with crystallisation.

The metallasiloxane and metallasilsesquioxane complexes were used as precursors for the preparation of lanthanide-doped silica nanoparticles. It has been shown, using Eu³⁺ complexes, that silica nanoparticles with small sizes and quasi-spherical structures can be formed using controlled thermolysis. These nanoparticles retain their original characteristic

lanthanide luminescence properties and acquire a broad luminescent baseline which is prevalent in all samples and becomes enhanced post-thermal treatment. Indeed, these nanoparticles resist quenching in ambient conditions, unlike their siloxane precursors, and retain their strong emissive properties over significant periods of time. The nanoparticles' luminescent properties are quenched upon dispersion in aqueous solvents, due to their porous nature and the possible presence of Eu^{3+} ions on their surfaces.

Further characterisation and investigations of the thermolysis of rare earth siloxanes are required in order to tune the sizes of the resulting nanoparticles prepared. An investigation into the growth of nanoparticles and the possibility of controlling their morphology through careful control of the thermal heating technique could yield different shaped nanostructures.

The thermolysis method presents a simple and promising technique of preparing nanoparticles from corresponding siloxane precursors. The properties of the nanoparticles can be altered by changing the metal centre of the precursors used to prepare them. Indeed, their siloxane complex structures provide an appropriate inorganic cluster to allow the formation of small sized nanoparticles. This technique could be used to prepare nanoparticles doped with rare earth and other metal centres for a variety of potential applications.

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Chapter 5

Magnetic Nanomaterials as Potential MRI Contrast Agents

5.1 Introduction

Magnetic nanoparticles and their assemblies continue to be of great interest in nanotechnology research due to their unique size-dependent magnetic properties, which differ from bulk magnetic materials and may be tuned through the assembly process. As a result, they have potential for use as magnetic recording devices and in biomedicine, such as vehicles for targeted drug delivery,¹⁻³ as mediators for hyperthermia⁴ and as contrast agents for magnetic resonance imaging (MRI).⁵⁻⁸ MRI, in particular, is a powerful non-invasive technique in medical research that can rapidly map out the spatial distribution of the ^1H signal intensity. There has been increased focus on MRI in recent years, due to the numerous ways in which different signal intensities are produced, *i.e.* contrast, arising from ^1H nuclei with different chemical or physical properties conferred by their immediate environment. Magnetic colloids act to reduce the T_1 (spin-lattice) or T_2 (spin-spin) relaxation times of the surrounding tissues, resulting in local changes in the MRI signal intensity.⁹

Currently available MRI contrast agents include those which are capable of enhancing the signal in T_1 -weighted images, such as gadolinium chelates; as well as those which provide strong contrast in T_2 -weighted images, such as superparamagnetic iron oxide (SPIO).¹⁰⁻¹³ The nanoparticulate nature of the SPIO can present benefits over traditional chelate materials as they hold opportunities for surface modification, allowing easy chemical distribution and biological transportation.

Numerous studies have been conducted towards the development of new MRI contrast agents based on magnetic nanoparticles.^{10,14-17} Dextran-coated iron oxide nanoparticles have been applied in clinical and molecular imaging for the last 20 years.^{12,13} Progress in the development of low field MRI opens up further prospects for the investigation of new types of contrast agents which operate at low fields.¹⁸ Low field systems could pave the future for MRI, as their use of lower energy radio frequency (RF) means that patients are less likely to develop side effects, such as RF burns.¹⁹ Downsides,

such as poor image quality, could be significantly improved by using contrast agents designed to work efficiently in these ranges. Magnetic particle imaging (MPI), which has been heralded as one of the most promising approaches for *in vivo* imaging, may provide a flexible and low cost diagnostic tool for a range of conditions.^{7,20}

Recently, Corr *et al.* reported the preparation of iron oxide nanoparticles stabilised with polyelectrolytes which form ordered nanowires through magnetic alignment (Figure 5.1).²¹ Single-stranded Herring DNA, which may be classed as a bioactive polyelectrolyte, was shown to successfully stabilise magnetic fluids, producing unprecedentedly high relaxivity.²² NMRD analysis of suspensions stabilised with synthetic polyelectrolytes demonstrated the potential to tune the relaxivity through the reaction conditions. The resulting colloids again had high relaxivity at low fields and showed potential for *in vivo* MRI diagnostics.²³

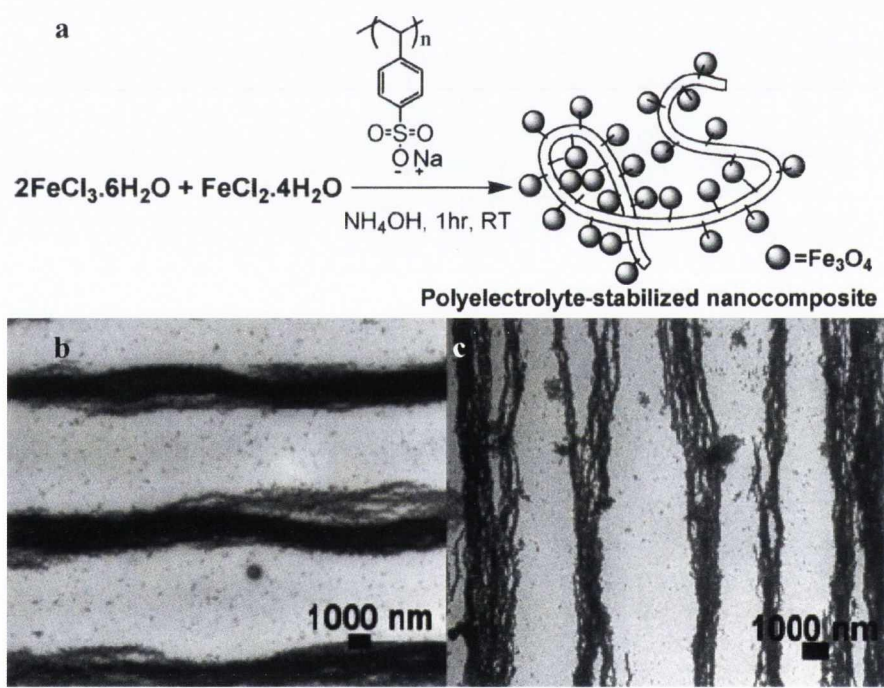


Figure 5.1: (a) Scheme showing the preparation of polyelectrolyte-stabilised magnetite nanoparticles;²¹ (b) and (c) TEM images of the polyelectrolyte-stabilised magnetite nanoparticles in the presence of an external magnetic field.²³

Cobalt ferrite (CoFe_2O_4) nanomaterials have also shown promise for MRI applications, due to their chemical stability, high magnetocrystalline anisotropy and coercivity.²⁴⁻²⁶ There has been extensive research on the chemical and magnetic properties of cobalt ferrite nanocrystals prepared by different methods.^{15,27-33} Similarly, the preparation and characterisation of manganese ferrite (MnFe_2O_4) nanoparticles as hyperthermia agents and MR probes make these types of ferrites very attractive.^{31,34} The interpretation of nuclear magnetic resonance dispersion (NMRD) profiles, which represent the relaxation behaviour of aqueous magnetic suspensions, allows a quantitative assessment of their efficiency as MRI contrast agents, *i.e.* determination of the spin-lattice relaxivity, r_1 .³⁵ The frequency dependence of the relaxivity provides insight into the critical interaction between the water molecules and the contrast agent.

The use of a stabiliser in nanochemistry is important for two reasons. Firstly, it allows the particles to remain stable in aqueous suspensions for long periods of time, a characteristic which is attractive for a multitude of applications. Secondly, it is widely known that particles in suspensions can undergo spontaneous changes of structure, morphology, and can grow in size during ageing *via* the Ostwald ripening process. Therefore, coating magnetic particles with stable materials is one method of preparing them for biomedical applications. Coatings can also facilitate further modification of the surfaces to carry therapeutic agents or to act as target-specific moieties.^{36,37} The use of commercially available polyelectrolytes can assist with stabilising particles and also can act as templating materials, assisting in the alignment of magnetic nanoparticles into 1-D linear arrays in the presence of an external magnetic field.²³ Sheparovych *et al.* used polyelectrolytes to link Fe_3O_4 nanoparticles in the presence of a magnetic field, yielding linear wire-like assemblies of magnetic particles (Figure 5.2).³⁸

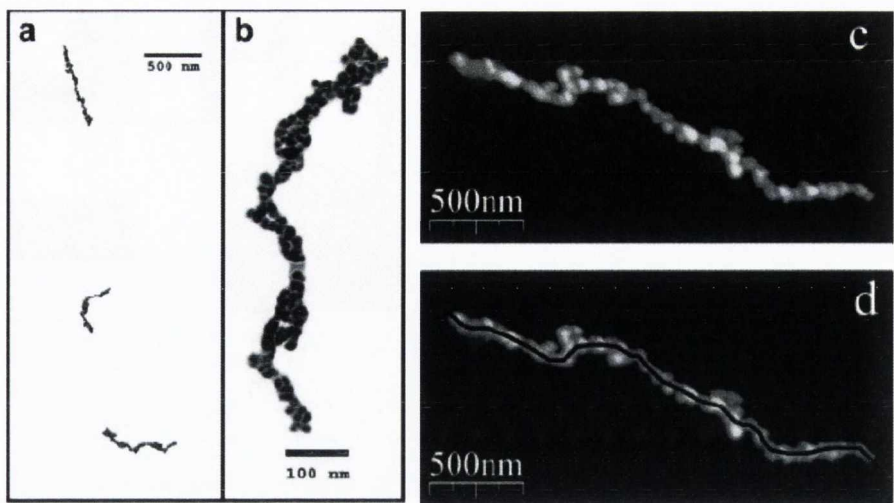


Figure 5.2: (a) and (b) TEM images, (c) and (d) AFM images of the magnetic wire-like structures stabilised with a positively charged polyelectrolyte poly(2-vinylN-methylpyridinium iodide).³⁸

5.2 Aims

The aims of the work presented in this chapter involve investigations of various magnetic nanoparticles as potential MRI contrast agents, including cobalt ferrite and manganese ferrite based magnetic nanocomposites. In a new approach for these types of particles, commercially available polyelectrolytes will be utilised to act as both nanowire assembly templates and water stable surfactants in the *in situ* synthesis of ferrite nanocomposites by co-precipitation. The nanocomposite materials will be characterised in terms of their size, magnetisation and relaxivity properties. We plan to study the relaxivity of new nanomaterials in aqueous suspensions by the NMRD technique. Our hope is that the magnetic relaxivity properties of these new nanocomposites will provide insights into the organisation of magnetic colloids of ferrite materials in suspension.

In this study, the negatively charged polyelectrolyte, poly(sodium-4-styrene) sulfonate (PSSS) (Figure 5.3) will be used.

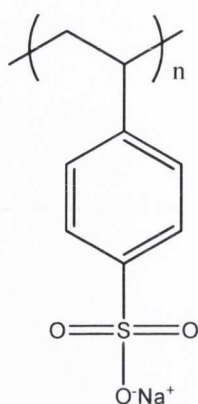


Figure 5.3: Structure of poly(sodium-4-styrene) sulfonate (PSSS), $n=70,000$.

5.3 Preparation and Characterisation of Cobalt Ferrite Nanoparticles

Cobalt ferrite nanoparticles were prepared using traditional co-precipitation techniques (Scheme 5.1).³⁹ Co-precipitation was carried out using ammonium hydroxide solution, which was added to a solution of iron (II) chloride and cobalt (II) nitrates and subsequently reacted for 1 hour at 80-90 °C using different agitation methods, including magnetic stirring and sonication (see experimental section for details). This yielded cobalt ferrite (CoFe_2O_4) nanoparticles which were present as a strongly magnetic black precipitate. The reactant Fe^{2+} iron salts in this scheme are oxidised to Fe^{3+} ions in the resulting $\text{Co}^{(2+)}\text{Fe}^{(3+)}_2\text{O}_4$ nanoparticles due to the nitrate ions from the cobalt (II) nitrate salts used in the reaction. The nanoparticles did not form stable aqueous suspensions. The particles were characterised using Transmission Electron Microscopy (TEM), Fourier-Transform Infrared (FTIR) and Raman spectroscopy, X-Ray Diffraction (XRD) and magnetisation measurements.



Scheme 5.1: Reaction sequence showing the preparation of cobalt ferrite nanoparticles using co-precipitation.

5.3.1 Characterisation of Cobalt Ferrite Nanoparticles

5.3.1.1 TEM Characterisation

TEM demonstrated nanoparticles which were quasi-spherical in shape and varied in size depending on the method of agitation used during preparation (Figure 5.4). The

nanoparticles prepared using magnetic stirring were 23.5 ± 7 nm in diameter, whereas those prepared using ultrasonic treatment were 13.5 ± 5 nm in diameter.

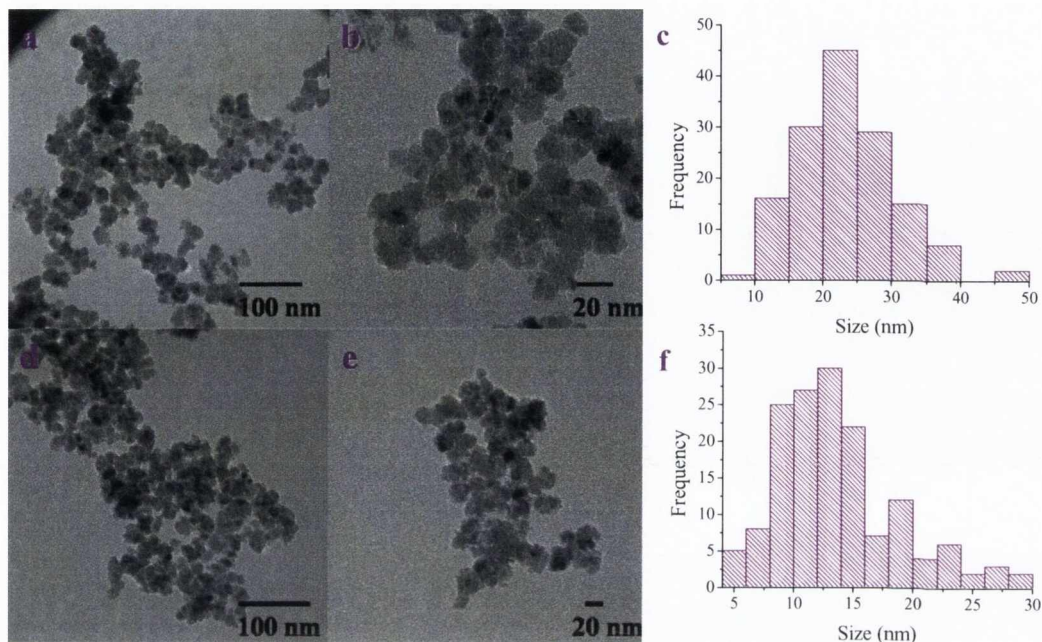


Figure 5.4: (a) and (b) TEM images and (c) histogram showing size distribution of cobalt ferrite nanoparticles prepared using heat and magnetic stirring; (d) and (e) TEM images and (f) histogram showing size distribution of cobalt ferrite nanoparticles prepared using ultrasonic treatment.

The particles prepared using heat and magnetic stirring were larger in diameter than those prepared using ultrasound. These findings are in agreement with a similar trend reported by Morel and co-workers.⁴⁰ Their use of a sonochemical approach during the coprecipitation of Fe_3O_4 yielded nanoparticles which were smaller in size than those prepared using mechanical stirring. This is due to the nucleation of the metal ions occurring *via* cavitation. Some effects of sonication which are thought to contribute to reduced particle sizes include the shock waves generated during bubble implosion which hinders agglomeration and the excellent mixing conditions created by acoustic cavitation.⁴¹

5.3.1.2 FTIR and Raman Spectroscopy

FTIR spectroscopy (Figure A3.1, Appendix 3) gave peaks at $570\text{--}580\text{ cm}^{-1}$ which represent Fe-O stretches. Literature shows a faint absorption band at 667.05 cm^{-1} which is

assigned to the stretching vibration mode of Co-O bond.⁴² Our results show this to appear as a shoulder on the Fe-O peaks. A broad peak around $3440\text{--}3460\text{ cm}^{-1}$ represents water and OH^- groups.

Raman spectroscopy of the dried powder cobalt ferrite nanoparticle samples (Figure 5.5) shows the optically active Raman modes characteristic of the cubic inverse-spinel structure of cobalt ferrite.⁴³ The highest frequency Raman mode at 680 cm^{-1} is assigned to the T-site mode, which reflects the local lattice effect in the tetrahedral sublattice. The peak at 465 cm^{-1} is assigned to the O-site mode, which reflects the local lattice effect in the octahedral sublattice. The other peaks were found to be at $613, 543, 300\text{ cm}^{-1}$. These values are all in good agreement with the 5 optically active modes ($A_{1g}+E_g+3F_{2g}$) characteristic of the cubic inverse spinel structure $O_h^7 (Fd3m)$ space group.⁴³

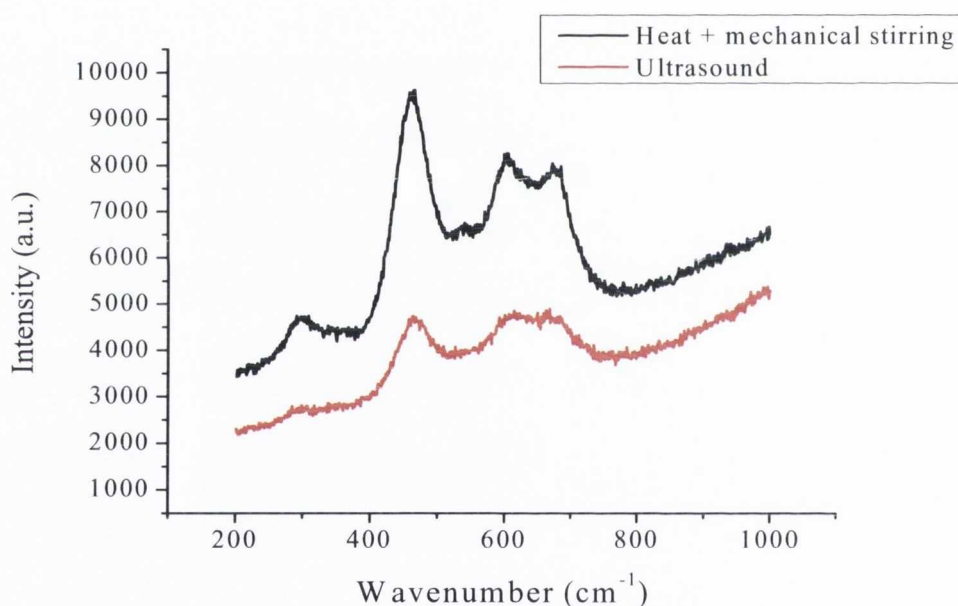


Figure 5.5: Raman spectra of samples of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red).

5.3.1.3 X-Ray Diffraction

Overnight X-ray diffraction patterns were collected of the cobalt ferrite dried powder samples (Figure 5.6). The reflection peaks can be readily indexed to the (220), (311), (400), (331), (422), (511) and (440) planes of spinel CoFe_2O_4 with a cubic symmetry.⁴⁴ The broad peak at $20\text{--}22^\circ 2\theta$ corresponds to silica, from the gel used to hold

the sample in place during measurement. The diffractogram peaks were broad in nature, indicating the nanocrystalline nature of the sample.

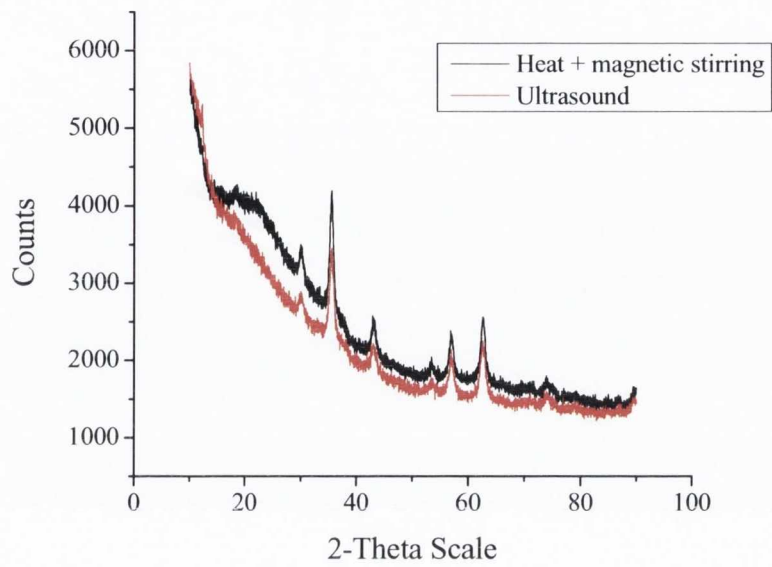


Figure 5.6: XRD pattern of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red) which correspond with the JCPDS database for CoFe_2O_4 .

5.3.1.4 Magnetisation Measurements

Samples of nanoparticles were characterised using Vibrating Sample Magnetometry (VSM). Magnetisation measurements show that nanoparticles prepared using magnetic stirring have higher saturation magnetisation at 1 T ($57.6 \text{ Am}^2/\text{kg}$) than those prepared using ultrasound ($36.9 \text{ Am}^2/\text{kg}$) (Figure 5.7). These values are lower than the accepted value of bulk CoFe_2O_4 of $80 \text{ Am}^2/\text{kg}$ at room temperature, but are comparable with similar cobalt ferrite nanoparticles ($61.50 \text{ Am}^2/\text{kg}$).^{45,46} This discrepancy between the samples is due to the size difference; it is well-recognised that smaller sized particles provide lower saturation magnetisation. This decreased magnetisation is thought to be due to an amorphous surface layer which is magnetically inactive.⁴⁷ A narrow hysteresis loop can be seen in the magnetisation spectra (inset Figure 5.7), which is due to the ferromagnetic nature of the particles. It should be noted that the materials do not fully saturate at 1 T, indicating the presence of a paramagnetic or superparamagnetic phase.

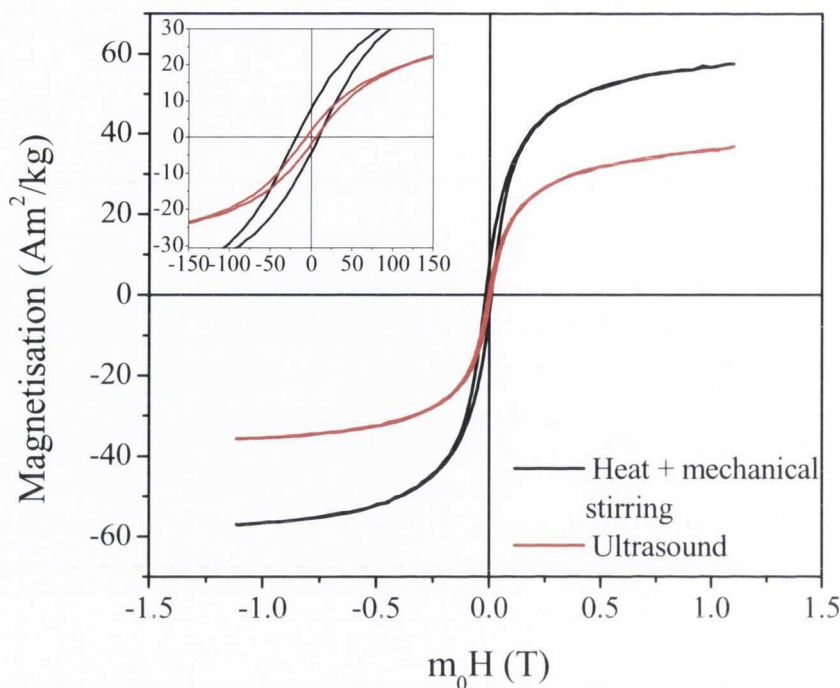


Figure 5.7: Magnetisation curves of cobalt ferrite nanoparticles prepared using heat and magnetic stirring (black) and ultrasound treatment (red); inset shows close-up of hysteresis loop.

Magnetic stirring and heating was adopted as the method for preparing particles hereafter as this yielded particles which were more uniform in their size, with smaller standard deviations as well as higher saturation magnetisation.

5.4 Preparation and Characterisation of Cobalt Ferrite-Polyelectrolyte Nanocomposites

Cobalt ferrite-polyelectrolyte nanocomposites were prepared using traditional co-precipitation techniques (Scheme 5.1)³⁹ with the *in situ* addition of poly(sodium-4-styrene) sulfonate (PSSS) polyelectrolyte as a stabiliser and assembly director. Variation of the reagent ratios proffered five stable nanocomposite suspensions, detailed in Table 5.1. It should be noted that the aqueous suspensions of cobalt ferrite-PSSS demonstrated long-term stability (over three years).

The concentrations used in these experiments were selected on the basis of previous work carried out in the area.²¹ It was found that the reagent concentrations and ratios

selected presented nanocomposites with the best characteristics, in terms of their stability, size and NMRD behaviour.

Aqueous suspensions of nanocomposites were characterised by TEM, photon correlation spectroscopy (PCS), nuclear magnetic resonance dispersion (NMRD) and inductively coupled plasma atomic emission spectroscopy (ICP-AES); dried solid powder samples of the precipitates were characterised by Raman and FTIR spectroscopy, XRD and magnetisation measurements.

5.4.1 Characterisation of Cobalt Ferrite-Polyelectrolyte Nanocomposites

5.4.1.1 TEM and PCS Characterisation

The PSSS-stabilised cobalt ferrite nanoparticles that were prepared demonstrated long-term stability in aqueous suspension. TEM and PCS measurements were carried out on all suspensions and the results are shown in Table 5.1.

Table 5.1: Characteristics of PSSS-stabilised cobalt ferrite nanocomposite samples.

Sample	Total [initial metal] (mM)	[PSSS] (mM)	[Initial metal] : [PSSS] ratio (~monomer ratio)	d_{TEM} ^[a] (nm)	d_{hyd} ^[b] (nm) (PDI)	r_l at 0.01MHz (s ⁻¹ mM ⁻¹)
1	42.9	0.204	210 (0.62)	32 ± 8	119 (0.160)	257.46
2	42.9	0.041	1046 (3.08)	42 ± 11	130 (0.167)	226.33
3	42.9	0.020	2145 (6.31)	59 ± 17	262 (0.195)	153.76
4	30	0.072	417 (1.23)	43 ± 21	307 (0.215)	125.32
5	42.9	0.409	105 (0.31)	26 ± 16	366 (0.168)	103.49

[a] d_{TEM} refers to the average diameter of primary nanoparticles calculated from >100 particles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions index; r_l refers to the relaxivity of the magnetic fluids.

On drying a drop of the stable aqueous suspensions onto a TEM grid in the absence of a magnetic field, the nanoparticles were well dispersed (Figure 5.8). Close examination of the micrographs (Figure 5.8f) reveals quasi-spherical particles with an average size which ranges from 25-60 nm. These micelle-like structures appear to be made up of smaller nanoparticles, held together by the PSSS polyelectrolyte. Importantly, for samples prepared for TEM in this way, no significant long-range macroscopic order persists. Histograms showing the size and size distribution amongst the samples can be seen in Figure 5.9. The primary particle size, d_{TEM} , was found to increase with increasing metal to monomer ratio (Figure 5.10). This suggests that increasing the amount of metal results in an extended nanoparticle growth phase and is consistent with all samples having a similar concentration of nucleation sites along the negatively charged polyelectrolyte backbone.

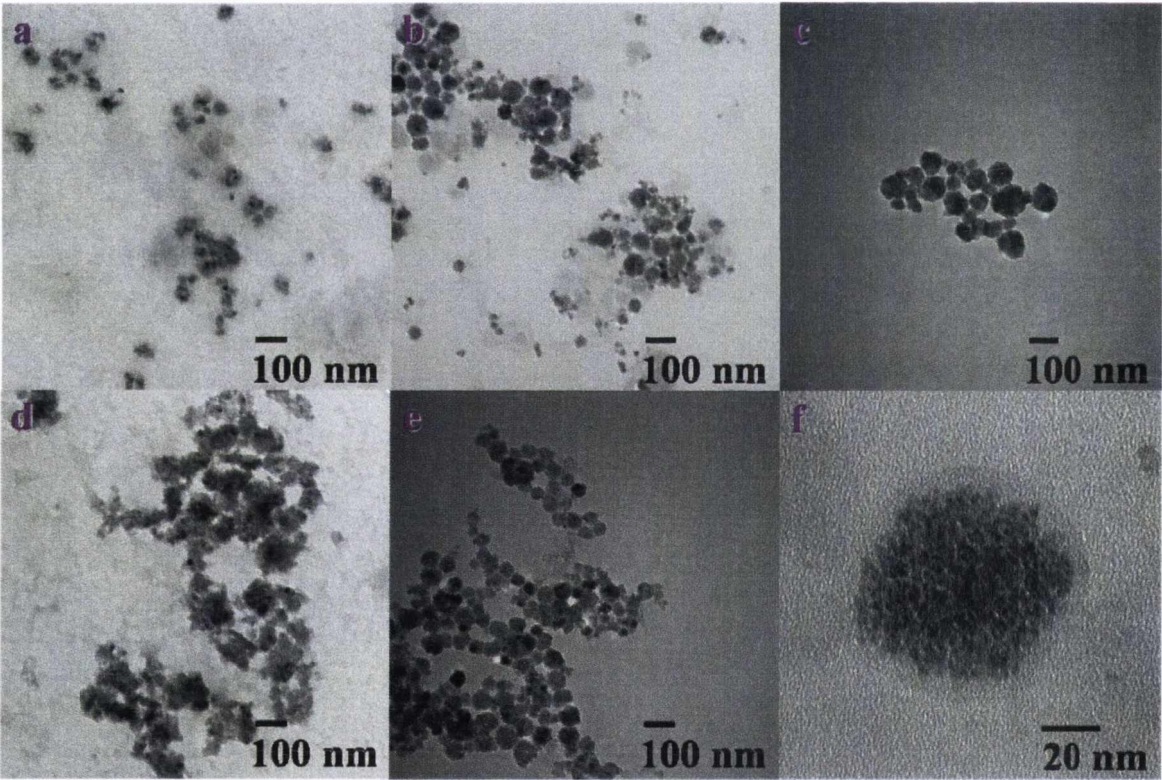


Figure 5.8: TEM images of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1: (a) Sample 1; (b) Sample 2; (c) Sample 3; (d) Sample 4; (e) Sample 5; (f) close-up of sample 2 showing vesicle arrangement.

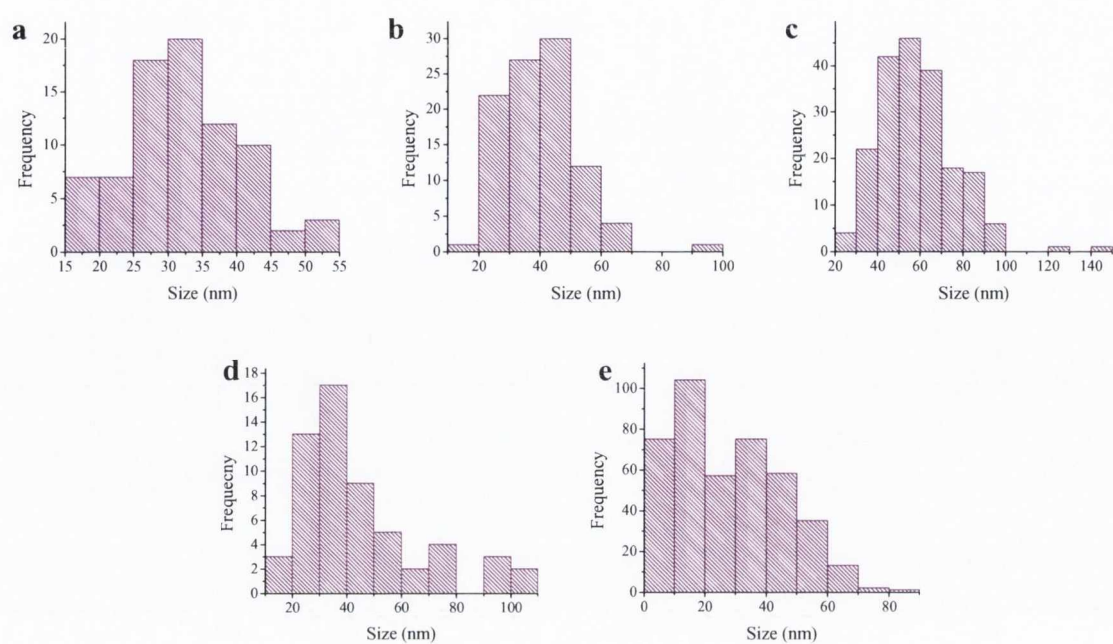


Figure 5.9: Histograms showing size distribution of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1; (a) to (e) represent samples 1-5 sequentially.

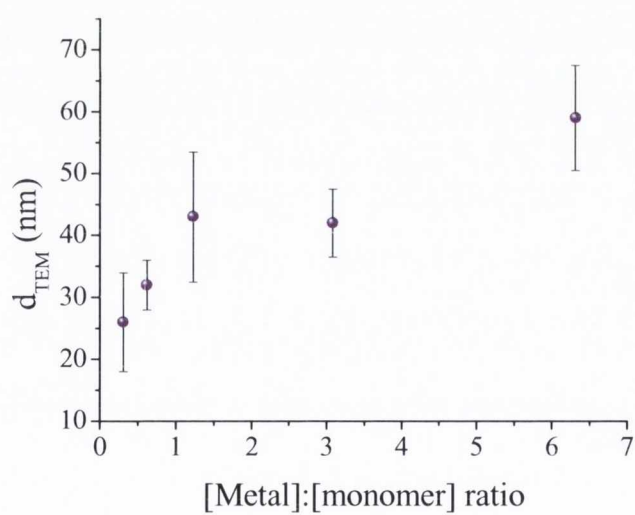


Figure 5.10: Graph showing increasing primary particle size with increasing metal to monomer ratio.

Upon drying a drop of the stable aqueous suspensions onto TEM grids in the presence of a permanent 0.5 T external magnetic field oriented in the plane of the grid, as the composites appeared as compact parallel 1-D linear arrays or ‘nanowires’, as expected

(Figure 5.11). The aspect ratio of these ‘nanowires’ varies considerably between samples. The assemblies only survive the drying process intact when magnetised by the presence of the external field, Figure 5.8 and Figure 5.11. The behaviour of the composites in a magnetic field is attributed to the templating effect of the polyelectrolyte stabiliser, which cross-links magnetic nanoparticles, resulting in these nanowire-like assemblies.

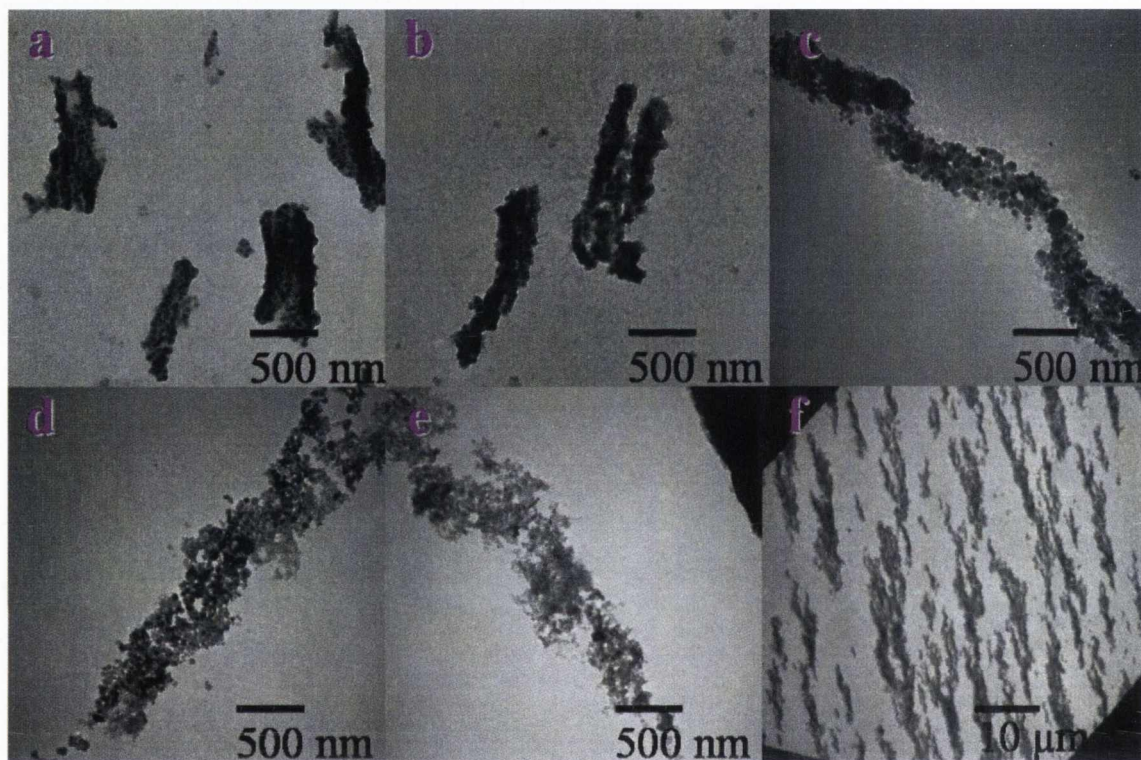


Figure 5.11: TEM images of PSSS-cobalt ferrite nanocomposites prepared according to Table 5.1 in the presence of a magnetic field at x 10,000 magnification: a) Sample 1; b) Sample 2; c) Sample 3; d) Sample 4; e) Sample 5; f) Sample 4 at x 400 magnification.

The hydrodynamic behaviour of all suspensions has been investigated by PCS (Table 5.1). The observed hydrodynamic diameters are in the range of 120 to 370 nm, which are significantly larger than the nanoparticle sizes determined by electron microscopy. In addition to being a stabilising agent, the polyelectrolyte can also act as a template for the formation of composites once the nanoparticles have been formed. Given the relatively low degree of polymerisation, $X \sim 340$, the assemblies are the result of hydrogen bonding and van der Waals interactions between different polyelectrolyte chains. It may also be possible that dipolar interactions between adjacent nanoparticles and cross-

linking between polyelectrolyte molecules contribute to this process, causing larger hydrodynamic radius values. In all cases, however, the polydispersity indices (PDI values) were <0.2 indicating good monodispersity and excellent stability of the suspended nanocomposites.^{48,49} The suspensions remained stable and neither their hydrodynamic size nor polydispersities were changed by extended exposure to magnetic field strengths of up to 1.6 T. Therefore any magnetically induced structural reorganisation of the nanocomposites, which might be anticipated for strongly dipolar nanoparticles in close physical proximity, is reversible in suspension.

5.4.1.2 FTIR and Raman Spectroscopy

FTIR spectroscopy reveals bands as expected for cobalt ferrite and confirms the presence of the PSSS stabiliser (Figure 5.12). The band at 580 cm^{-1} can be assigned to the Fe-O stretching mode. The shoulder around 670 cm^{-1} on the Fe-O band is due to the Co-O stretching vibrational mode.⁴² Sulfonate vibrational modes are seen at 828 and 773 cm^{-1} . The bands observed in the 1008 - 1180 cm^{-1} range originate from the symmetric and asymmetric C-H stretches of the polyelectrolyte. The bands observed in the 1410 - 1500 cm^{-1} range can be assigned to CH_2 bending vibrational modes. Aromatic C-H bonds and C-C stretches can be seen at 2921 cm^{-1} and 1633 cm^{-1} respectively.⁵⁰ The broad peak centred at 3440 - 3460 cm^{-1} represents water and OH^- groups.

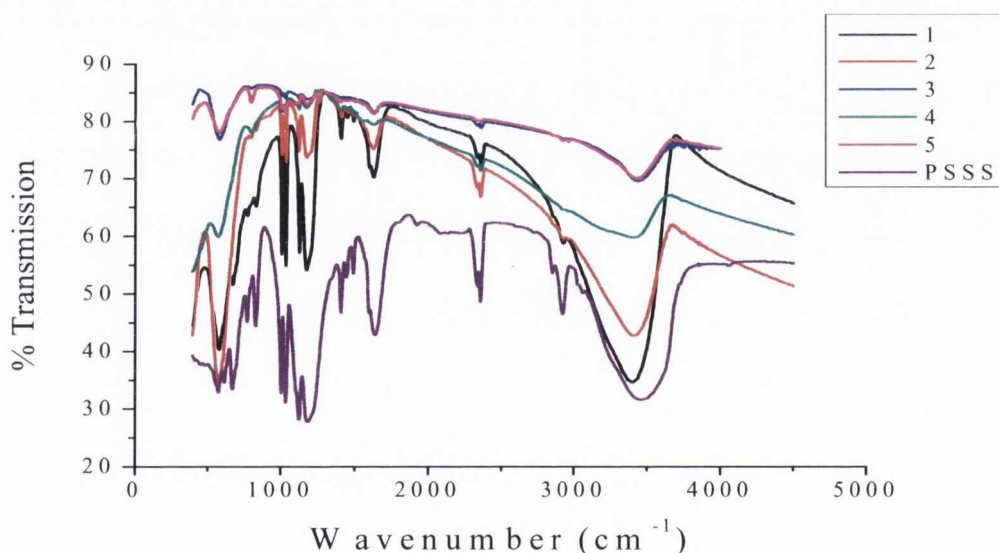


Figure 5.12: FTIR spectra of PSSS-cobalt ferrite nanocomposites samples 1-5, prepared according to Table 5.1.

As with the previous samples, Raman spectroscopy of the dried powder cobalt ferrite-polyelectrolyte nanocomposites (Figure 5.13) shows the optically active Raman modes characteristic of the cubic inverse-spinel structure of cobalt ferrite.⁴³ The peaks were found to be at 688, 618, 563, 470, 314 cm^{-1} . These values are all in good agreement with the 5 optically active modes ($A_{1g}+E_g+3F_{2g}$) characteristic of the cubic inverse spinel structure $O_h^7 (Fd3m)$ space group.⁴³

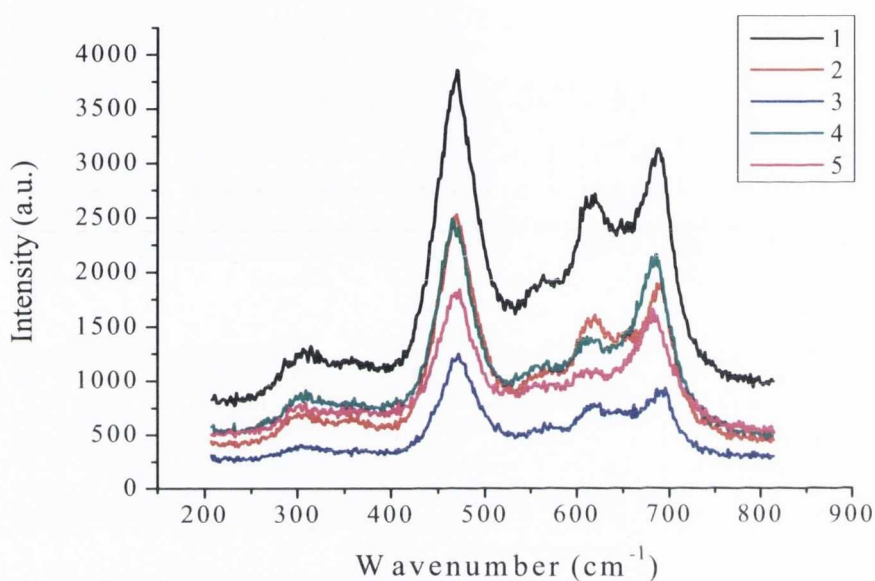


Figure 5.13: Raman spectra of PSSS-cobalt ferrite nanocomposites samples 1-5, prepared according to Table 5.1.

5.4.1.3 X-Ray Diffraction

XRD diffractograms were recorded for all dried powder samples and a typical diffraction pattern is shown in Figure 5.14. The reflection peaks can be readily indexed to the (220), (311), (400), (331), (422), (511) and (440) planes of spinel CoFe_2O_4 with a cubic symmetry.⁴⁴ The broad peak at 20-22 2θ corresponds to silica, from the gel used to hold the sample in place during measurement. The diffractograms were all found to be broad in nature, indicative of the nanocrystalline nature of the samples.

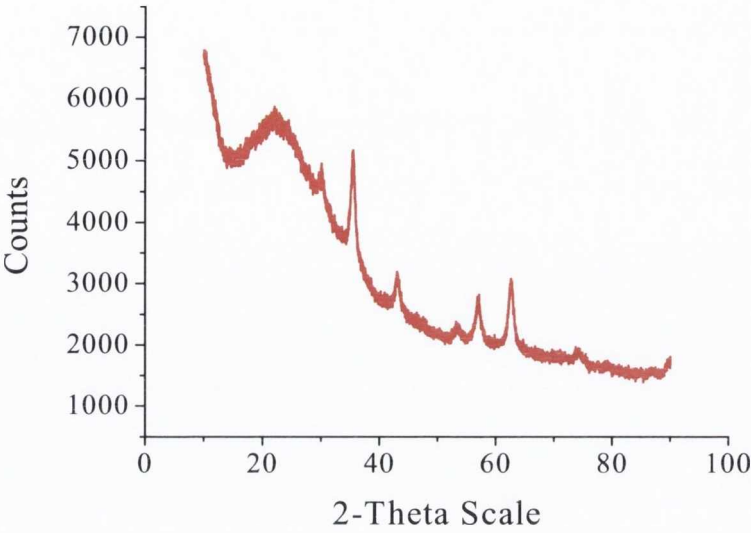


Figure 5.14: Typical XRD pattern for sample of PSSS-stabilised cobalt ferrite nanoparticles which corresponds with the JCPDS database for CoFe_2O_4 .

5.4.1.4 Magnetisation measurements

Magnetisation measurements were carried out on solid samples of the nanoparticles and a typical magnetisation curve is shown in Figure 5.15. The magnetisation curves showed the nanoparticles to be ferromagnetic in nature. The magnetic saturation of the samples were in the range $40\text{--}50\text{ Am}^2/\text{kg}$, which is somewhat lower than previously prepared cobalt ferrite nanoparticles ($57.6\text{ Am}^2/\text{kg}$) but is comparable with the magnetisation of typical biopolymer-magnetic nanocomposites ($40\text{--}50\text{ Am}^2/\text{kg}$).⁵¹

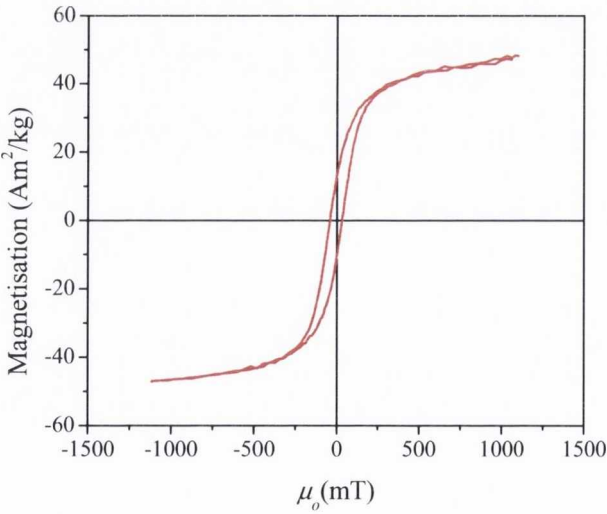


Figure 5.15: Typical magnetisation curve of sample of PSSS-stabilised cobalt ferrite nanoparticles.

5.4.1.5 NMRD Characterisation

The suspensions prepared demonstrated excellent stability and their dramatic response to an applied magnetic field led to a detailed investigation of their magnetic resonance characteristics. NMRD measurements were carried out on samples which demonstrated long-term stability, *i.e.* those that remained suspended and unchanged in water for several months. These NMRD profiles are shown in Figure 5.16. The spin-lattice relaxation enhancement per mM of iron, or relaxivity, r_1 , is given by Equation 1.

$$r_1 = (R_{1obs} - R_{1H_2O})/[Fe] \quad (1)$$

Where R_{1obs} is the measured relaxation rate of a suspension ($R_{1obs} = 1/T_{1obs}$, where T_{1obs} is the observed spin-lattice relaxation time) and R_{1H_2O} is the measured relaxation rate in the absence of any nanoparticles. The r_1 values are critical as they measure the contrast efficacy of the suspension for T_1 -weighted imaging applications. The NMRD profile displays r_1 over a wide range of magnetic fields, and hence ^1H Larmor frequencies. The r_1 dependence provides insight into the relaxation mechanisms of the stable suspension of the agent.⁵²

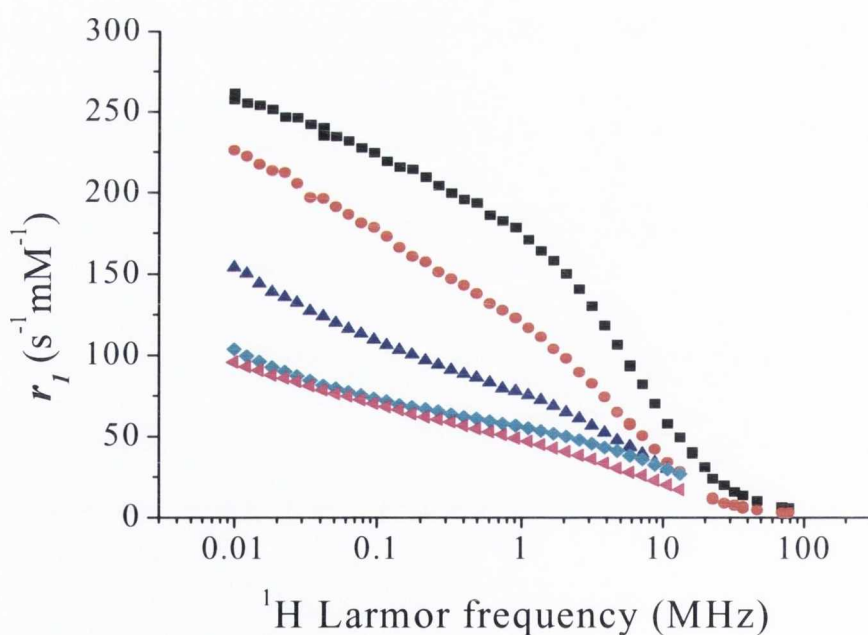


Figure 5.16: ^1H NMRD profiles for the stable CoFe_2O_4 suspensions: samples 1 (■), 2 (●), 3 (▲), 4 (◆) and 5 (◄), prepared according to Table 5.1. The relaxivities have been calculated in terms of the iron content of the samples (according to Equation 1).

The behaviour of all the suspensions in the high frequency range (≥ 10 MHz) is very similar, irrespective of the reaction conditions used or the physical properties of the resulting clusters. There is a significant decrease in the relaxivity at very high frequency (40–100 MHz), where the behaviour is predominantly outer sphere in nature.^{53,54} In this region, relaxation arises from diffusion of the solvent molecules in the environment of magnetic particles. The frequency dependence is therefore similar for dispersed nanoparticles and aggregates of any size.

In the low frequency range ($\nu_L \leq 1$ MHz), the shape of the relaxation profiles for all the suspensions changes significantly, indicating a change in the relaxation mechanism. In this frequency range, the relaxivity of all magnetic nanoparticle suspensions is determined by the rate of fluctuations of the magnetic moments. The principle mechanism governing the relaxation process is the movement of the nanoparticles in solution. This means that the relaxation time (T_1) is shorter at lower frequencies. This in turn gives rise to a higher relaxation rate at lower frequency (since $R_1 = 1/T_1$). This type of behaviour is noted for more clustered materials, where there are larger particles or aggregates. In the case of superparamagnetic materials, this is termed the Néel process, and a low frequency relaxivity plateau is usually observed, with $r_1 < 5 - 20 \text{ s}^{-1} \text{ mM}^{-1}$.⁵⁴

Previously, Corr *et al.* reported that the relaxation of PSSS-stabilised Fe_3O_4 suspensions could be tuned across the range from super- to non-superparamagnetic by varying the iron to polymer ratio.²¹ Their work showed that the reactant ratio strongly influenced the low frequency relaxivity. This ratio determined the number of nucleation sites during the co-precipitation reaction, and hence fixed the strength of the inter-particle interactions along the PSSS backbone. It was thought that similar effects would be seen for PSSS-stabilised cobalt ferrite magnetic nanoparticles due to their inherently greater magnetocrystalline anisotropy, which could lead to potentially greater relaxivity at low frequency, which was the case. The PSSS-stabilised cobalt ferrite suspensions showed non-superparamagnetic behaviour, irrespective of the reactant ratio. The reactant ratio offered some control over the primary nanoparticle size, but the nanoparticles grew in size to well above the superparamagnetic limit. It is well known that cobalt confers increased intrinsic magnetocrystalline anisotropy upon individual nanoparticles.⁵⁵ This would promote the loss of superparamagnetism, even for smaller nanoparticle sizes than we

obtained. The cobalt ferrite-PSSS suspensions were found to be ferromagnetic (Figure 5.15).

The relaxivity recorded for sample 1 ($r_1 = 257 \text{ s}^{-1}\text{mM}^{-1}$ at 0.01 MHz) is the highest we obtained in this study and is very similar to the highest reported values which have been obtained for iron-oxide stabilised with single-stranded herring DNA ($r_1 = 269 \text{ s}^{-1}\text{mM}^{-1}$ at 0.01 MHz).²² For all the cobalt ferrite suspensions, a reasonable inverse correlation is observed between r_1 and the average hydrodynamic size, d_{hyd} , (Figure 5.17). It has been shown that in the presence of a magnetic field, the nanoparticle assemblies form compact structures in suspension (Figure 5.11). It is thought that the relatively higher surface area to volume ratio of the smaller aggregates results in higher relaxivity, as more iron is accessible to the solvent molecules. Indeed, the suspensions with the highest relaxivities, samples 1 and 2, were found to form more compact ‘nanowires’ on drying in the presence of a magnetic field. Samples 3-5 had lower relaxivity values at 0.01 MHz. These samples showed greater hydrodynamic sizes and appeared as larger, less dense aggregates in TEM. The core nanoparticle size, according to TEM, does not appear to influence the relaxivity, see Table 5.1. This is surprising, since the magneto-crystalline anisotropy energy ΔE_{anis} is proportional to the volume of the nanoparticle.⁵⁴ It is likely that this effect is obscured by a range of other contributing factors.

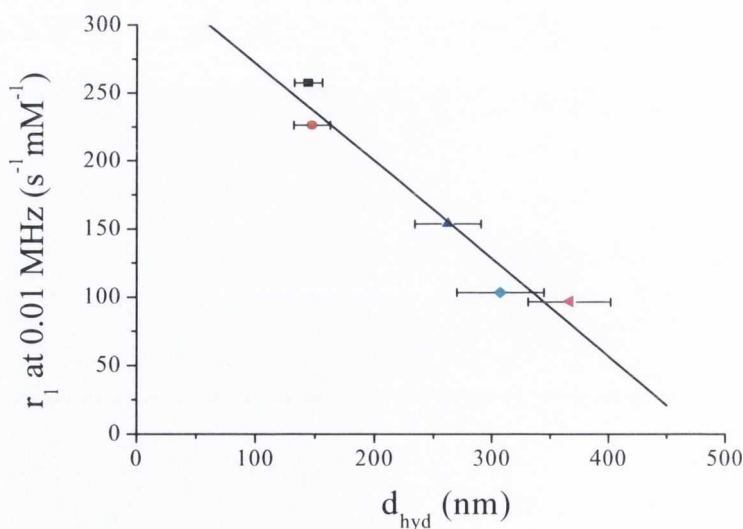


Figure 5.17: Low frequency relaxivity of the suspensions plotted as a function the hydrodynamic size as measured by PCS: samples 1 (■), 2 (●), 3 (▲), 4 (◆) and 5 (◄). The error bars represent one standard deviation in d_{hyd} . The straight line is a least squares fit to the data; $y = -0.72(9)x + 343(25)$, $R^2 = 0.95$.

In this study, we have defined the relaxivity of the suspensions in terms of the iron content only, following the normal convention. In fact, determination of the relaxivity per mM of total metal, including cobalt, does not provide any additional insight.

There is a generally accepted theory for the interpretation of the spin-lattice relaxation enhancement of superparamagnetic colloids,⁵⁴ which has been successfully applied to study their magnetic resonance properties.^{21,53,56} In the present case of suspensions of cobalt ferrite nanoparticles, the relaxation mechanism is not superparamagnetic which is expected, due to their inherently greater magnetocrystalline anisotropy. Currently there is no detailed theory explaining the low frequency behaviour of non-superparamagnetic systems. However, it is established that the presence of nanoscale order can significantly affect the ¹H relaxivity. These changes can arise from amplification of the contrast effect due to the presence of multiple relaxation centres, whether they are gadolinium ions⁵⁷ or magnetic nanoparticles.

5.5 Preparation and Characterisation of Manganese Ferrite Nanoparticles

Manganese ferrite nanoparticles were prepared similarly to cobalt ferrite using traditional co-precipitation techniques (Scheme 5.2).³⁹ Co-precipitation was carried out using ammonium hydroxide solution, which was added to a solution of iron (III) and manganese (II) which was subsequently reacted for 2 hours under reflux under argon at 100 °C using magnetic stirring. This yielded manganese ferrite nanoparticles which were present as a black precipitate which was strongly magnetic. The nanoparticles did not form stable aqueous suspensions. The particles were characterised using TEM, FTIR and Raman spectroscopy, XRD and magnetisation measurements.



Scheme 5.2: Reaction sequence showing the preparation of manganese ferrite nanoparticles using co-precipitation.

5.5.1 Characterisation of Manganese Ferrite Nanoparticles

5.5.1.1 TEM Characterisation

TEM demonstrated nanoparticles which were quasi-spherical in shape with a diameter of 11 ± 3 nm (Figure 5.18). The histogram in Figure 5.18(c) demonstrates that although the nanoparticles have a narrow size distribution, there is the presence of a small amount of larger, aggregated particles as well as a population of smaller ones. It should be noted that the nanoparticles were not stable in aqueous suspension.

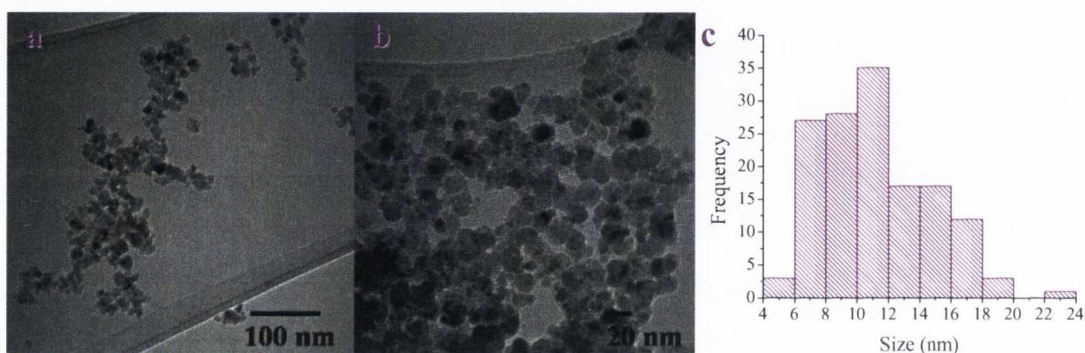


Figure 5.18: (a) and (b) TEM images and (c) histogram showing size and size distribution of manganese ferrite nanoparticles.

5.5.1.2 FTIR and Raman Spectroscopy

FTIR spectroscopy (Figure A3.2) revealed a peak at 570 cm^{-1} which represents Fe-O stretching. Literature shows absorption between 600 and 750 cm^{-1} can be assigned to Mn-O within the MnFe_2O_4 structure.^{58,59} In our results, this appears as a peak at 670 cm^{-1} . A broad peak from 3440 - 3460 cm^{-1} represents water and OH^- groups.

Raman spectroscopy of the dry powder of nanoparticles (Figure 5.19) shows the optically active Raman modes characteristic of the spinel structure of manganese ferrite.^{60,61} The highest frequency Raman mode at 618 cm^{-1} is assigned to the O-site mode, which reflects the local lattice effect in the octahedral sublattice, and the peak at 444 cm^{-1} is assigned to the T-site mode, which reflects the local lattice effect in the tetrahedral sublattice. The other peaks were found to be at 322 and a faint shoulder at 600 cm^{-1} . These values are all in good agreement with the 4 Raman active modes ($A_{1g} + E_g + 2T_{2g}$).⁶²

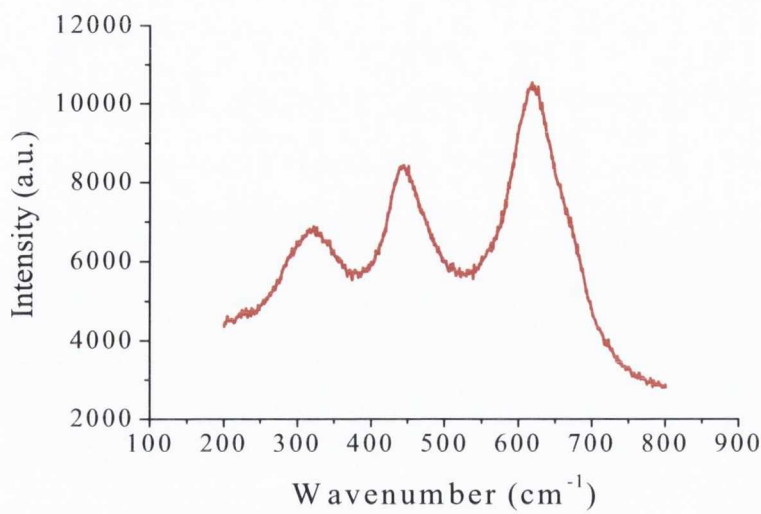


Figure 5.19: Raman spectrum of manganese ferrite nanoparticles prepared by co-precipitation.

5.5.1.3 X-Ray Diffraction

Overnight XRD diffraction patterns were collected for the dried powder sample (Figure 5.20). The reflection peaks can be readily indexed to the (220), (311), (400), (331), (422), (511) and (440) planes of spinel MnFe_2O_4 with a cubic symmetry with the space group $Fd3m$.^{63,64} The broad peak at 20-22 2θ corresponds to silica, from the gel used to hold the sample in place during measurement. The diffractogram peaks were broad in nature, indicating the nanocrystalline nature of the sample.

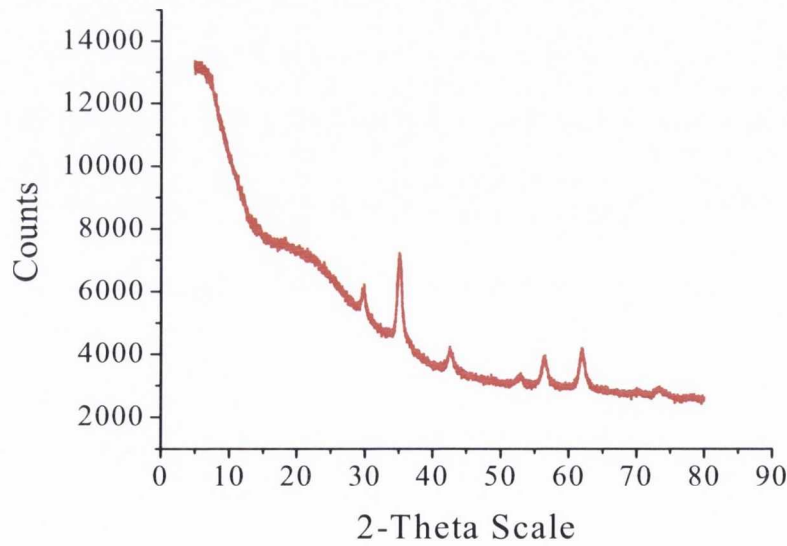


Figure 5.20: XRD pattern of manganese ferrite nanoparticle prepared by co-precipitation which corresponds with the JCPDS database for MnFe_2O_4 .

5.5.1.4 Magnetisation Measurements

Magnetisation measurements show that the nanoparticles prepared have a saturation magnetisation at 1 T of $60.1 \text{ Am}^2/\text{kg}$ (Figure 5.21). This is lower than the reported value for bulk manganese ferrite ($80 \text{ Am}^2/\text{kg}$).⁶⁵ However, the value obtained is typical of nanosized manganese ferrite of this size range, which is reported in the literature to be about $40\text{--}50 \text{ Am}^2/\text{kg}$ for sub-50 nm diameter particles.^{47,66} The absence of a hysteresis loop indicates the superparamagnetic nature of the particles.

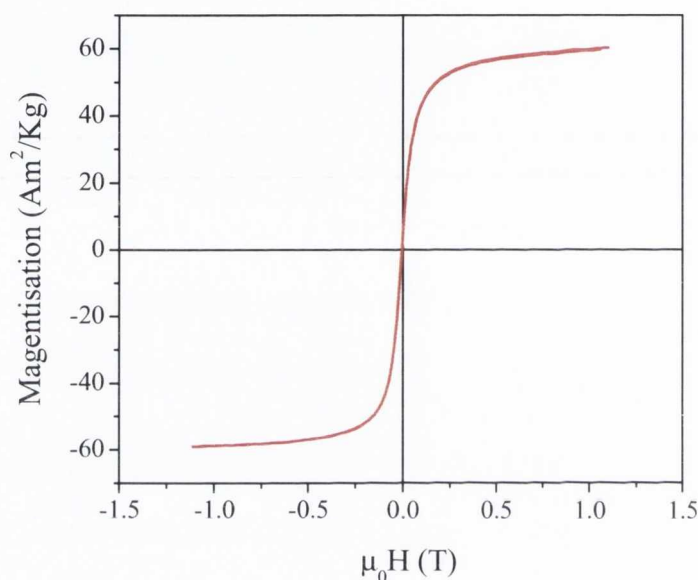


Figure 5.21: Magnetisation curve of manganese ferrite nanoparticles prepared using co-precipitation.

5.6 Preparation and Characterisation of Manganese Ferrite-Polyelectrolyte Nanocomposites

Manganese ferrite-polyelectrolyte nanocomposites were prepared similarly to cobalt ferrite analogues using traditional co-precipitation techniques (Scheme 5.2)³⁹ with the addition of PSSS polyelectrolyte as a stabiliser and assembly director. A series of nanocomposite suspensions were prepared. However, the only stable composite suspension which exhibited a response to a magnetic field was prepared using a ratio of metal to PSSS of 2083:1 (comparable to sample 3 prepared in Section 5.4).

The aqueous suspension of nanocomposites was characterised by TEM, PCS, NMRD and ICP-AES; the dried solid powder of the precipitate was characterised by Raman and FTIR spectroscopy and XRD and magnetisation measurements.

5.6.1 Characterisation of Manganese Ferrite-Polyelectrolyte Nanocomposites

5.6.1.1 TEM and PCS Characterisation

TEM and PCS measurements were carried out on the sample which demonstrated good stability in aqueous suspension, giving a diameter according to TEM (d_{TEM}) of 12 ± 4 nm. On drying a drop of the stable aqueous suspension onto a TEM grid in the absence of a magnetic field, the nanocomposites appeared as quasi-spherical particles which were well dispersed (Figure 5.22). Closer examination of the images once again reveals composites which appear as micelle-like structures made up of smaller nanoparticles held together by the PSSS polyelectrolyte (Figure 5.22b). Again, the absence of any long range structure for particles prepared for TEM in this way is an important factor in the behaviour of the suspension.

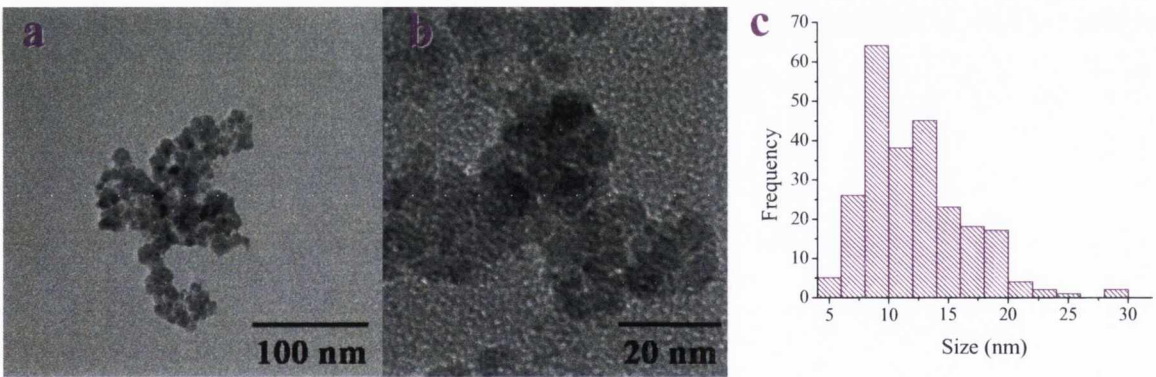


Figure 5.22: (a) and (b) TEM images of PSSS-manganese ferrite nanocomposite at different magnifications and (c) histogram showing the size distribution of the sample.

Upon drying a drop of the aqueous suspension onto a TEM grid in the presence of a permanent 0.5 T magnetic field, oriented in the plane of the grid, the composites aligned into 1-D linear arrays or ‘nanowires’ (Figure 5.23).

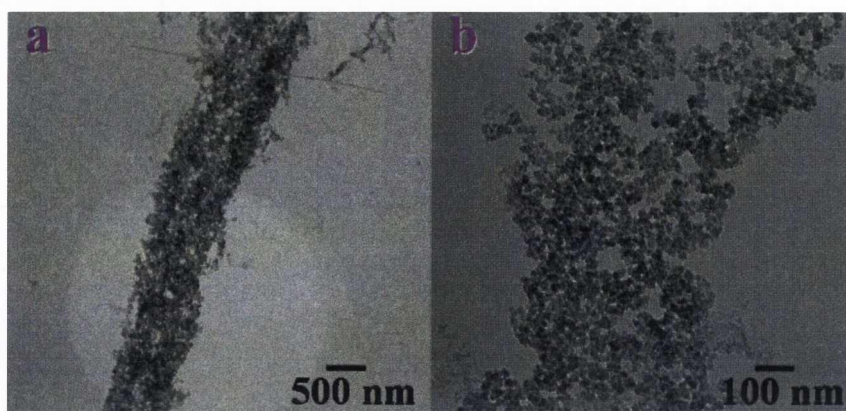


Figure 5.23: (a) and (b) TEM images of PSSS-manganese ferrite nanocomposite in the presence of a magnetic field at different magnifications.

The hydrodynamic radius (d_{hyd}) of the suspension, as measured by PCS was 145 nm. This value is significantly larger than the size as measured by TEM. Once again, this can be attributed to the assemblies of PSSS-stabilised composites having strong hydrogen bonding, dipolar and van der Waals interactions between the polyelectrolyte chains. The PDI value of 0.185 indicates excellent monodispersity and stability of the suspension. The nanocomposites remained stable with a low PDI after extended exposure to magnetic field strengths of up to 1.6 T, showing that magnetic reorganisation is reversible in suspension, as would be anticipated for superparamagnetic species.

5.6.1.2 FTIR and Raman Spectroscopy

FTIR spectroscopy (Figure A3.3) revealed a peak at 570 cm^{-1} which represents Fe-O stretching. A peak at 670 cm^{-1} can be assigned to Mn-O vibrations within the MnFe_2O_4 structure.^{58,59} The bands observed in the range $1008\text{--}1160\text{ cm}^{-1}$ originate from the symmetric and asymmetric C-H stretches of the polyelectrolyte. The peaks between 1500 and 2360 cm^{-1} represent the CH_2 , C-C and aromatic C-H bonds of the polyelectrolyte.⁵⁰ A broad peak from $3440\text{--}3460\text{ cm}^{-1}$ represents water and OH^- groups.

Raman spectroscopy of the dry powder of nanoparticles (Figure 5.24) shows the Raman active modes characteristic of the spinel structure of manganese ferrite.^{60,61} The peaks, found at 322 , 444 , 600 and 618 cm^{-1} are in good agreement with the 4 optically active modes ($A_{1g}+E_g+2T_{2g}$).⁶²

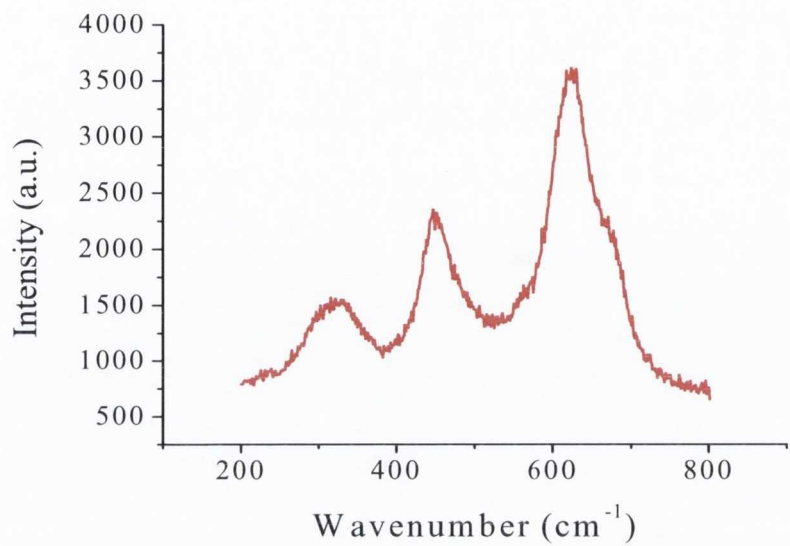


Figure 5.24: Raman spectrum of PSSS-manganese ferrite nanocomposite.

5.6.1.3 X-Ray Diffraction

Overnight XRD diffraction patterns were collected for the dried powder sample (Figure 5.25). The reflection peaks can be readily indexed to the (220), (311), (400), (331), (422), (511) and (440) planes of spinel MnFe_2O_4 with a cubic symmetry.^{63,64} The broad peak at 20-22 2θ corresponds to silica, from the gel used to hold the sample in place during measurement. The diffractogram peaks were broad in nature, indicating the nanocrystalline nature of the sample.

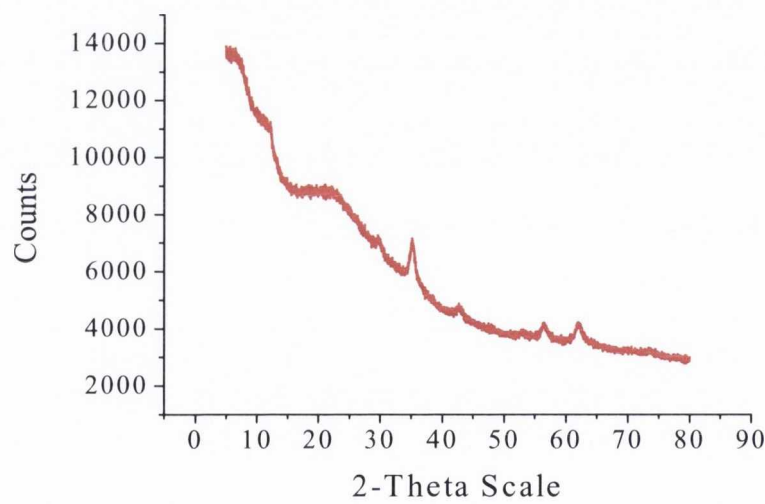


Figure 5.25: XRD pattern of PSSS-manganese ferrite nanocomposite which corresponds with the JCPDS database for MnFe_2O_4 .

5.6.1.4 Magnetisation Measurements

Magnetisation measurements were carried out on the solid powder of PSSS-manganese ferrite nanocomposite (Figure 5.26). The curve demonstrates the superparamagnetic nature of the particles, which have a saturation magnetisation value of $36.1 \text{ Am}^2/\text{kg}$, this is lower than the value for unstabilised manganese ferrite (Figure 5.21). Such a decrease can be expected due to the added weight contribution of the non-magnetic polyelectrolyte component.

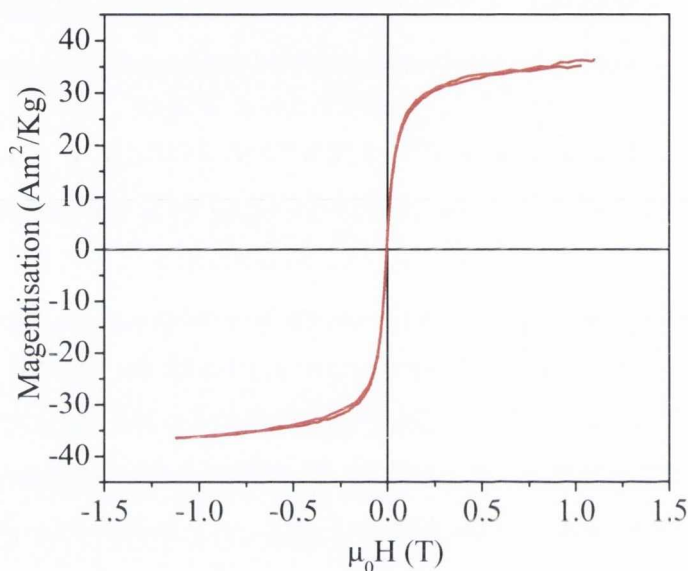


Figure 5.26: Magnetisation curve of PSSS-manganese ferrite nanocomposite.

5.6.1.5 NMRD Characterisation

The suspension prepared demonstrated excellent stability and the response of the nanocomposites to an external magnetic field made them appropriate for investigation by NMRD. The NMRD profile is shown in Figure 5.27, where the relaxivity, r_1 , is given by Equation 1. The behaviour of the suspension is different to the behaviour of the PSSS- CoFe_2O_4 composites presented in Section 5.4.1.5. The relaxation enhancement is significant and the profile exhibits an r_1 maximum of $37.8 \text{ s}^{-1}\text{mM}^{-1}$ in the range of 0.5–2 MHz. The low frequency plateau is at an elevated r_1 value ($24.7 \text{ s}^{-1}\text{mM}^{-1}$), higher than would be expected for purely superparamagnetic species ($<15 \text{ s}^{-1}\text{mM}^{-1}$). In fact, the profile of the composite differs from that reported for purely superparamagnetic samples and

similarly prepared PSSS-stabilised magnetite suspensions (Figure 5.28), where the r_I maxima are in the range 5-20 MHz.^{21,54}

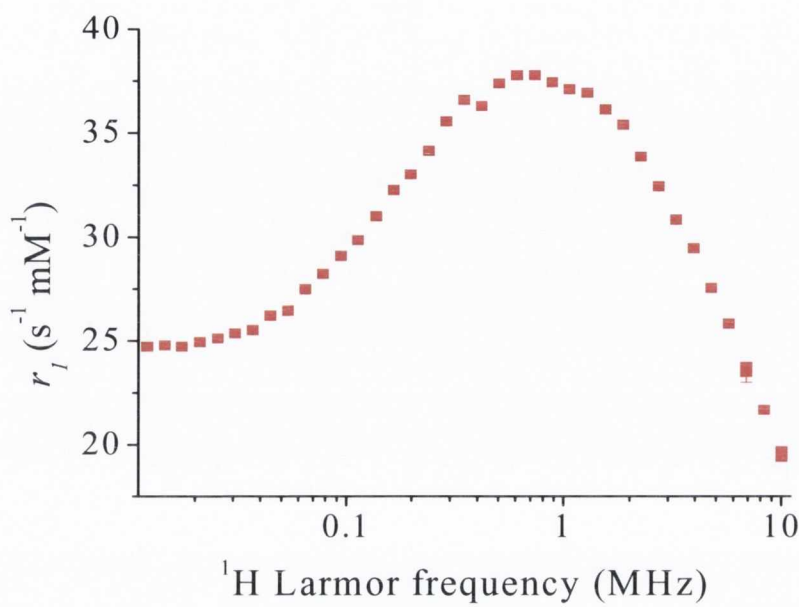


Figure 5.27: ^1H profile of the stable MnFe_2O_4 suspension. The relaxivity has been calculated in terms of the iron content of the sample (according to Equation 1).

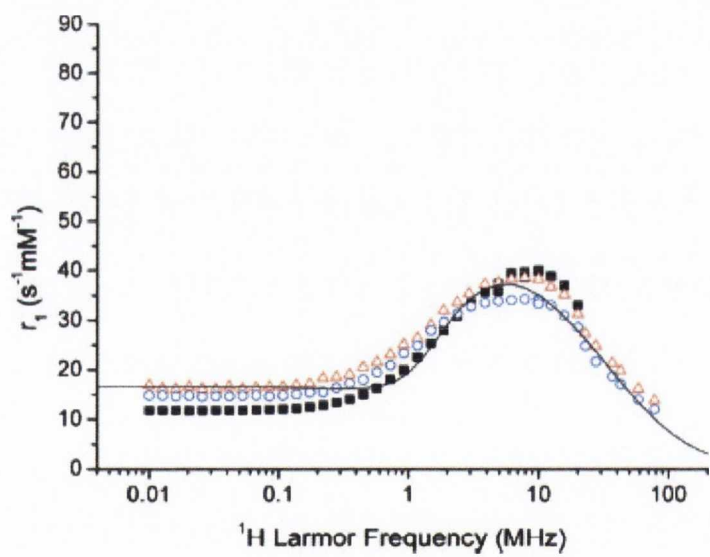


Figure 5.28: NMRD profiles for PSSS-magnetite nanoparticle suspensions with diameters of 6.5 ± 1 nm ($\blacksquare$), 7.0 ± 1.1 nm ($\circ$) and 7.1 ± 1 nm ($\triangle$), solid line represents a simulation for a superparamagnetic nanoparticle dispersion with $d_{\text{TEM}} = 12$ nm, $\Delta E_{\text{anis}} = 1$ GHz, and $M_s = 49$ Am²/kg.²¹

Lower frequency r_1 maxima have been observed for single stranded-DNA-stabilised Fe_3O_4 nanocomposites and 12 nm clusters of PSSS-stabilised Fe_3O_4 nanocomposites.^{21,67} This behaviour was attributed to the composites existing as a two-phase system, comprising ‘magnetically aggregated’ and ‘magnetically dispersed’ components. The presence of these two systems confers a larger local magnetic moment when compared to purely superparamagnetic materials; this presents improved magnetic ordering and higher relaxivity. The increased low field relaxivity seen in our sample is consistent with this theory and can be said to arise from the increased magnetic anisotropy energy from the inclusion of manganese ions in the spinel iron oxide lattice and the presence of more clustered materials, where there are larger particles or aggregates. Despite this, the NMRD data conforms acceptably to the theory developed by Muller and co-workers for relaxation by superparamagnetic nanoparticles.⁵⁴ The theory is strictly applicable to suspensions of monodisperse, sub-20 nm, particles.

5.7 Conclusions

We have demonstrated an efficient method for preparing magnetic fluids of a range of spinel ferrite nanoparticles stabilised by polyelectrolytes using an *in situ* co-precipitation technique. The advantage of this method is that it is a quick, inexpensive one-step procedure in which parameters can be varied to produce magnetic fluids with tuneable relaxivities. These nanocomposite materials align into 1-dimensional linear arrays in the presence of a magnetic field – a phenomenon which is reversible in suspension. The nanocomposites demonstrate remarkably high relaxivity values at low field, indeed the highest obtained in the cobalt ferrite-PSSS study ($257 \text{ s}^{-1}\text{mM}^{-1}$ at 0.01 MHz) is comparable with previously reported DNA-stabilised iron oxide nanoparticles.²² It was found that the spin-lattice relaxivity of PSSS- CoFe_2O_4 samples showed an inverse correlation with their hydrodynamic radii, indicative of the larger surface area to volume ratio of the smaller composites allowing the iron molecules greater access to the surrounding water.⁶⁸ PSSS- MnFe_2O_4 nanocomposites demonstrate superparamagnetic behaviour, with an r_1 maximum of $37.8 \text{ s}^{-1}\text{mM}^{-1}$ in the range of 0.5-2 MHz. These values are comparable with PSSS- Fe_3O_4 nanocomposites of similar sizes and they demonstrate an elevated low frequency plateau indicative of a two-phase magnetic system in suspension.

Our study provides insights into the interaction of diffusing H₂O molecules with the surface layers of the magnetic nanocomposites, information which will be relevant to the design of the next generation of magnetic fluids. In addition, such materials may find direct application as contrast agents, particularly in ultra low-field applications in medicine, such as ultra low-field magnetic resonance imaging (ULF-MRI).^{19,69} Low field technologies have the advantages of reduced equipment costs and improved portability.⁷⁰ A further advantage arises from the very large natural variation in low frequency contrast between different tissue types, which may provide new imaging modalities, such as simultaneous structural (ULF-MRI) and functional (magnetoencephalography) imaging.⁷¹ Our work suggests that high contrast nanoparticulate agents that operate in the microtesla field range may have a lower limit of detection due to their high relaxivity at low frequency, a feature that is critical for molecular imaging.⁷² This potential has been a driving force for the development of nanoparticle technologies which can compete with molecular imaging agents.

When compared to some of the commercially available iron oxide contrast agents, it is found that most of our magnetic fluids have a higher relaxivity at 20 MHz (Table 5.2). Therefore, these new magnetic fluids could have some very important applications in clinical MRI. Future work will include the *in vivo* testing of these fluids.

Table 5.2: Relaxivity values, r_1 , at 20 MHz for commercially available MRI contrast agents compared to our polyelectrolyte stabilised nanocomposites.

Magnetic fluid	r_1 at 20 MHz
Gd-DTPA	4.5
Ferumoxil	3.2
Ferumoxtran	22.7
Ferumoxide	23.7
PSSS-CoFe ₂ O ₄ (sample 1)	31.1
PSSS-MnFe ₂ O ₄	19.4

Further research is required in the development of synthetic strategies which can fine-tune the control of the relaxivity of the suspensions, as well as elucidate the

mechanism of relaxation of these composites at these low frequencies. We anticipate that this ongoing work will provide further physical insight into the relaxation mechanisms and frequency dependencies of r_l . We believe this work could stimulate further investigations into ferrite nanomaterials for their application as contrast agents in low field MRI technologies.

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Chapter 6

Multimodal Magnetic Core-Shell Nanostructures

6.1 Introduction

Nanomaterials with multiple modalities including magnetism, specific UV-vis absorption and photoluminescence properties and appropriate surface functionalities for biomolecular conjugation have become increasingly attractive in recent years due to their versatility and their wide range of potential applications.^{1,2} By tuning the nature of the core, shell and ligand of a particulate system, its biocompatibility, biofunctionality and behaviour can be carefully controlled and nanocomposites can be synthesised for a wide range of applications in diagnostics and therapeutics.³ In particular, magnetic-luminescent nanomaterials present great interest in biomedicine, especially in the emerging field of nanomedicine, where biosensing, biological separation, molecular imaging and anticancer therapy are being explored.^{1,4}

Magnetic nanoparticles have been utilised as efficient diagnostic tools as MRI contrast agents,⁵ as mediators for hyperthermic cancer treatments⁶ and as drug delivery vehicles.^{4,7} For all of these applications, the unique response of the nanoparticles to a magnetic field allows them to be manipulated and targeted to carry out particular tasks. In addition, fluorescence is a sought-after property in materials for biomedical applications, as it allows materials to be tracked and visualised within the body. Currently, semiconductor quantum dots (QDs) are heavily researched, thanks to their tuneable emission characteristics and small sizes. They have shown promise in *in vitro* and *in vivo* studies, where they can be used to target tumour cells and as probes for bioimaging.^{8,9} However, toxicity issues have yet to be fully resolved. Organic dyes offer strong luminescence intensities and good water solubility and have proven useful in bio-imaging.¹⁰⁻¹²

Coating of magnetic nanomaterials can be beneficial for several reasons. Firstly, coating can improve colloidal stability and provide useful surface functionalities. Additionally, nanoparticle coating is extremely important for the synthesis of multimodal nanocomposites in order to address the challenge of preventing quenching of a luminescent moiety by a magnetic core. Silica as a coating material presents an excellent opportunity to

solve these problems using core-shell designs. Using silica as a coating material has proven popular, with examples including colloidal systems such as nanoscale metals, QDs, magnetic or ceramic nanoparticles and polymers. This is due to its high stability (particularly in aqueous solutions), ease of coating procedure allowing variation of shell thicknesses, its chemical inertness, strength, optical transparency, porosity and its processability, allowing further interesting surface modification.¹³ Methods of coating nanomaterials with silica include the classical aqueous Stöber method,¹⁴ reverse micelle reaction,¹⁵ polymer and surfactant mediated coating,¹⁶ or assembly of silica colloids on nano- and micro- particles by layer-by-layer (LbL) deposition.¹⁷

The magnetic stimulus responsive behaviour of magnetic nanoparticles makes them ideal candidates as building blocks for the preparation of 1-, 2- and 3-dimensional nano- and microstructures. It has been shown that linear magnetic structures have the potential to outperform nanoparticles in biomedical tasks thanks to their larger aspect ratio.¹⁸ The successful assembly of magnetic nanoparticles into well-defined nanostructures not only depends on the ability to control precisely their composition, shape and size, but also on the modification of the magnetic particle surface with the desired functionality that mediates interactions that allow assembly and maintain stability. To date, the main approaches for preparing magnetic nanoparticle composite assemblies have included use of a polymeric template to direct the formation of 1, 2, and 3-dimensional structures; and the formation of magnetic nanoparticles followed by assembly using polymers.¹⁹

The utilisation of an external magnetic field to assist with assembly of magnetic nanoparticles is an interesting concept which could lead to a simple method of preparing more complex 1-dimensional structures. Indeed, Ni nanowires prepared by hydrothermal synthesis can be aligned, in the presence of stabilisers, using an external magnetic field during synthesis.²⁰ FeS₂ prepared in the presence of a magnetic field have yielded microparticle assemblies.²¹ In addition, an *in situ* magnetic field during the preparation of Co nanocrystals can form necklace-like chains several microns in length.²² Post-preparation, a magnetic field can often be used to align magnetic nanoparticles (such as Fe₃O₄) into linear wire-like arrays.²³ For example, Sheparovych and co-workers formed magnetic nanowires by assembly of nanoparticles *via* controlled evaporation of colloidal suspensions in the presence of a magnetic field (Figure 6.1).²⁴ These wires were formed

using superparamagnetic nanoparticles in the presence of a polyelectrolyte, leading to permanently linked magnetic nanowires which were flexible and demonstrated a response to a magnetic field.

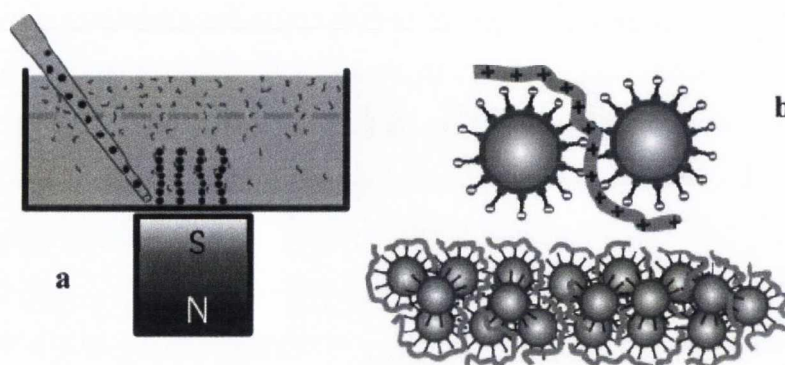


Figure 6.1: (a) Preparation of magnetic nanowires and (b) schematic representation of the structure of magnetic nanowires stabilised with a polyelectrolyte.²⁴

Finally, new interesting hollow multifunctional nanostructured materials have been recently envisaged as very promising drug delivery agents.⁷ Recently, Liu *et al.* have synthesised ‘yolk-shell’ composites consisting of various cores (including silica nanoparticles and magnetite nanoparticles) with mesoporous silica shells which possess a hollow space in which they have encapsulated ibuprofen and monitored its release (Figure 6.2).²⁵ These composites were prepared using a core-vesicle templating method followed by annealing to ‘shrink’ the core layer and develop porosity. The preparation of similar structures with different core materials and with the additional functionality of fluorescence could enhance their potential applications, allowing them to be monitored in cells.

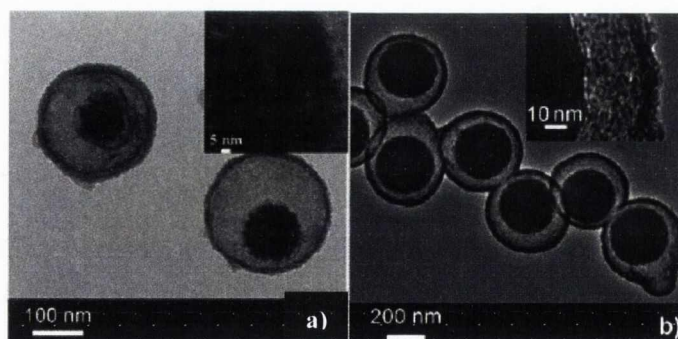


Figure 6.2: TEM images of (a) hollow silica shells with magnetite nanoparticle core and (b) hollow silica shells with silica nanoparticle core prepared using vesicle templating method.²⁵

6.2 Aims

The main aim of this part of the work is to develop new magnetic core-shell nanostructures with a range of potential applications. To produce these, we plan to use a sol-gel approach under different conditions to provide nanomaterials with variable shell thicknesses. We intend to use selected oxide materials (e.g. silica, titania) to form shells which can be further modified with materials to increase their functionality.

In addition, we plan to prepare functionalised nanomaterials with different aspect ratios, including linear arrays and nanowires. These nanoarrays may be useful in biomedicine, as 1-dimensional structures have shown benefits over traditional nanoparticles in biological sensing and flow cytometry.¹⁸ Another aim of this part of our work is to prepare and investigate bi-functional nanomaterials which have both magnetic and fluorescent components.

It is expected that these new multimodal magnetic nanomaterials will find a variety of applications, as they can be readily coated with different materials such as drug molecules and luminescent moieties. In addition, they can be manipulated by an external magnetic field.

6.3 Silica Coated Magnetic Materials

Magnetic materials based on iron oxides have been coated using a modified Stöber method.¹⁴ This method was chosen due to its simple two-step procedure which yields nanoparticles with a silica shell of controllable size. In addition, its aqueous environment throughout ensures biocompatibility.

6.3.1 Preparation of Silica Coated Magnetite

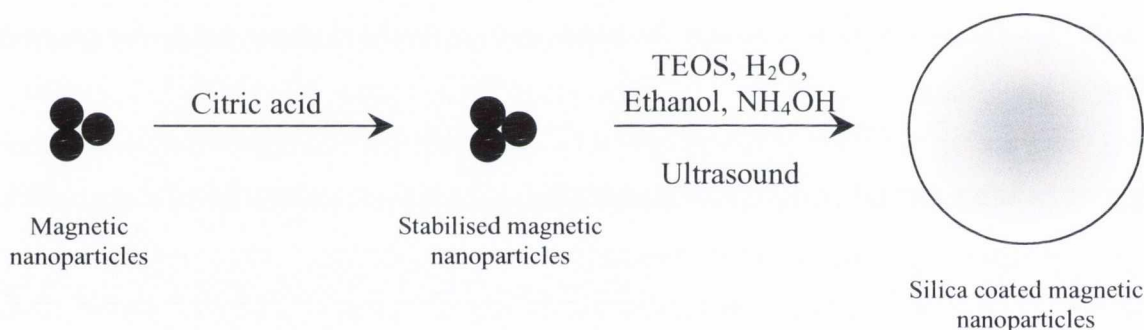
Superparamagnetic magnetite nanoparticles were prepared using a traditional aqueous co-precipitation method (Scheme 6.1). Co-precipitation of an aqueous solution of iron (II) and iron (III) chlorides was carried out using sodium hydroxide and subsequently reacted for 1 hour at 40-50 °C using magnetic stirring. This yielded magnetite (Fe_3O_4) nanoparticles which were present as a strongly magnetic black precipitate. The purity of the magnetite nanoparticles is governed by the ratio of $\text{Fe}^{2+}:\text{Fe}^{3+}$, which must be kept at 1:2

under strict non-oxidising conditions until the addition of the base. Impurities of maghemite can appear in the product if this is not the case.



Scheme 6.1: Reaction sequence showing the preparation of magnetite nanoparticles using co-precipitation.

Magnetite nanoparticles were coated with silica using a modified Stöber sol-gel technique which involves the hydrolysis and condensation of tetraethylorthosilicate (TEOS) onto the surface of the magnetite nanoparticles (Scheme 6.2).¹⁴ The silica shell thickness can be varied by altering the concentration of the silica source, see experimental section for more details. The thickness of the silica shell can affect the magnetic properties of the nanoparticles due to its non-magnetic nature, causing a reduction in saturation magnetisation.



Scheme 6.2: Representation of preparative procedure used to coat magnetic nanoparticles with a silica shell.

6.3.2 Characterisation of Magnetite-Based Nanoparticles

The nanoparticles were characterised using Transmission Electron Microscopy (TEM), Photon Correlation Spectroscopy (PCS), Fourier Transform Infrared (FTIR) and Raman spectroscopy, X-Ray Diffraction (XRD) and magnetisation measurements.

6.3.2.1 TEM and PCS Measurements

Silica coated magnetite nanoparticles with silica shells of different thickness were prepared according to Table 6.1. TEM and PCS allowed the determination of nanoparticle sizes and the thickness of the silica shell. PCS of magnetite nanoparticles showed the

particles to be unstable in the absence a stabiliser. TEM images show that the silica coated particles can contain multiple inclusions of magnetite nanoparticles (several core particles) (Figure 6.3). Histograms in Figure 6.4 show the size distribution of the particles prepared.

The average diameter according to PCS is greater than that calculated using TEM in all cases, which is expected due to hydrodynamic interactions between particles in water suspensions. Zeta potential measurements confirm the formation of suspensions of nanoparticles with negative surface charges.

Table 6.1: Characteristics of magnetite and silica coated magnetite with different shell thicknesses.

Sample	[TEOS] (mM)	d _{TEM} ^[a] (nm)	d _{hyd} ^[b] (nm) [PDI]	Zeta Potential (mV)	Magnetisation Saturation at 293 K (Am ² /kg)
Magnetite	0	9 ± 2	---	---	41.12
1	4.03	53 ± 11	238; 57 [0.398]	-36 ± 6	16.01
2	7.78	107 ± 17	145 [0.038]	-41.5 ± 17	12.92
3	15.55	123 ± 16	344 [0.064]	-46.1 ± 18	9.96

[a] d_{TEM} refers to the average diameter of particles calculated from >100 particles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions index.

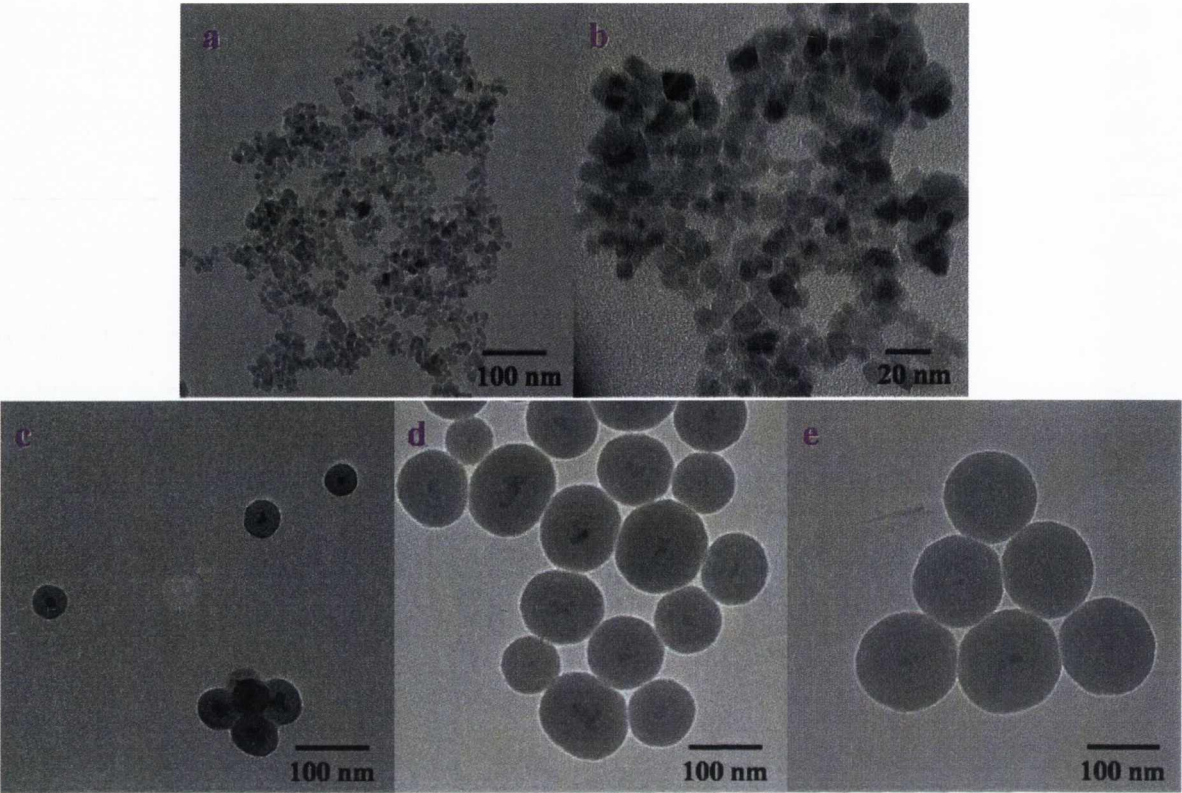


Figure 6.3: TEM images (a) and (b) magnetite nanoparticles, (c) sample 1, (d) sample 2 and (e) sample 3, prepared according to Table 6.1.

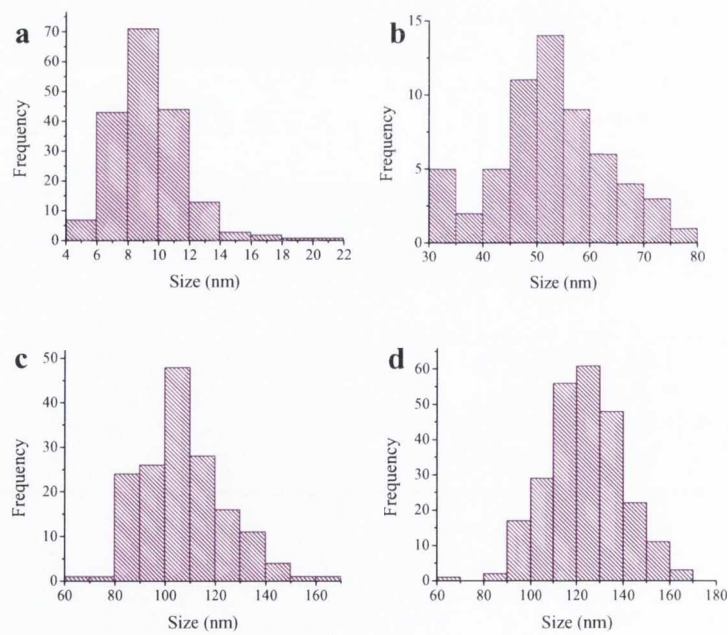


Figure 6.4: Histograms showing size distribution of (a) magnetite nanoparticles; (b) sample 1; (c) sample 2 and (d) sample 3, prepared according to Table 6.1.

6.3.2.2 FTIR and Raman Spectroscopy

FTIR spectroscopy of the prepared nanoparticles displays peaks at 570-580 cm^{-1} which represent Fe-O stretches (*Figure A4.1, Appendix 4*). Spectra of silica coated nanocomposites confirms the presence of a silica shell on all samples, displaying stretches at 1100 cm^{-1} , which are assigned to asymmetric Si-O-Si stretching vibrations. For all samples, the presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at 1629 cm^{-1} . A broad stretching vibration centred at 3440-3460 cm^{-1} represents contributions from both symmetrical (ν_1) and asymmetrical (ν_3) modes of the O-H bonds which are attached to the surface iron atoms.

Raman spectra recorded for all composites (*Figure A4.2*) display peaks at 670 and 190 cm^{-1} , which are representative of the A_{1g} and T_{2g} modes of magnetite respectively; broad peaks centred at 340 and 500 cm^{-1} can represent E_g and T_{2g} modes of magnetite. These appear with relatively high intensities due to an overlap with T_1 and E modes of maghemite impurities in the sample.²⁶⁻²⁸ The presence of maghemite in the samples is likely to be due to oxidation of the sample during measurement due to heating from the high intensity of the laser. The emerging peak at 945 cm^{-1} observed in samples 1, 2 and 3 can be assigned to Si-OH stretching vibrations.^{29,30} The peak at 750 cm^{-1} represents the bending vibrations of silicon and oxygen in the Si-O-Si bond.³¹

6.3.2.3 X-Ray Diffraction

An XRD pattern was recorded of magnetite nanoparticles (*Figure 6.5*). The pattern corresponds well to the JCPDS database for magnetite in the cubic phase. The average particle size has been calculated from the peak width at half maximum of the most intense peak at 35.5 degrees 2θ , using the Debye-Scherrer equation.³² The average particle size was found to be 10.57 nm. This is in agreement with average diameter calculations based on TEM imaging. The peaks at 12.2 and 74 degrees 2θ appear due to the lamp present in the XRD machine. The peak at 23 degrees 2θ is due to the silica gel used to adhere the sample to the glass holder.

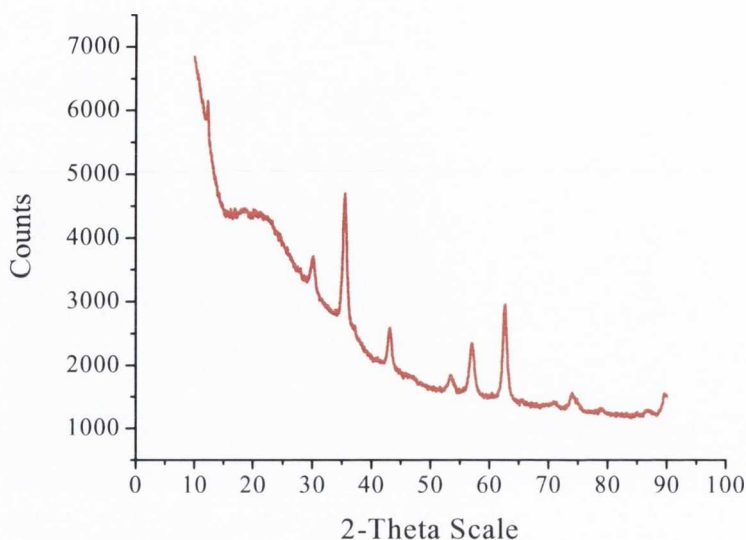


Figure 6.5: XRD pattern for magnetite nanoparticles synthesised by co-precipitation, which corresponds with the JCPDS database for Fe_3O_4 .

6.3.2.4 Magnetisation Measurements

Magnetisation measurements were carried out on all of the samples to determine the extent of reduction in saturation magnetisation by the presence of a silica shell with varying thickness (Figure 6.6). All samples demonstrate typical superparamagnetic characteristics as expected. Magnetite nanoparticles show a saturation magnetisation value at room temperature (M_s) of $41.1 \text{ Am}^2/\text{kg}$. This is considerably less than that reported for bulk magnetite ($M_s = 92 \text{ Am}^2/\text{kg}$), however, the value obtained is comparable to reported values for magnetite prepared in this manner ($M_s = 40 - 50 \text{ Am}^2/\text{kg}$).³³⁻³⁵ As expected, the increased thickness of the silica shell caused a decrease in the saturation magnetisation, as silica is a non-magnetic material.

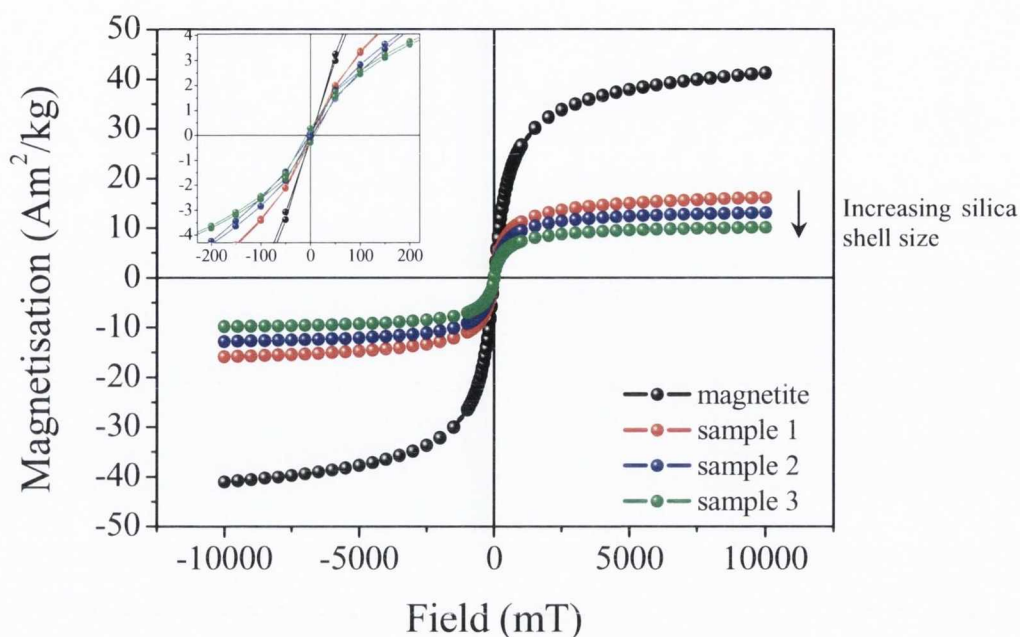


Figure 6.6: Magnetisation curves of samples of magnetite and silica coated magnetite nanoparticles at 293 K; inset shows absence of hysteresis, demonstrating superparamagnetism. Samples prepared according to Table 6.1.

6.3.3 Preparation of Silica Coated Ferrites

Cobalt ferrite (CoFe_2O_4) and manganese ferrite (MnFe_2O_4) nanoparticles were prepared using a co-precipitation technique which is described in Chapter 5. This method is similar to the preparation of magnetite nanoparticles, where an aqueous solution of metal salts prepared in a de-oxygenated system are precipitated using a base, see experimental section for more details. The ferrite nanoparticles were then coated with silica shells using the same technique as previously discussed, which is represented in Scheme 6.2.

6.3.4 Characterisation of Ferrite-Based Nanoparticles

The nanoparticles were characterised using TEM, PCS, FTIR and Raman spectroscopy, XRD and magnetisation measurements.

6.3.4.1 TEM and PCS Measurements

Silica coated cobalt ferrite and manganese ferrite nanoparticles were prepared according to Table 6.2. TEM and PCS confirm the sizes of the particles prepared and allow

determination of the thickness of the silica shell. PCS measurements of the uncoated ferrite nanoparticles showed the particles to be unstable in the absence of a stabiliser. TEM images show silica coated particles can contain multiple magnetic particle cores (Figures 6.7 and 6.9). Histograms in Figures 6.8 and 6.10 show the size distribution of the particles prepared. As expected, the average hydrodynamic diameter according to PCS is greater than that calculated using TEM in all cases. Zeta potential measurements confirm the nanoparticle suspensions have negative surface charges.

Table 6.2: Characteristics of ferrite and silica coated ferrite nanoparticles with different shell thicknesses.

Sample	[TEOS] (mM)	d _{TEM} ^[a] (nm)	d _{hyd} ^[b] (nm) (PDI)	Zeta Potential (mV)	Magnetisation Saturation at 293 K (Am ² /kg)
Cobalt ferrite	0	12 ± 4	---	---	57.57
4	2.24	46 ± 11	178 [0.310]	-42.8 ± 7	9.32
5	4.03	59 ± 15	164 [0.291]	-45.3 ± 6	9.16
Manganese ferrite	0	11 ± 3	---	---	60.11
6	4.03	51 ± 11	375 [0.237]	-34.4 ± 13	10.68

[a] d_{TEM} refers to the average diameter of particles calculated from >100 particles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions index.

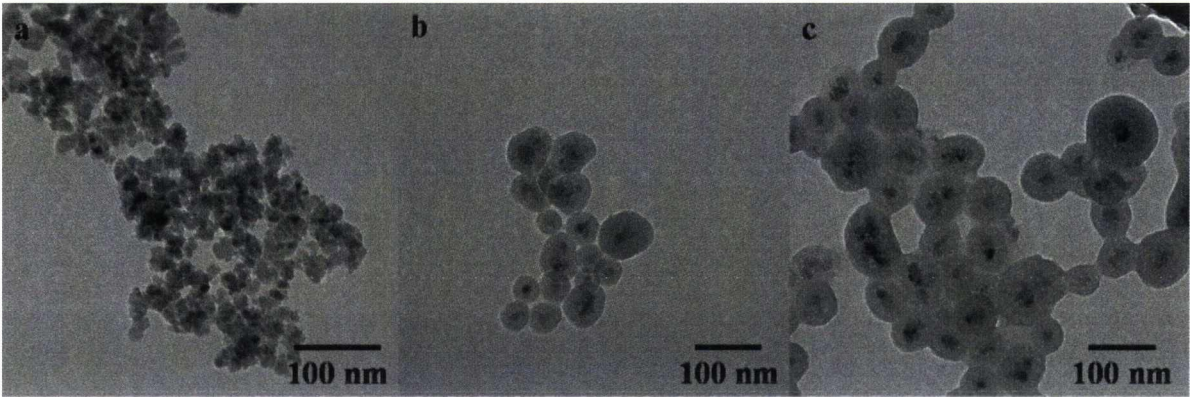


Figure 6.7: TEM images of (a) cobalt ferrite nanoparticles; (b) sample 4 and (c) sample 5, prepared according to Table 6.2.

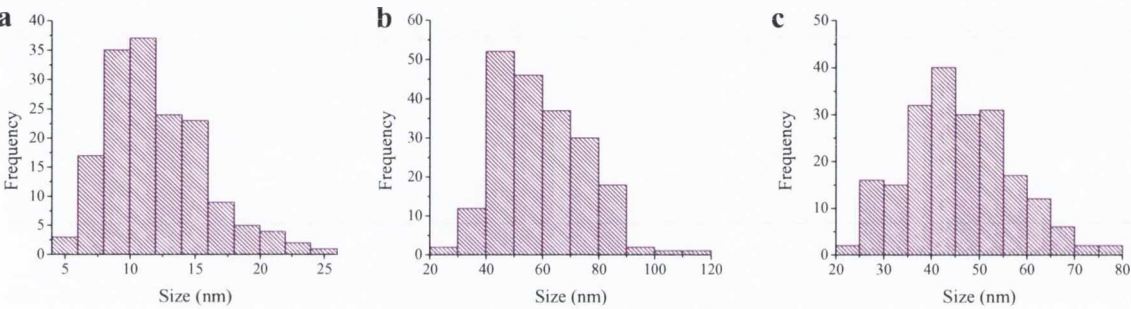


Figure 6.8: Histograms showing size distribution of (a) cobalt ferrite; (b) sample 4 and (c) sample 5, prepared according to Table 6.2.

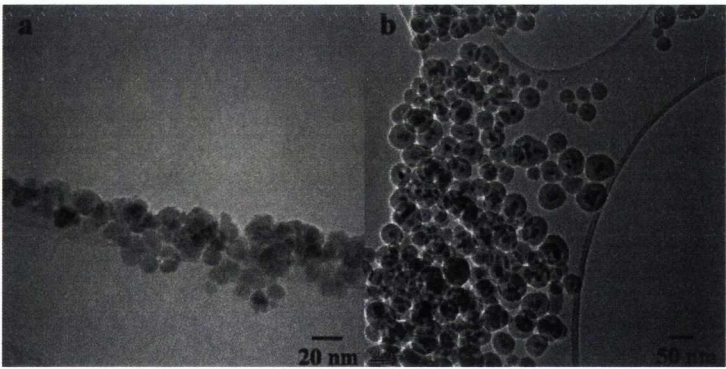


Figure 6.9: TEM images of (a) manganese ferrite nanoparticles and (b) sample 6, prepared according to Table 6.2.

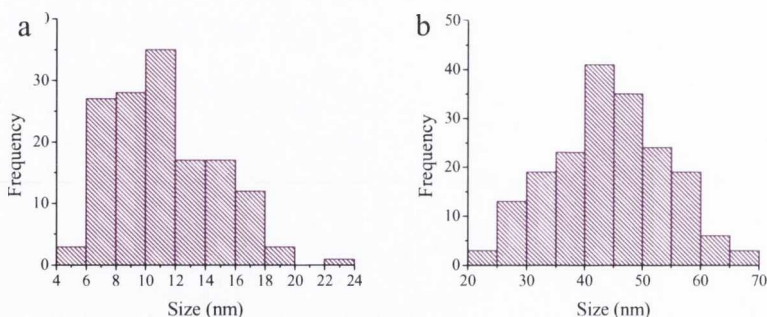


Figure 6.10: Histograms showing size distribution of (a) manganese ferrite nanoparticles and (b) sample 6, prepared according to Table 6.2.

6.3.4.2 FTIR and Raman Spectroscopy

FTIR spectroscopy of the cobalt ferrite and manganese ferrite particles (*Figures A4.3 and A4.4* respectively) displayed stretches at $570\text{--}580\text{ cm}^{-1}$ which represent Fe-O. In the cobalt ferrite spectrum, a shoulder at $\sim 670\text{ cm}^{-1}$ on this peak can be assigned to the stretching vibrational mode of Co-O.³⁶ For manganese ferrite, a peak at 670 cm^{-1} represents Mn-O stretching vibrations.³⁷ FTIR spectra of silica coated magnetic nanocomposites confirms the presence of the silica shell on all samples, displaying stretches at 1100 cm^{-1} , which are assigned to asymmetric Si-O-Si stretching vibrations. For all samples, the presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at 1629 cm^{-1} . A broad stretching vibration centred at $3440\text{--}3460\text{ cm}^{-1}$ represents contributions from both symmetrical (ν_1) and asymmetrical (ν_3) modes of the O-H bonds which are attached to the surface iron atoms.

Raman spectroscopy of the particles shows the optically active modes as expected for the cubic spinel structures of both cobalt ferrite and manganese ferrite based samples (*Figures A4.5 and A4.6*). For the cobalt ferrite samples, the highest frequency Raman mode is at 680 cm^{-1} , which can be assigned to the T-site mode, which reflects the local lattice effect in the tetrahedral sublattice. The peak at 465 cm^{-1} represents the O-site mode, which reflects the local lattice effect in the octahedral sublattice. The values are all in good agreement with the 5 optically active modes ($A_{1g} + E_g + 3F_{2g}$) characteristic of the cubic inverse spinel structure of cobalt ferrite.³⁸ For manganese ferrite, the highest frequency mode at 618 cm^{-1} is assigned to the O-site mode while the peak at 444 cm^{-1} represents the T-site mode. All peaks were in good agreement with the 4 active Raman modes ($A_{1g} + E_g$

+ $2T_{2g}$).²⁷ For all silica-coated samples, the emerging peak at 750 cm^{-1} represents the bending vibrations of silicon and oxygen in the Si-O-Si bond.³¹

6.3.4.3 X-Ray Diffraction

XRD patterns of the samples of magnetic nanoparticles were recorded and compared with the JCPDS database (Figure 6.11). The patterns corresponded well to the JCPDS database for cobalt ferrite and manganese ferrite in the cubic phase. The average particle size has been calculated accordingly from the peak width at half maximum of the peak at 35.5° 2θ , using the Debye-Scherrer equation.³² The average particle size for cobalt ferrite nanoparticles was found to be 10.14 nm . The average particle size for manganese ferrite nanoparticles was found to be 11.78 nm . These values are in agreement with average diameter calculations based on TEM imaging (Table 6.2). The peaks at 12.2° and 74° 2θ appear due to the lamp present in the XRD machine. The peak at 20° 2θ is due to the silica gel used to adhere the sample to the glass holder.

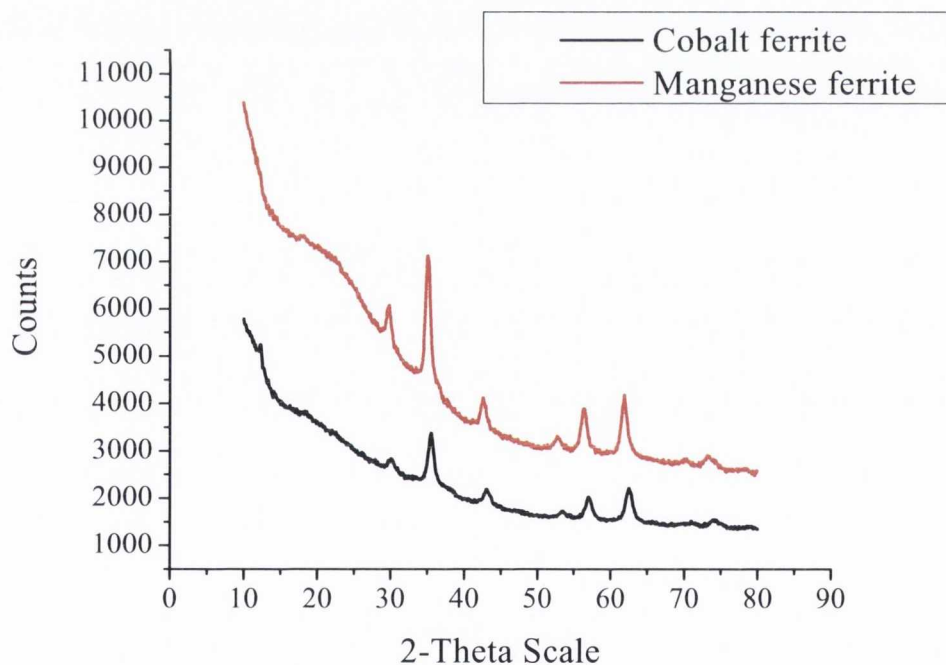


Figure 6.11: XRD patterns for cobalt ferrite (black) and manganese ferrite (red) nanoparticles prepared by co-precipitation, which correspond to the JCPDS database for CoFe_2O_4 and MnFe_2O_4 respectively.

6.3.4.4 Magnetisation Measurements

Magnetisation measurements were carried out on all of the samples to determine the extent of reduction in saturation magnetisation by the addition of a silica shell of varying thicknesses to magnetic nanoparticles. Cobalt ferrite based samples were found to be superparamagnetic in nature, with almost immeasurable remanence and coercivity (Figure 6.12). Cobalt ferrite nanoparticles show a saturation magnetisation value at room temperature (M_s) of $57.57 \text{ Am}^2/\text{kg}$. This is less than that reported for bulk cobalt ferrite ($M_s = 80 \text{ Am}^2/\text{kg}$),³⁹ however, M_s is often lower for nanoparticles and our value is comparable to similar sized nanoparticles of cobalt ferrite ($M_s = 60 \text{ Am}^2/\text{kg}$).³⁹ As expected, increasing the thickness of the silica shell causes a decrease in the saturation magnetisation, as silica is a non-magnetic material.

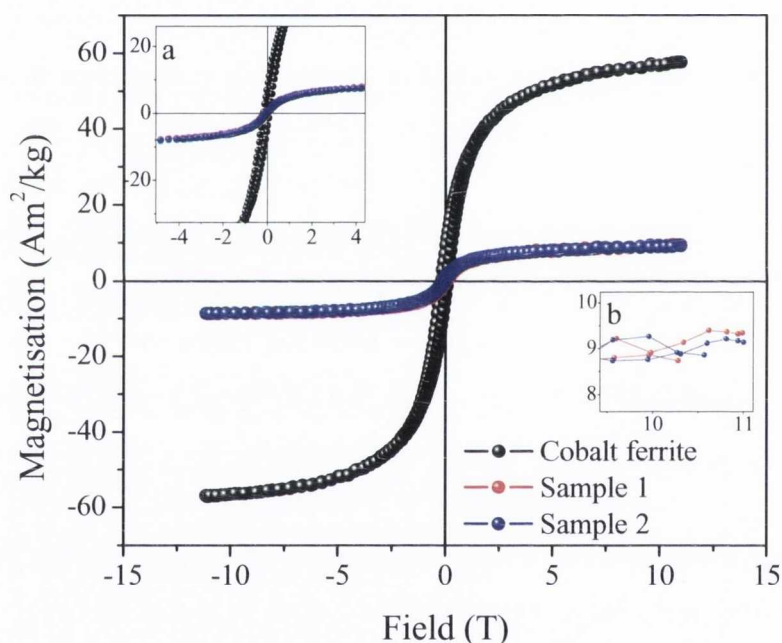


Figure 6.12: Magnetisation curves for cobalt ferrite and silica coated cobalt ferrite at 293 K; inset (a) shows very narrow hysteresis loop for all samples; inset (b) shows the saturation magnetisation difference between samples with different size silica shells. Samples prepared according to Table 6.2.

Manganese ferrite samples were found to be superparamagnetic (Figure 6.13). Manganese ferrite nanoparticles show a saturation magnetisation value at room temperature (M_s) of $60.11 \text{ Am}^2/\text{kg}$. Again, this is lower than that reported for bulk manganese ferrite ($M_s = 80 \text{ Am}^2/\text{kg}$),⁴⁰ however, our value is comparable to sub-50 nm sized nanoparticles of

manganese ferrite ($M_s = 40\text{--}50 \text{ Am}^2/\text{kg}$).^{41,42} Following a similar trend to previous samples, the addition of a silica shell causes a decrease in the saturation magnetisation.

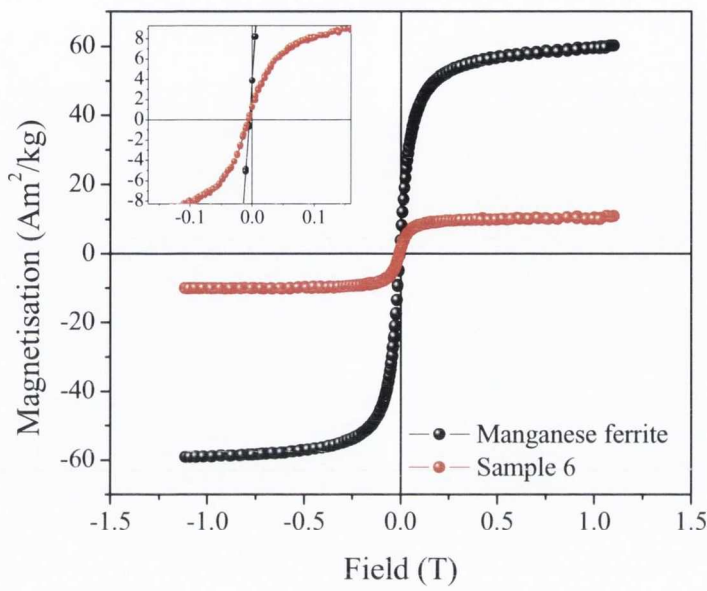
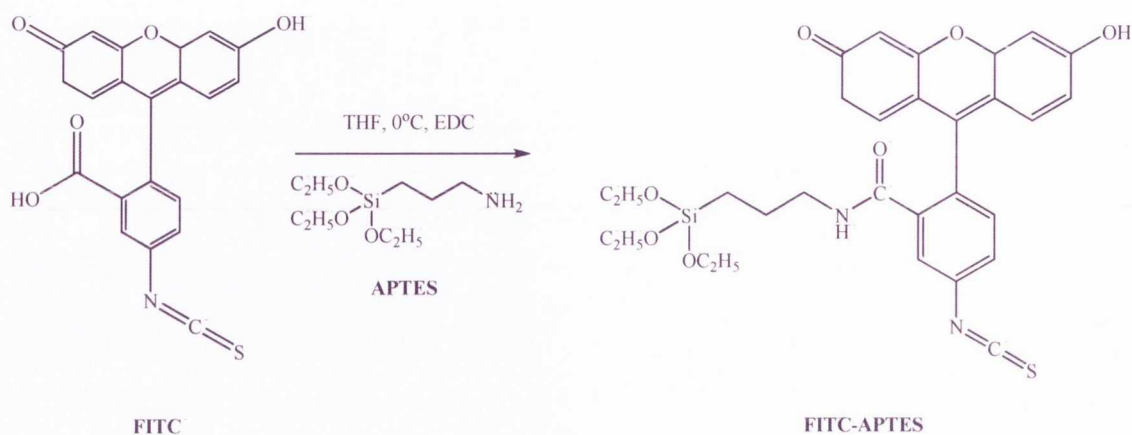


Figure 6.13: Magnetisation curves for manganese ferrite and silica coated manganese ferrite (sample 6) at 293 K; inset shows absence of hysteresis loop for both samples. Samples prepared according to Table 6.2.

6.4 Magnetic-Luminescent Nanocomposites

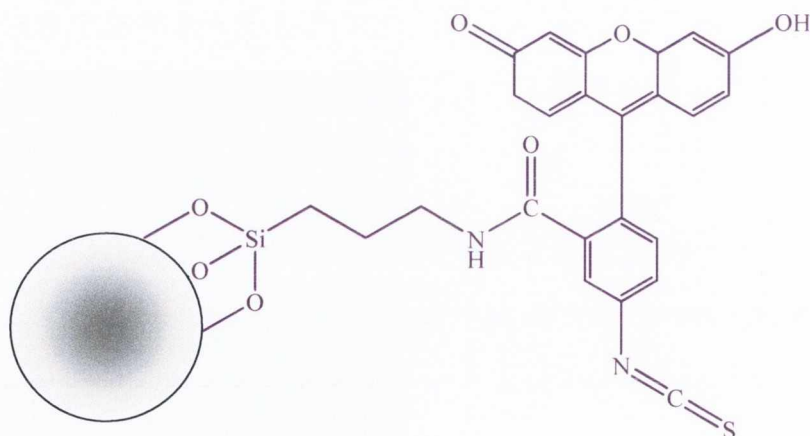
6.4.1 Synthesis of Magnetic-Luminescent Nanocomposites

In order to prepare magnetic-luminescent nanoparticles, fluorescein isothiocyanate (FITC) was bound onto the surface of silica coated magnetic nanocomposites. This was carried out by using carbodiimide coupling to bind FITC to aminopropyltriethoxysilane (APTES) using EDC (EDC = N-[3-Dimethylaminopropyl]-N'-ethylcarbodiimide-hydrochloric acid). EDC is a water soluble compound which promotes the formation of an amide bond between carboxylic acids and amines by activating the carboxyl to form a urea intermediate which can react readily with the amino group. The synthesis of the FITC-APTES derivative is presented in Scheme 6.3. All of the reactions were carried out under argon using Schlenk techniques in order to prevent hydrolysis of the triethoxysilane groups.



Scheme 6.3: Preparation of FITC-APTES fluorescent moiety.

The FITC-APTES derivative was then covalently bound to the surface silanol groups on silica coated nanoparticles according to Scheme 6.4. The silica coated magnetic nanoparticles used were the smallest size prepared (~50 nm diameter), due to these having the highest saturation magnetisation values, allowing ease of manipulation by a magnetic field. FITC-conjugated magnetic nanocomposites were prepared using different magnetic cores, including magnetite and cobalt ferrite. FITC coated silica coated magnetite will hereafter be denoted as $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$, while FITC coated silica coated cobalt ferrite will be referred to as $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{FITC}$.



Scheme 6.4: Covalently linked FITC molecule on silica coated magnetic nanocomposite.

6.4.2 Characterisation of Magnetic-Luminescent Nanocomposites

6.4.2.1 TEM Imaging

TEM images show the silica coated magnetic nanoparticles prepared both before and after functionalisation with FITC dye (Figure 6.14). The sizes of the particles do not change after functionalisation, implying a monolayer of APTES-FITC is bound to the silica shell.

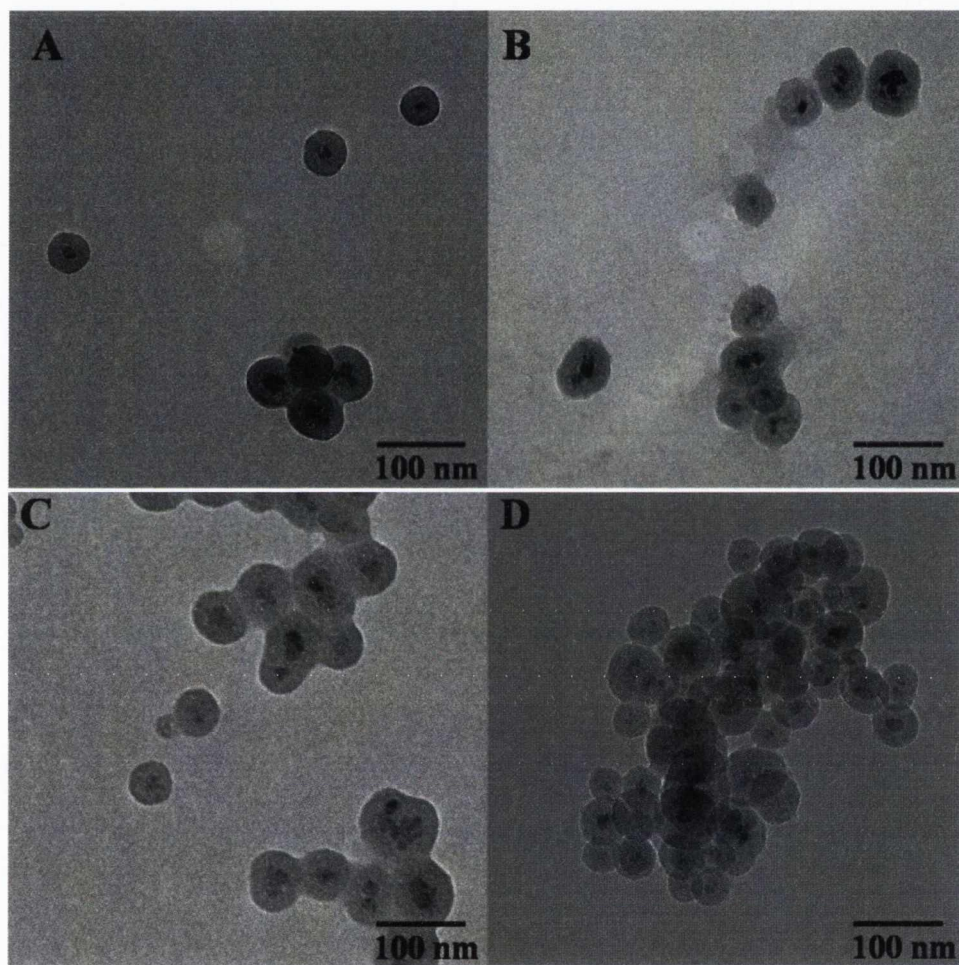


Figure 6.14: TEM images of (a) silica coated magnetite; (b) FITC-linked silica coated magnetite; (c) silica coated cobalt ferrite; (d) FITC-linked silica coated cobalt ferrite; at x50,000 magnification.

6.4.2.2 UV-vis and Photoluminescence Spectroscopy

The nanocomposites were washed with THF and water and isolated using magnetic separation to ensure that the only luminescence observed in the samples was due to bound

fluorescein groups. Absorbance spectra of the free, unbound FITC and the FITC-conjugated nanocomposites were carried out in water (Figure 6.15). The absorbance maximum for free FITC dye in water is centred at 488 nm. The absorbance value for both of the samples of dye-bound nanoparticles has been redshifted by 12 nm in the case of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites; and by 17 nm for the $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites. The shift can be explained by the binding of the dye to the particle surface and particle aggregation effects.

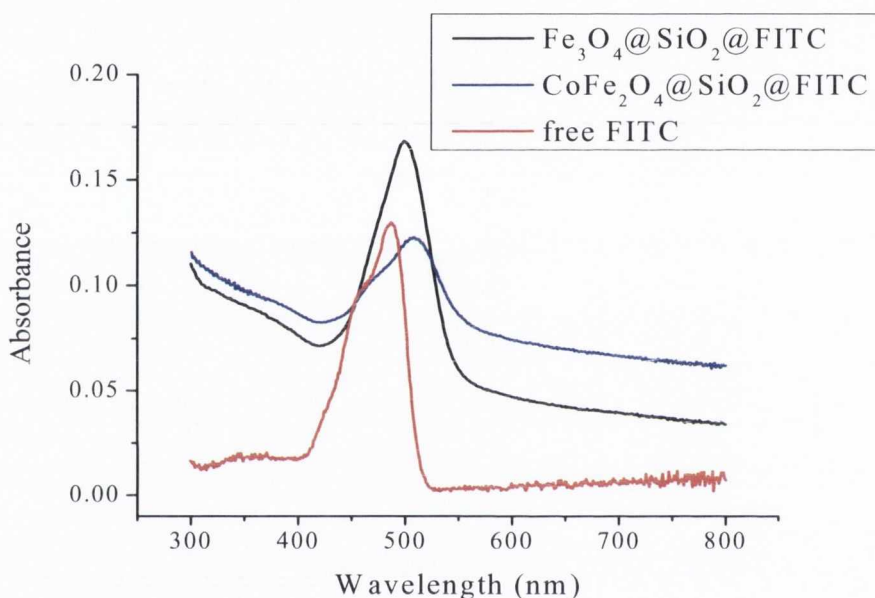


Figure 6.15: UV-visible absorption spectra of samples of FITC-bound silica coated magnetic nanoparticles and free FITC dye.

Photoluminescence spectra of the samples of FITC-bound silica coated magnetic nanoparticles dispersed in water were recorded and compared to the spectrum of free FITC dye dissolved in water (Figure 6.16). All emission spectra were obtained using an excitation wavelength (λ_{ex}) of 488 nm. The emission maximum of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites is centred at 550 nm, while for $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites, it is at 530 nm. These values are redshifted compared to the free FITC emission maximum, at 518 nm. This shift is again due to the particle functionalisation, cross-linking and aggregation effects.

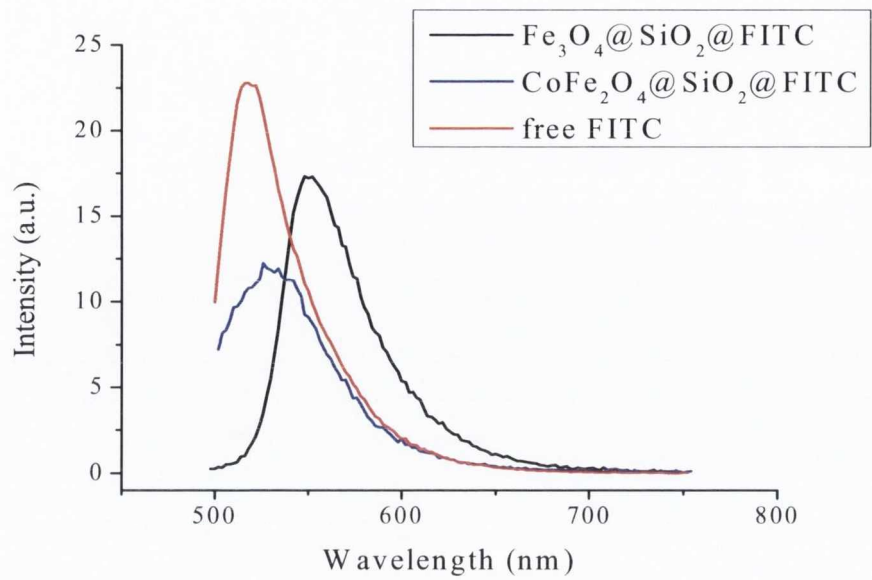


Figure 6.16: Photoluminescence spectra of samples of FITC-bound silica coated nanoparticles and free FITC dye, $\lambda_{ex} = 488 \text{ nm}$.

6.4.2.3 Biological Imaging

The $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites were imaged in *in vitro* experiments to demonstrate their potential for biological imaging applications. An aqueous suspension of the nanocomposites was incubated with A549 epithelial lung cancer cells for different periods of time up to 24 hours before the cells were fixed and embedded in epoxy resin. The resin was cut using a microtome to provide 80 nm thick slices before imaging using electron microscopy (Figure 6.17). After a time of just 20 minutes, nanoparticles can be seen to be entering cells and endosomes (Figure 6.17a). After two hours, nanoparticles have entered lysosomes and multivesicular bodies (Figures 6.17 b and c). After 24 hours, nanoparticles appear to have infiltrated a series of organelles within the cell, where the organelles appear to be filled almost to capacity in many cases (Figures 6.17 d-i). The mechanism of uptake appears to be *via* endocytosis, as can be seen in Figure 6.17 f, where nanoparticles are being engulfed by the cellular membrane.

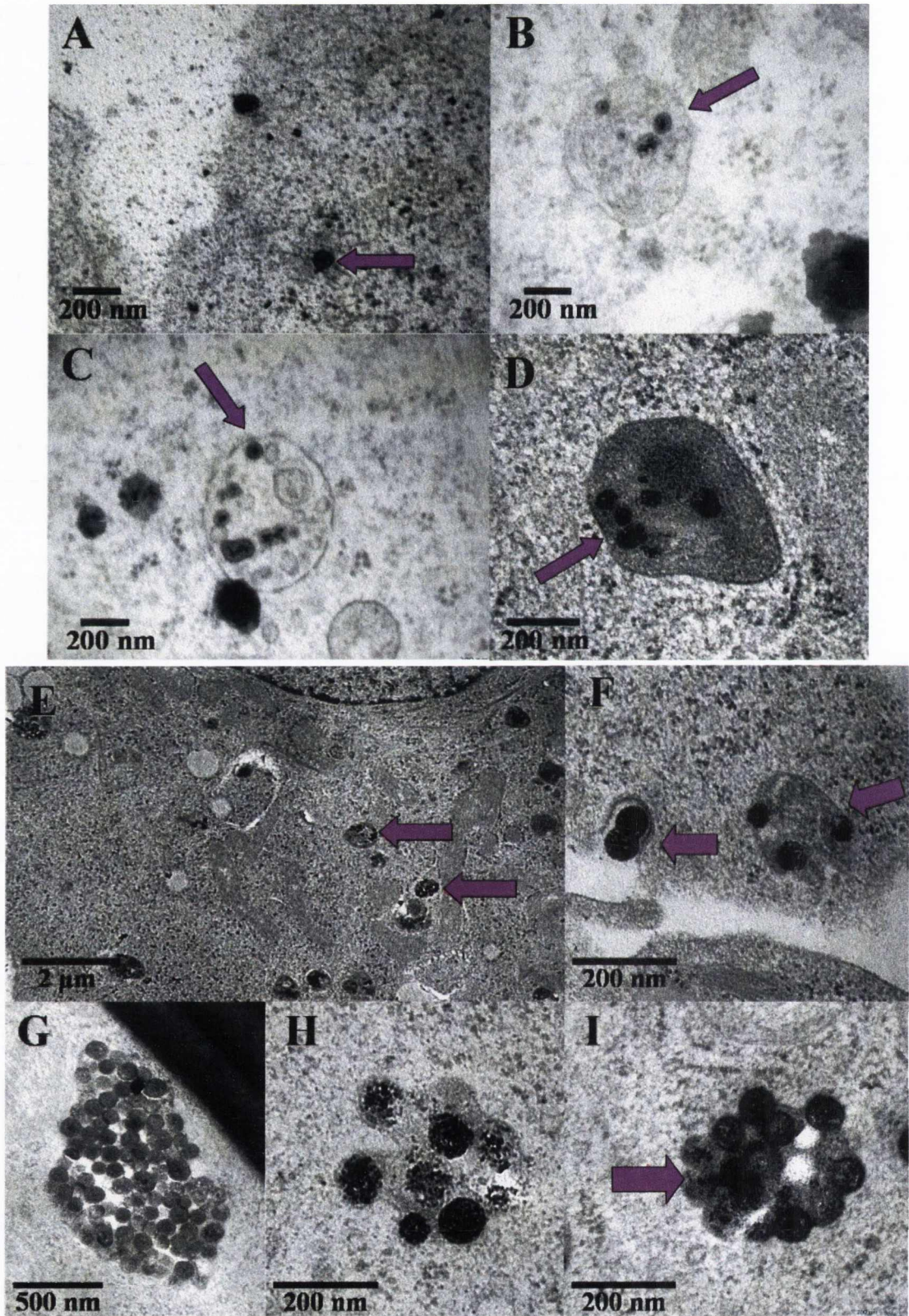


Figure 6.17: Electron microscope images of A549 cells incubated with $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites (53 ± 11 nm); images (a) to (i) at different magnifications; arrow indicates particles inside various organelles.

The nanocomposites which were incubated with A549 cells were also characterised using confocal imaging (Figure 6.18). The presence of the covalently bound FITC dye displayed the nanoparticles as green. The nuclei of the cell were dyed blue using Hoechst dye and the lysosomes can be seen in red, due to eurrhodin dye staining. The images show that some nanoparticles form large aggregates outside the cells. Those particles which enter the cell, however, appear to be located in the cytoplasm, most likely in the lysosome organelle.

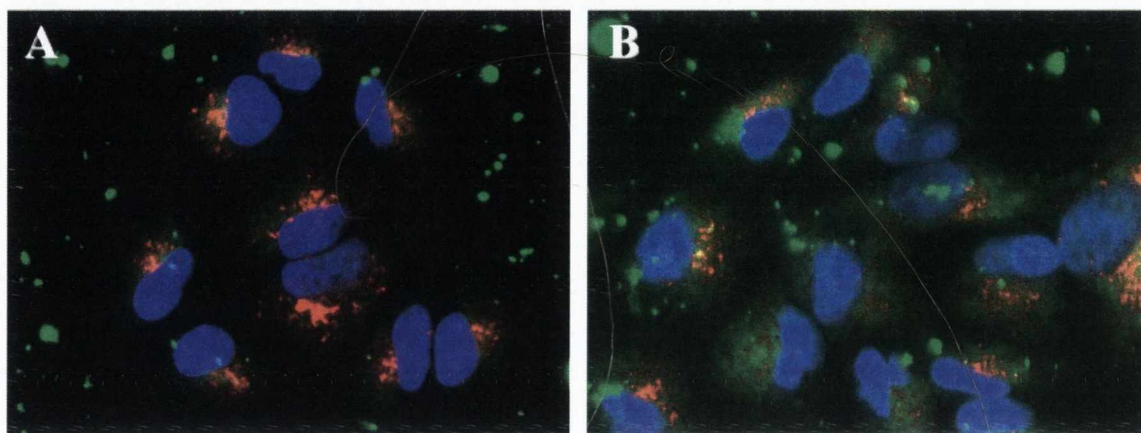


Figure 6.18: Confocal images of A549 cells incubated with $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposites (53 ± 11 nm).

6.4.3 Preparation of Magnetic Nanorattle Structures

Nanorattle-like structures were prepared by reacting $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{FITC}$ nanocomposite samples with TEOS in an attempt to provide an additional protective outer layer of silica, see experimental section for more details.

6.4.3.1 TEM Imaging and Analysis

High resolution TEM imaging and High Angle Annular Dark Field (HAADF) Scanning Transmission Electron Microscopy (STEM) imaging of the structures clearly shows their hollow interior nature (Figure 6.19). The inner magnetic core has moved to the edge in many samples, showing that the interior is ‘empty space’. As a result, the structures have been referred to as ‘nanorattles’.

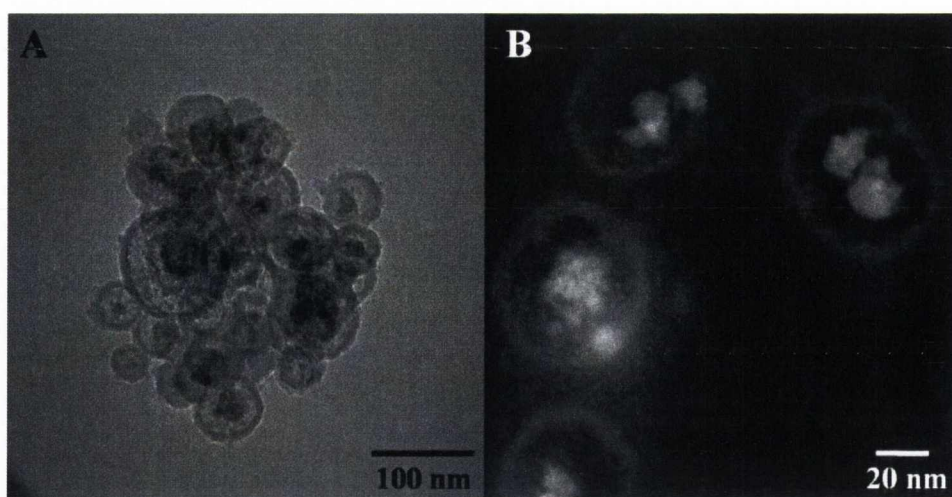


Figure 6.19: (a) TEM image and (b) HAADF STEM image of ‘nanorattle’ structures.

The hollow interior of the nanorattle was confirmed by Electron Energy Loss Spectroscopy (EELS) analysis of HAADF STEM images (Figures 6.20 and 6.21), which demonstrates the clear difference between a ‘hollow’ and ‘non-hollow’ structure. A linescan EELS experiment was carried out on two individual nanoparticles; this allowed monitoring of the intensity of the HAADF intensity across each particle. It also monitored the presence of different elements across this linescan. Figure 6.20 displays the ‘hollow’ nanostructure and its analysis. In Figure 6.20b, the linescan experiment demonstrates that silicon is present on the outer surface of the particle, the outer edges of the magnetic core, and the centre of the sphere. Oxygen can be seen to be present across the sphere, with a lower intensity seen across the ‘hollow’ area of the particle. Carbon was also measured across the sample; it was found to vary across the linescan, with higher intensities in the outer silica shell layers, as expected from FITC embedded within the silica shell. In Figure 6.20c, the overall HAADF STEM intensity was measured and was found to have three distinct peaks and two obvious troughs, which represent the silica shell and inner magnetic core (in the case of the peaks) and the hollow space in between these (the troughs).

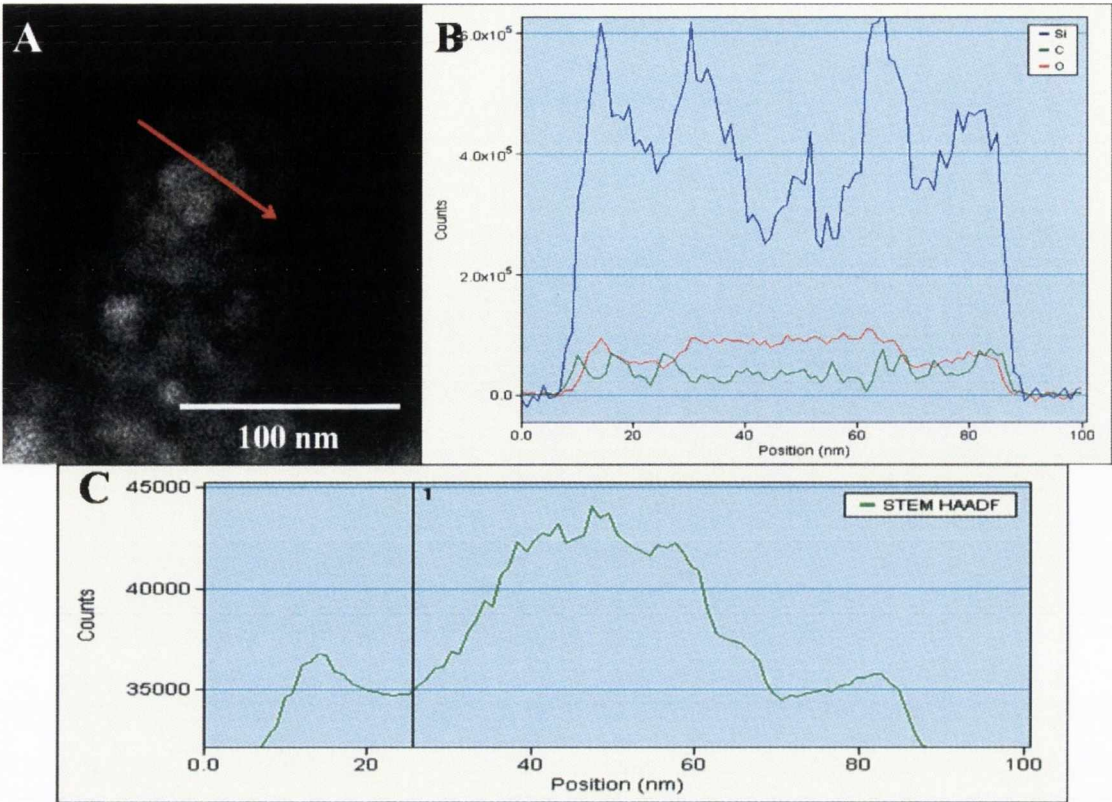


Figure 6.20: ‘Hollow’ structure: (a) HAADF STEM image with red arrow across which EELS linescan experiment was carried out; (b) Graph showing intensity of Si (blue line), C (green line) and O (red line) signals across the linescan experiment; (c) STEM signal graph showing intensity of signal.

Figure 6.21 displays a ‘non-hollow’ nanostructure and its analysis. In Figure 6.21b, the linescan experiment demonstrates that silicon is present across the entire sphere. It should be noted that the decrease in the centre of the linescan is due to the magnetic core, which absorbs some signal. Again, oxygen can be seen with a steady intensity across the sphere. Carbon was also measured across the sample; it was found to vary across the linescan, with highest intensities in the outer portions of the sphere (on the outer edge of the silica shell surface), representing FITC dye conjugated onto the surface as expected. In Figure 6.21c, the overall HAADF STEM intensity was measured and was found to have three distinct peaks, which represent the silica shell and inner magnetic core, and no obvious troughs.

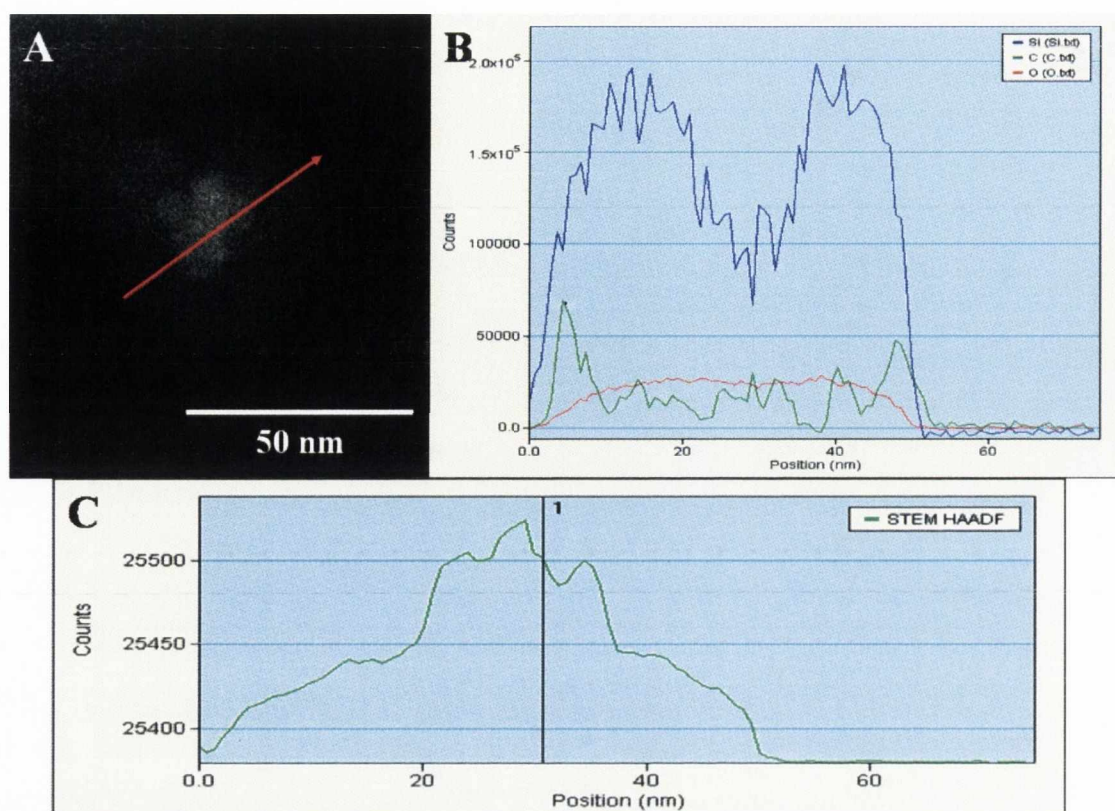


Figure 6.21: 'Non-hollow' structure: (a) HAADF STEM image with red arrow across which EELS linescan experiment was carried out; (b) Graph showing intensity of Si (blue line), C (green line) and O (red line) signals across the linescan experiment; (c) STEM signal graph showing intensity of signal.

From these results, we can suggest that the nanorattle-like structures have been formed as a result of the Kirkendall effect when the limited amount of water molecules at the surface of the FITC-conjugated nanoparticles hydrolyses the TEOS precursor, providing an outer silica shell.

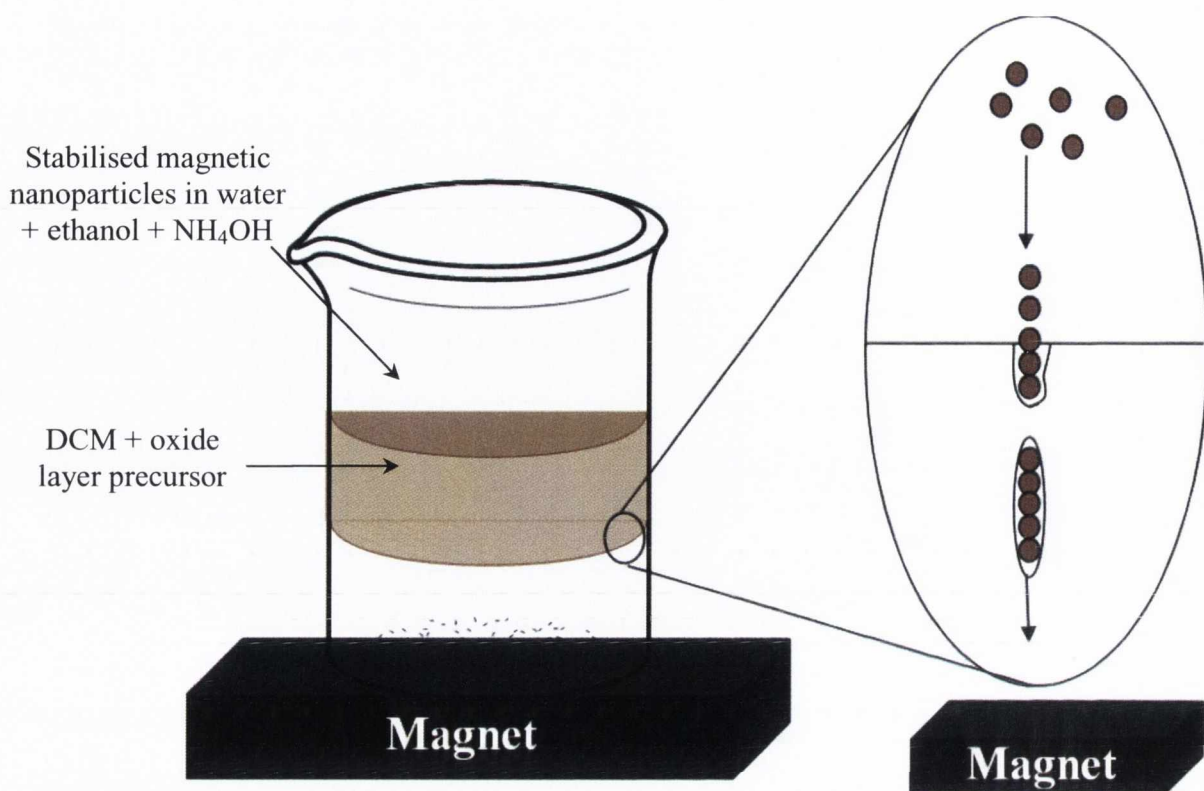
6.5 Magnetic Nanowires

An external magnetic field can be utilised to manipulate magnetic nanoparticles to form temporary linear arrangements. In this part of the chapter, we will discuss a new method of producing permanent magnetic nanowires from magnetic nanoparticles by coating them in the presence of a magnetic field to permanently retain their wire-like shape. This technology could be used to fabricate nanowires prepared from a variety of magnetic materials. In our work, we have prepared wires made from ferrites with thin silica and

titania shells. Using our one-step method, it is possible to incorporate different materials onto the surface of the magnetic wires by using a magnetically-induced reaction at the interface between bi-layers.

6.5.1 Trans-Phase Coating Technique

The principal procedures of this technique are schematically presented in Scheme 6.5. First, a two phase bi-layered system was prepared. This involved an aqueous phase containing magnetic nanoparticles and a reaction catalyst (ammonium hydroxide) and a high-density organic phase containing another reagent (such as tetraethylorthosilicate [TEOS] or titanium isopropoxide). The magnetic nanoparticles were then pulled through the organic phase using a magnet. An external magnetic field allows the bi-layer formed between the aqueous and organic phase to be breached, at the same time as causing the nanoparticles to align into nanowire structures. Their coating is initiated chemically by surface-bound water molecules and ammonium hydroxide catalyst reacting with the alkoxide precursor. The reaction is triggered by its movement across the interface between the two phases. This is presented in Scheme 6.5, where the trans-phase mechanism of coating can be seen in the inset. The nanowires produced by the initial presence of a magnetic field had a thin oxide shell causing their permanent alignment, even when the sample is removed from the magnetic field.



Scheme 6.5: Experimental setup for the preparation of magnetic nanowires from magnetic nanoparticles using magnets. The inset shows the alignment of the magnetic nanoparticles into nanowires and their coating which occurs by a chemical reaction initiated at the interface, triggered by the movement of the magnetic particles through the interface. DCM is dichloromethane solvent and NH_4OH is ammonium hydroxide solution.

We have successfully demonstrated the robustness of this method by using polyelectrolyte stabilised magnetic nanoparticles of cobalt ferrite ($\text{PSSS-CoFe}_2\text{O}_4$) and TEOS or titanium isopropoxide precursors to produce silica or titania coatings respectively.

6.5.2 TEM Imaging

Prior to coating, the PSSS-stabilised cobalt ferrite nanoparticles exist as spheres which are well-dispersed in solution and exhibit no 1-dimensional alignment (Figure 6.22).

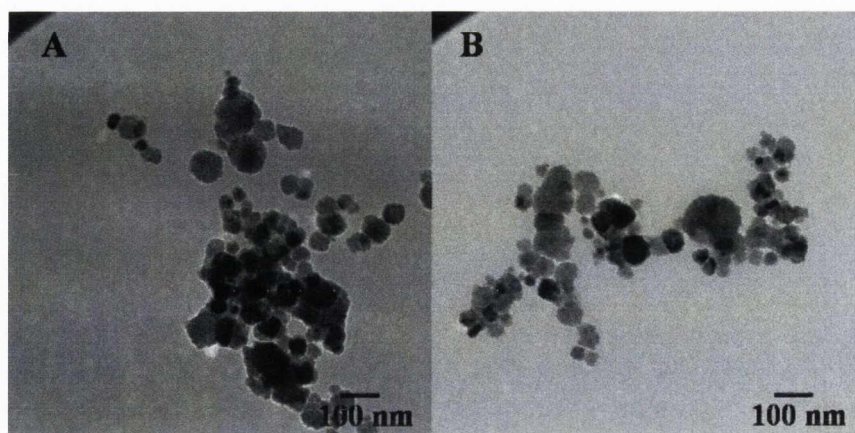


Figure 6.22: TEM images of PSSS-stabilised cobalt ferrite nanoparticles before coating showing monodispersity and no intrinsic alignment in the absence of a magnetic field.

After treatment with TEOS, silica coated cobalt ferrite nanocomposites in the shape of nanowires can be seen in Figure 6.23. The nanowires prepared were 445 ± 190 nm in width and were up to 20 μm in length. Nanowires can be seen to have formed throughout, and it should be noted that the nanowires remain flexible until dry. Indeed, they are capable of being manipulated by an external magnetic field, as can be seen in Figure 6.23d, where application of a magnetic field causes the wires to be aligned parallel to one another.

Variation of parameters shows that increasing the concentration of the catalyst in the magnetic layer does not cause larger wires to form (in terms of width, length or aspect ratio). Increasing the amount of silicon alkoxide (the silica precursor) does not affect the thickness of the resulting silica shell. Also, it should be noted that changing the concentration of the magnetic nanoparticles (*i.e.* top layer) does not appear to alter the resulting nanowire structure, it simply increases the yield of nanowires produced.

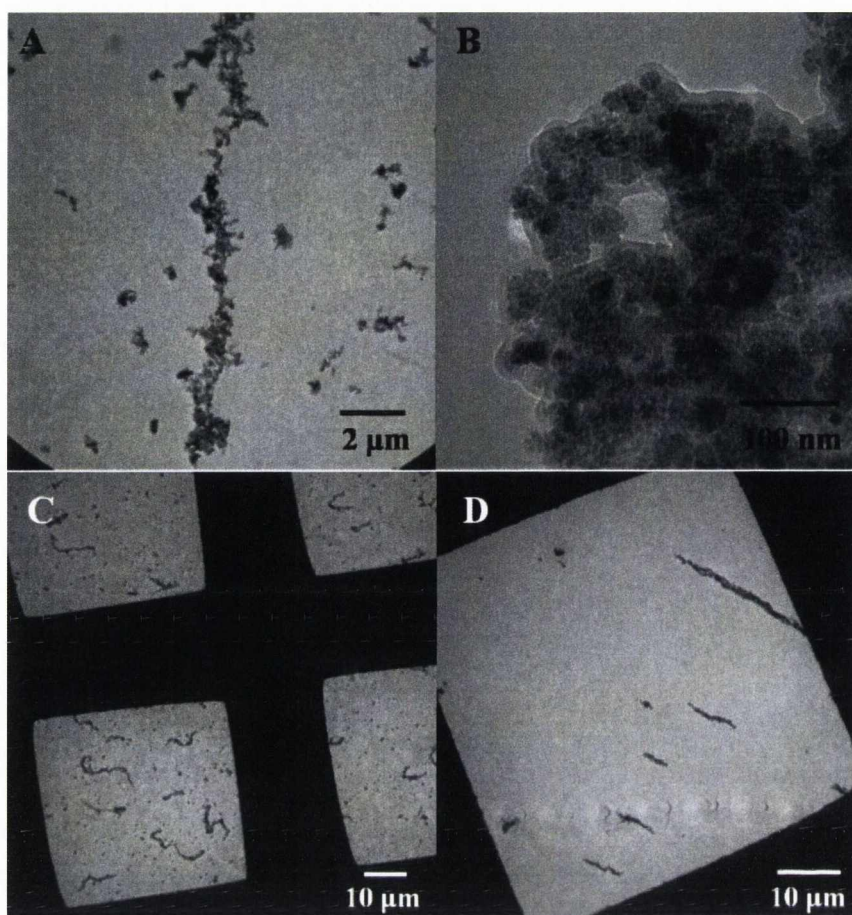


Figure 6.23: (a) and (b) Silica coating on cobalt ferrite nanoparticles – nanowires have been formed and coated with silica; (c) Silica coated nanowires which show non-parallel arrangement; and (d) Silica coated nanowires which have been aligned parallel to one another in the presence of an external magnetic field.

Variation of the composition of the magnetic nanoparticle sample used (see Table 6.3) to prepare the nanoparticles causes a change in the appearance of the resulting nanowire structures (Figure 6.24). PSSS-stabilised CoFe_2O_4 nanoparticles were prepared with two different concentrations of the polyelectrolyte stabiliser, PSSS. Sample 1 was prepared using a high concentration of PSSS; sample 2 was prepared using a low concentration of PSSS, according to Table 6.3.

Table 6.3: Details of PSSS-stabilised CoFe₂O₄ nanoparticles, their composition and characteristics.

Sample	[Metal]:[PSSS] ratio (~monomer ratio)	d _{TEM} (nm)	d _{hyd} (nm) [PDI]	Saturation Magnetisation (Am ² /kg)	Magnetic moment (Am ²)
1	210 (0.62)	32 ± 8	119 [0.160]	39.7	2.1 x 10 ⁻⁴
2	1046 (3.08)	42 ± 11	130 [0.167]	66.4	6.8 x 10 ⁻⁴

[a] d_{TEM} refers to the average diameter of particles calculated from >100 particles according to TEM measurements; [b] d_{hyd} refers to the hydrodynamic radius of the particles in aqueous suspension according to PCS measurements; PDI indicates the polydispersity index of the suspensions index.

In Figure 6.24, the effect of using the different magnetic nanoparticle samples to prepare silica coated nanowires can be seen. All other parameters and concentrations remained the same. The images in Figure 6.24a, b and c were prepared using PSSS-CoFe₂O₄ sample 1 and show shorter, narrower nanowires; 178 ± 67 nm in width and 20-50 µm in length. The images in Figure 6.24d, e, and f were prepared using PSSS-CoFe₂O₄ sample 2, where the nanowires have a very large aspect ratio and show long wires, stretching across TEM grid squares, and also have a thicker width and more ordered appearance; 1680 ± 900 nm in width and hundreds of microns in length.

Full characterisation of the samples of nanoparticles used to prepare the different nanowires in Figure 6.24 shows that they differ in their sizes and their magnetisation (Table 6.3). Sample 2 has higher magnetisation than sample 1, and this causes the nanowires formed using this sample to be longer and wider, due to the nanoparticles being pulled more strongly towards the magnet.

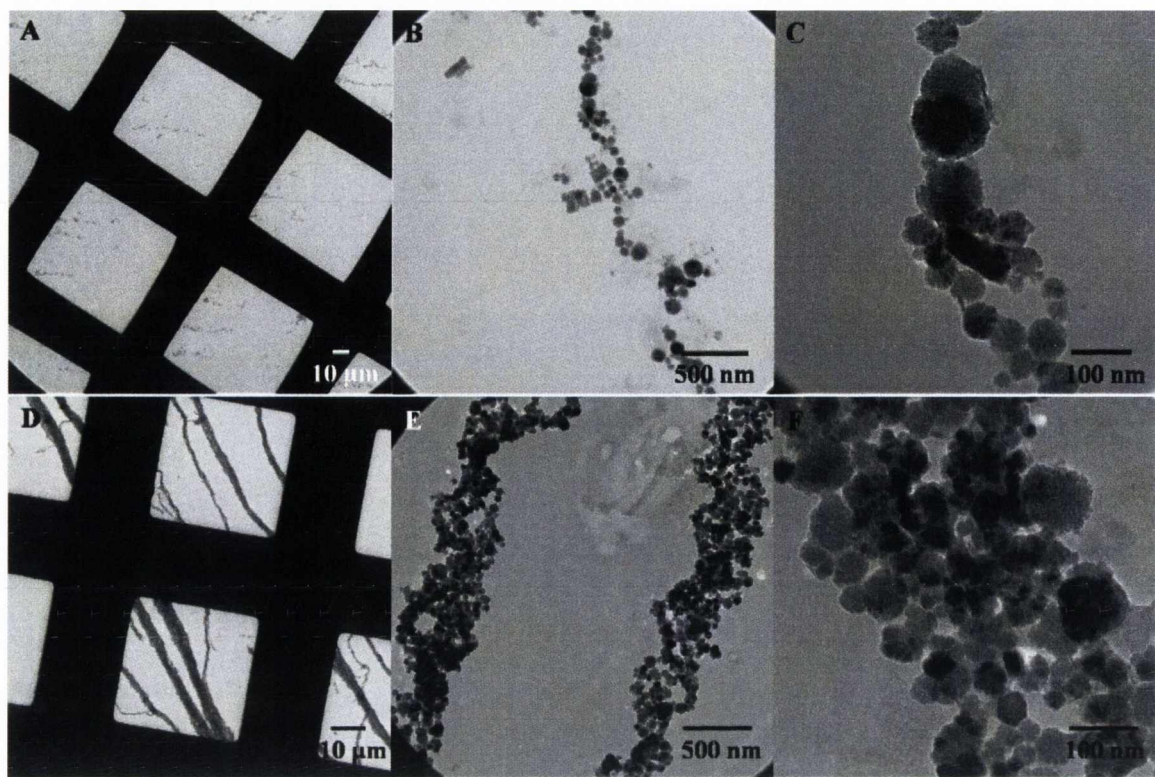


Figure 6.24: TEM images of silica coated nanowires formed: (a, b, c) using sample 1 PSSS-CoFe₂O₄ (images taken at different magnifications); and (d, e, f) using sample 2 PSSS-CoFe₂O₄ (images taken at different magnifications) which produce nanowires which have a higher aspect ratio and a more ordered appearance.

Nanowires prepared using samples of PSSS-CoFe₂O₄ according to Table 6.3.

Titania coated cobalt ferrite nanocomposites were also prepared and appear in Figure 6.25 as bunches of aligned nanowires. The nanowires prepared were 190 ± 70 nm in width and were up to 5 μ m in length. Again, the nanowires, which appear to have been formed throughout, were flexible and capable of manipulation using a magnetic field until dry. This is demonstrated in Figure 6.25d, where application of an external magnetic field caused the wires to align parallel to one another.

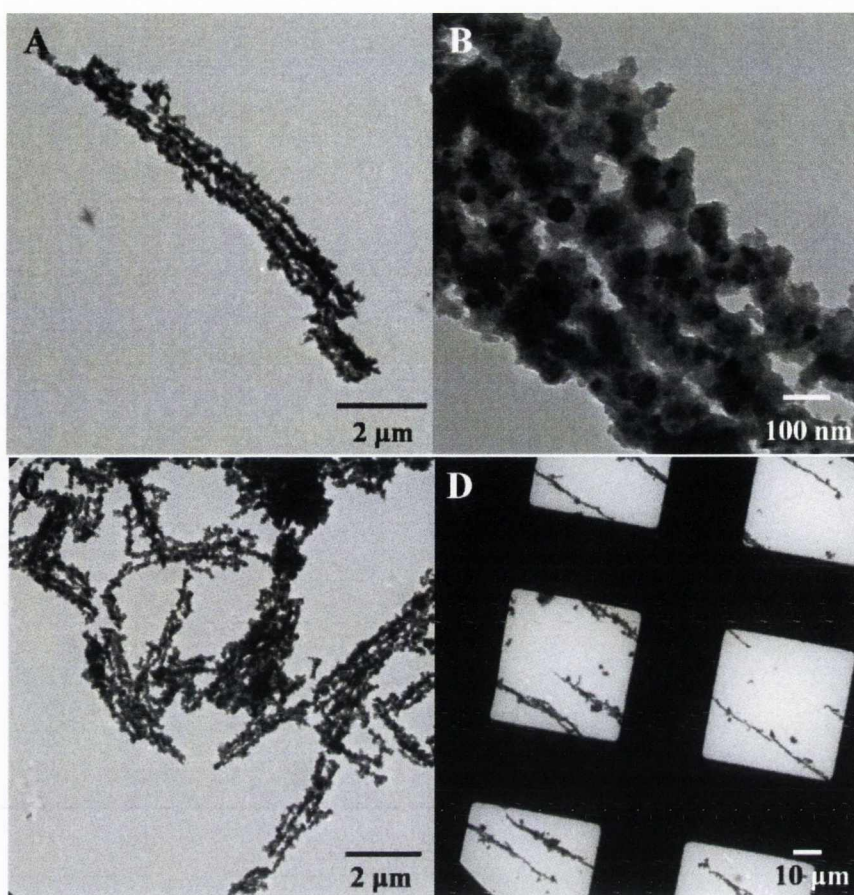


Figure 6.25: (a) and (b) Titania coating on cobalt ferrite nanoparticles – nanowires have been formed and coated with titania; (c) Titania coated nanowires which show non-parallel arrangement; and (d) Titania coating nanowires which have been aligned parallel to one another in the presence of an external magnetic field.

A control experiment was carried out in the absence of a magnetic field, where there was no movement of nanoparticles towards the interface; therefore no coating reaction occurred and no nanowire structures were formed. Nanowires are only formed due to the presence of the magnetic field triggering movement of the magnetic nanoparticles and the formation of an oxide coating at the interface.

6.5.3 FTIR and Raman Spectroscopy

FTIR of the nanowires confirmed the formation of a silica shell for samples prepared using TEOS (*Figure A4.7*), with stretches at $\sim 1100\text{ cm}^{-1}$, which are assigned to asymmetric Si-O-Si stretching vibrations. A distinct shoulder at $760\text{--}800\text{ cm}^{-1}$ can be seen

for the titania coated nanowire composites, which can be assigned to Ti-O-Ti stretching vibrations.⁴³ For all samples, the presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at 1629 cm^{-1} . A broad stretching vibration centred at $3440\text{--}3460\text{ cm}^{-1}$ represents contributions from both symmetrical (ν_1) and asymmetrical (ν_3) modes of the O-H bonds which are attached to the surface iron atoms.

Raman spectra of the nanocomposites displayed the Raman modes characteristic of the cubic inverse spinel structure of cobalt ferrite (*Figure A4.8*). Namely, peaks at 314 , 470 , 563 , 618 and 688 cm^{-1} which can be assigned to the optically active Raman modes.³⁸ The two most common polymorphs of titania are anatase and rutile. Anatase TiO_2 has six Raman active modes, at 144 , 197 , 399 , 513 , 519 and 639 cm^{-1} ; while rutile TiO_2 has four Raman active modes, at 143 , 447 , 612 and 826 cm^{-1} .⁴⁴ Raman spectroscopy of the titania coated nanoparticles shows peaks at 325 , 462 , 561 , 624 and 685 cm^{-1} which represent cobalt ferrite. Unfortunately, these peaks tend to overlap with the expected peaks due to titania, therefore we cannot confidently assign the phase of titania.

6.6 Conclusions

A range of core-shell nanostructured materials based on magnetic nanoparticles of magnetite, cobalt ferrite and manganese ferrite have been successfully prepared. These nanocomposites demonstrated bimodal magnetic and luminescent properties when conjugated with an organic dye. *In vitro* experiments involving incubation of the nanocomposites with cells demonstrated that the particles were easily uptaken by various organelles within the cells and were readily imaged using confocal microscopy.

Novel interesting nanorattle structures were prepared using these dye-coated silica-magnetic nanocomposites. The nanorattle structures showed a hollow area surrounding the magnetic core and an outer silica shell which contained the organic dye. A Kirkendall effect is the most likely reason for the formation of these interesting hollow nanostructures. However, at this stage, the mechanism of their formation is not quite clear and will require further research. These nanorattle-like nanostructures can find a range of applications including biological imaging, drug delivery and drug release systems.

We have also developed a new method of producing magnetic nanowire materials using a one-step magnetically induced trans-phase chemical reaction. This technique could

be used to prepare magnetic nanoparticles and nanowires for a range of magnetic nanomaterials of various shapes and with different coatings.

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Chapter 7

Conclusions and Future Work

7.1 Conclusions

In this work, a series of nanocomposite materials based on silica and magnetic-fluorescent silica nanoparticles have been prepared and investigated. These materials have a broad range of applications, particularly in the emerging field of nanomedicine.

The use of statistical studies has been demonstrated to be a good method for the optimised preparation of silica nanoparticles by varying the synthetic parameters used during preparation. These results allow the easy identification of the best conditions for the formation of small sized silica nanoparticles with a narrow size distribution. In addition, the statistical analyses provide a 3-D surface contour model which can be used as a ‘map’ to prepare tailor-made silica nanoparticles of a specific size. These statistical designs demonstrate the correlation between the concentrations of various parameters and the presence of any interactions which may affect the properties of the resulting nanoparticles. This statistical approach could be used for the optimised preparation of a variety of nanomaterials, not just silica – opening up new opportunities in the reproducible fabrication of nanoparticles or any synthetic system which possesses two or more variable parameters.

Luminescent silica nanoparticles were prepared using a number of different techniques. Extensive studies into the method of agitation used to prepare silica nanoparticles by the Stöber technique resulted in the formation of silica nanoparticles which demonstrated broad white luminescence, without the addition of traditional organic or metallorganic dyes. This emission was thought to originate from defects formed during their preparation and is the first time that such luminescence has been observed in nanoparticulate silica prepared in this way.

Multi-layered nanostructures with interesting hollow morphologies have been prepared using a dispersion of small droplets of aqueous solutions in an alkoxysilane precursor-containing organic solvent. Using this approach, we have shown the encapsulation of an organic dye inside the ‘nanoshells’, demonstrating that this method can be used to prepare a variety of nanomaterials with a broad range of potential applications.

In addition, new rare earth metallasiloxane and metallasilsesquioxane materials were used to prepare luminescent silica nanoparticles by using the simple yet promising technique of thermal treatment. The resulting nanoparticles proved to be small in size and often retained their characteristic lanthanide emission in addition to increasing underlying strong broad emission which is likely to be due to defect emission developed during thermolysis.

The work presented within also shows the preparation of polyelectrolyte-stabilised magnetic nanocomposites. These stable aqueous suspensions, which arrange into aligned chains in the presence of an external magnetic field, were characterised using nuclear magnetic resonance dispersion (NMRD). Some of the composites displayed very high r_1 relaxivities at low fields, which are higher than currently available nanoparticulate contrast agents. This demonstrated the great potential of these magnetic fluids as contrast agents for magnetic resonance imaging (MRI), particularly low field MRI technologies.

New multimodal magnetic-luminescent nanomaterials have been developed. Novel nanorattle-like structures which demonstrate magnetism and fluorescence are of particular interest. These structures appear to possess a hollow area surrounding the magnetic core with an outer shell which contains an organic dye. These offer great potential in the areas of drug delivery and drug release.

Finally, linear 1-dimensional nanowires have been prepared using a novel technique, which utilises an external magnetic field to initiate the trans-phase transport of magnetic nanoparticles and corresponding coating reaction. This has been demonstrated using cobalt ferrite nanoparticles and different oxide coatings, including silica and titania. The nanowire structures formed using this method respond to a magnetic field after coating and can be aligned.

In conclusion, it is believed that this work will contribute to the further development of several important areas of nano- and biotechnology.

7.2 Future Work

Future work will involve the further research and development of luminescent silica nanoparticles, stabilised nanocomposite ferrofluids and multimodal magnetic-luminescent nanoparticles.

Research into the nature of the defect emission emitted by silica nanoparticles will be carried out. In addition, protection of these particles from quenching upon dispersion into various solvents will be developed, through the investigation of different stabilisers, surfactants and functionalities.

The technique of thermal treatment should provide a new route to a multitude of nanomaterials. A detailed investigation of this technique and its parameters, such as heating rate, final temperature and the heating atmosphere will shed light on the mechanism of formation of the nanoparticles and manipulation of these parameters should produce nanostructures of different shapes and sizes. Additionally, metallasiloxane complexes including Er^{3+} and Gd^{3+} ions will be used to prepare silica-based nanostructures, which could be used as optical amplifiers in the telecommunications industry or as contrast agents in MRI.

Further development of stable magnetic fluids of ferrite nanocomposites is required to fine-tune the relaxivity values and their behaviour in response to a magnetic field. In addition, an investigation into their cytotoxicity and *in vivo* MRI testing will prove their efficacy as contrast agents.

7.2.1 Core-shell Multimodal Nanocomposites

Core-shell magnetic nanoparticles have been utilised to develop magnetisation measurements of individual nanoparticles of magnetic materials. This can be realised using a nano-SQUID magnetometer, where a single particle of silica coated magnetite can be placed onto a nano-SQUID surface (Figure 7.1). This unique measurement technique, which is still under development, allows an assessment of the magnetisation of individual magnetic nanoparticles for the first time.

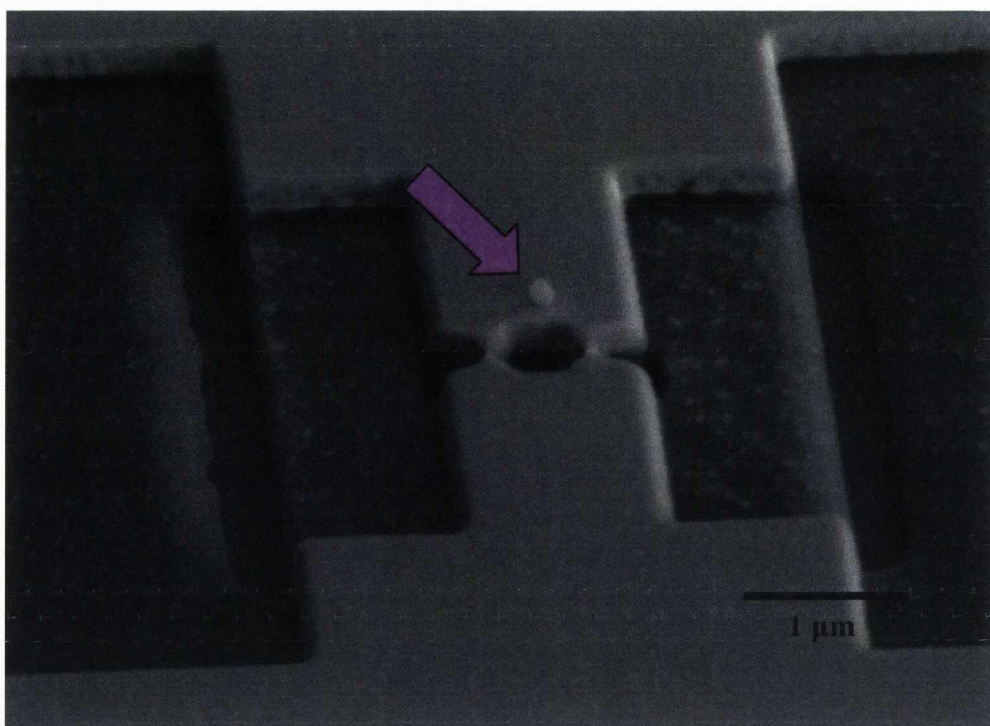


Figure 7.1: SEM image of single silica coated magnetite nanoparticle (indicated by the arrow) on a nano-SQUID machine (at x 50,000 magnification).

Core-shell nanocomposites which display nanorattle-like structures have a vast array of potential applications. Their hollow interior lends itself well to drug delivery, permitting encapsulation and controlled release. In addition, the rattle-like configuration of the internal magnetic core, which allows unhindered movement around its spherical shell could be used for magnetic sensing, using an optical response *via* luminescence quenching.

7.2.2 Magnetically Initiated Trans-phase Reactions

Our new approach towards the magnetic trans-phase formation of coated magnetic nanowires is currently under patent consideration. It is a promising method which may be used to develop composite materials by using magnetically assisted trans-phase delivery. This one-step approach could also be used for encapsulation and for the preparation of a wide variety of functionalised and coated magnetic materials. In addition, this method allows magnetically triggered reaction initiation (e.g. polymerisation, condensation etc.) at aqueous/organic interfaces. The resultant nanomaterials are capable of possessing multiple functionalities by the inclusion of different materials (e.g. organic dyes) in the bi-layer

system, which will be incorporated at the phase transition. In our future work, we plan to demonstrate that this approach could not only be used to prepare nanowire and nanocomposite materials, but could be used for magnetic destabilisation of microemulsion systems. This could be useful for techniques which require catalysis through the mixture of materials harboured in two different organic phases or emulsions. We believe that this technique has a range of potential applications, which will be developed in the future.

Appendix 1

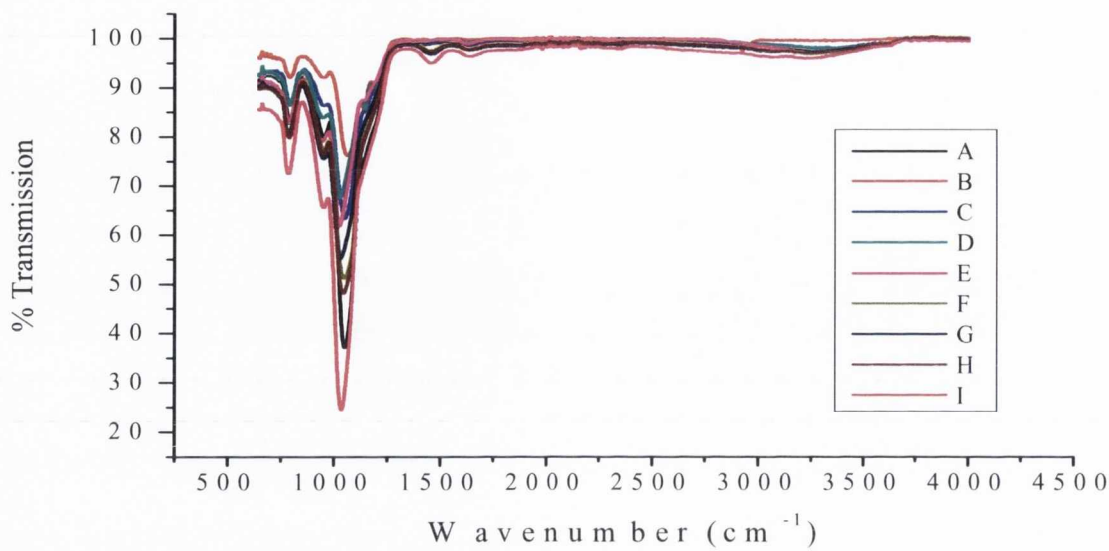


Figure A1.1: FTIR spectra of samples A-E prepared according to Table 3.1, Chapter 3.

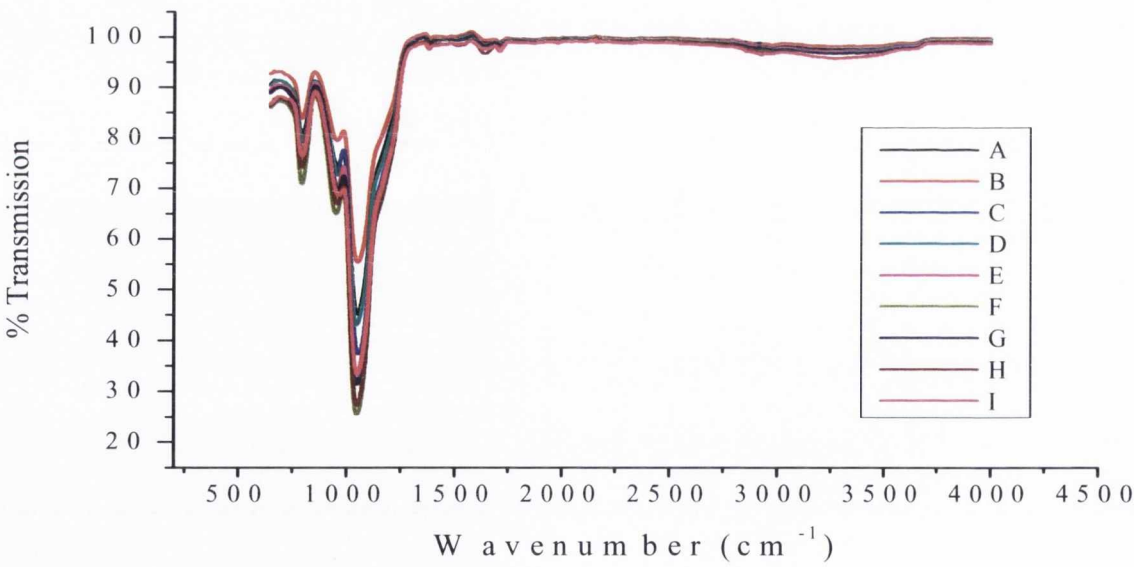


Figure A1.2: FTIR spectra of samples prepared according to the statistical study 1.

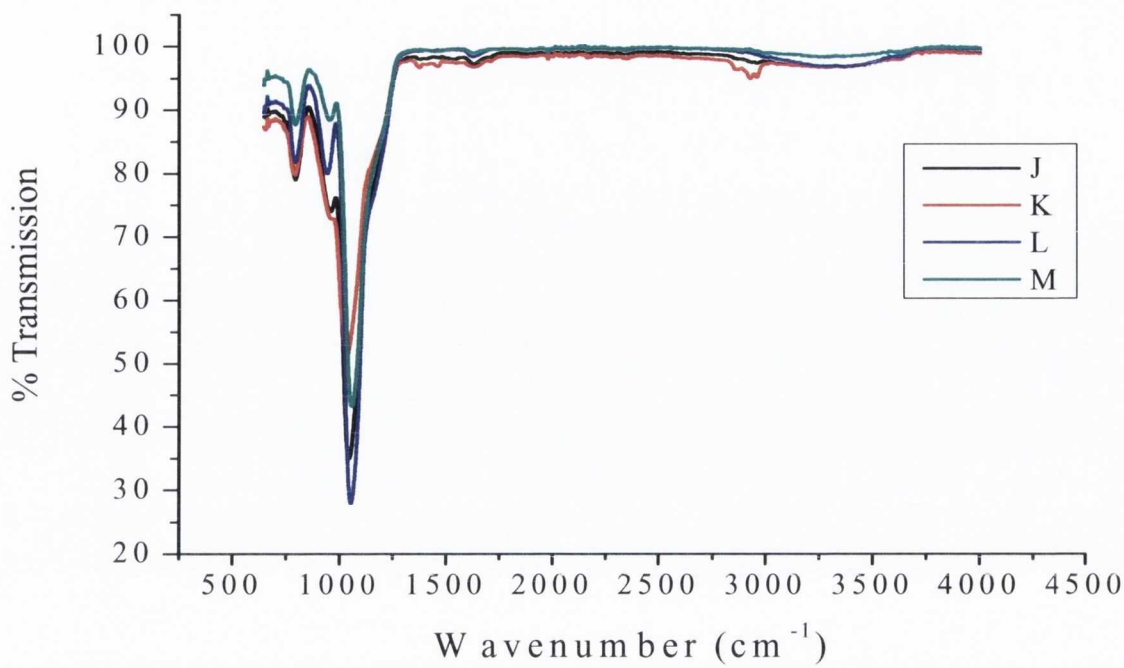


Figure A1.3: FTIR spectra of samples prepared according to the statistical study 2.

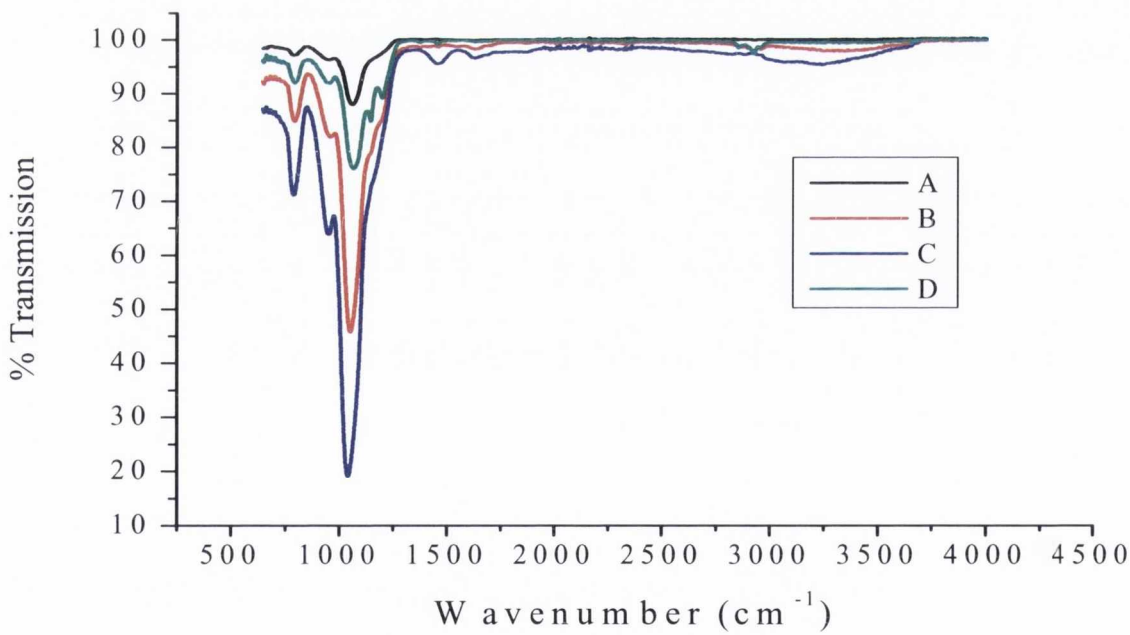


Figure A1.4: FTIR spectra of samples A-D prepared according to Table 3.5, Chapter 3.

Appendix 2

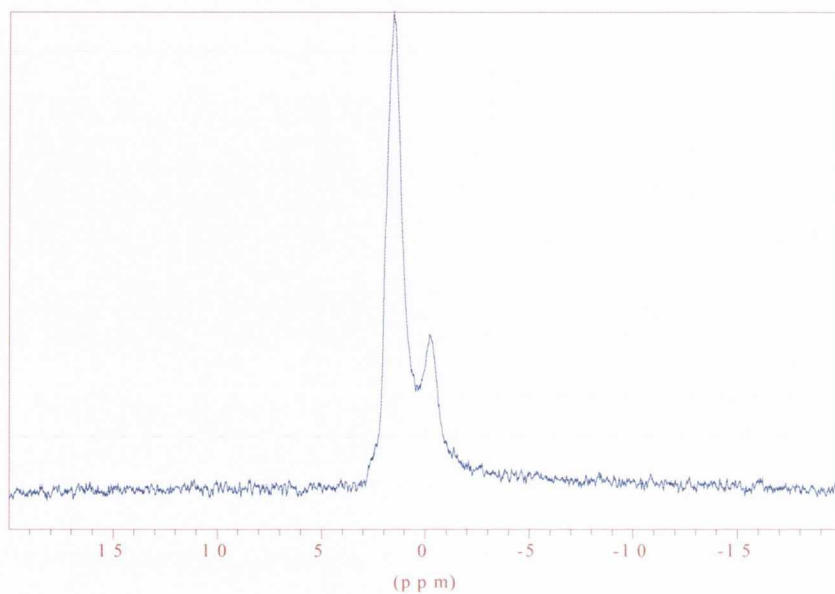


Figure A2.1: ^7Li NMR of **Compound 1** showing peaks at 1.56 and -0.20 ppm in a ratio of approximately 5:1.

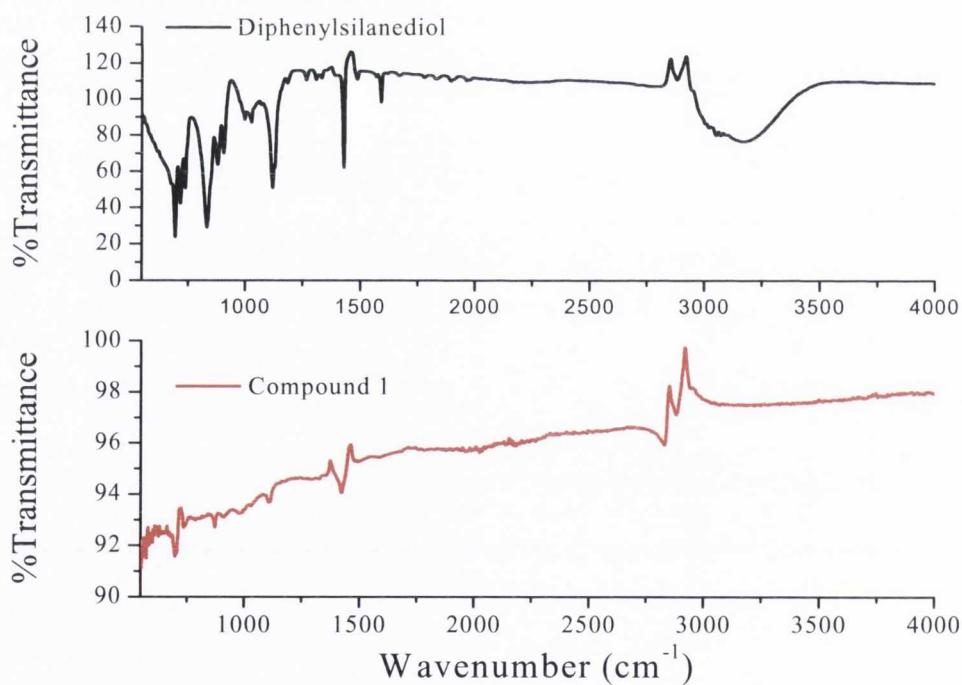


Figure A2.2: FTIR spectra of diphenylsilanediol and **Compound 1**.

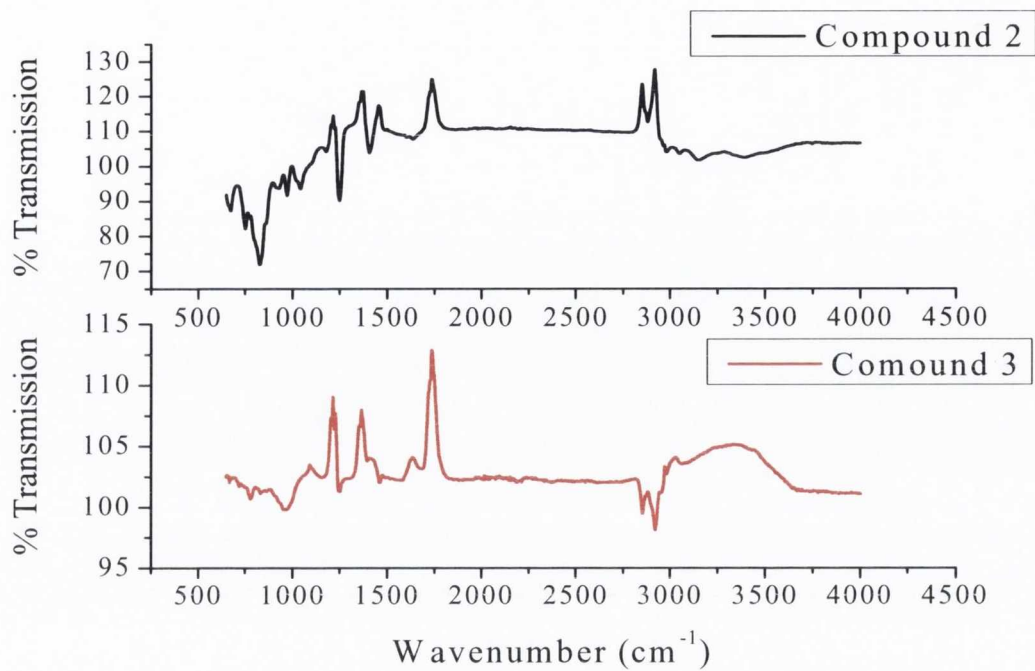


Figure A2.3: FTIR spectra of Compounds 2 and 3.

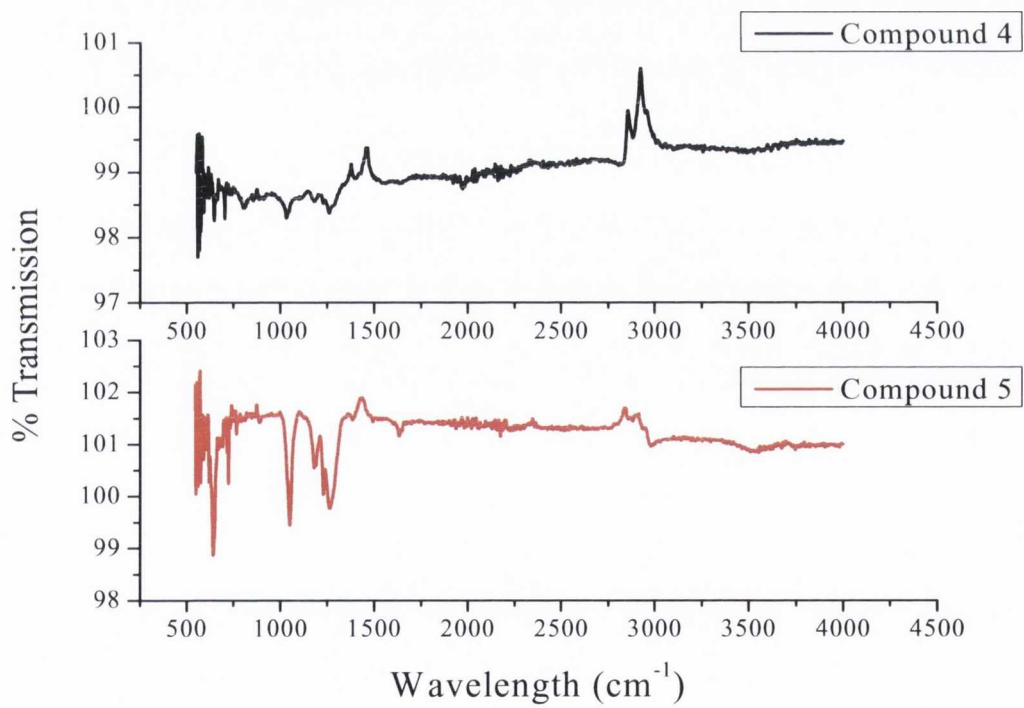


Figure A2.4: FTIR spectra of Compounds 4 and 5.

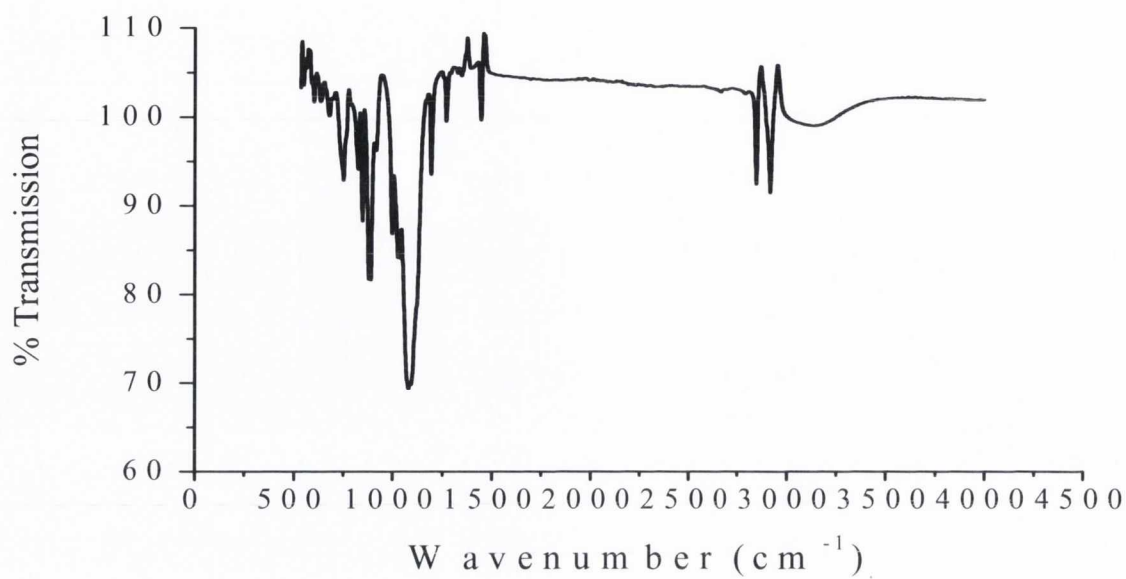


Figure A2.5: FTIR spectrum of $(c\text{-C}_6\text{H}_{11})_7\text{Si}_7(\text{OH})_3$ **Ligand A**.

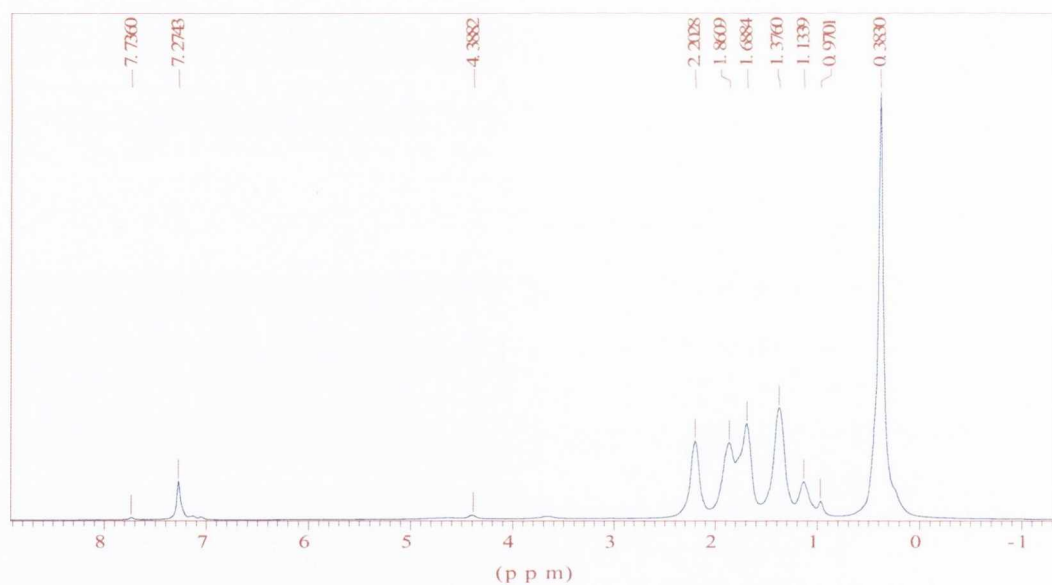


Figure A2.6: ^1H NMR spectrum of **Compound 6**.

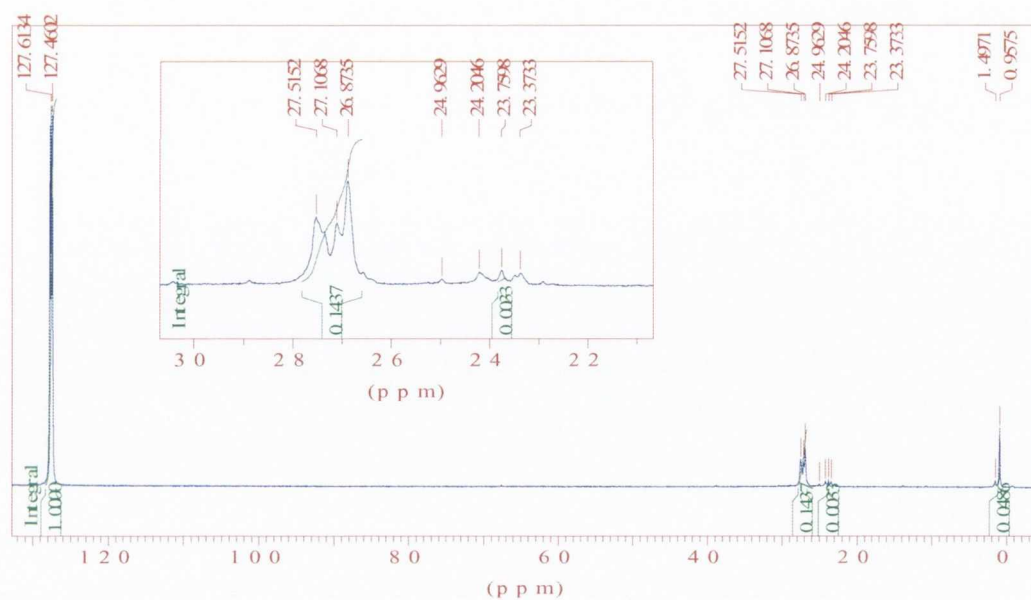


Figure A2.7: ¹³C NMR spectrum of Compound 6.

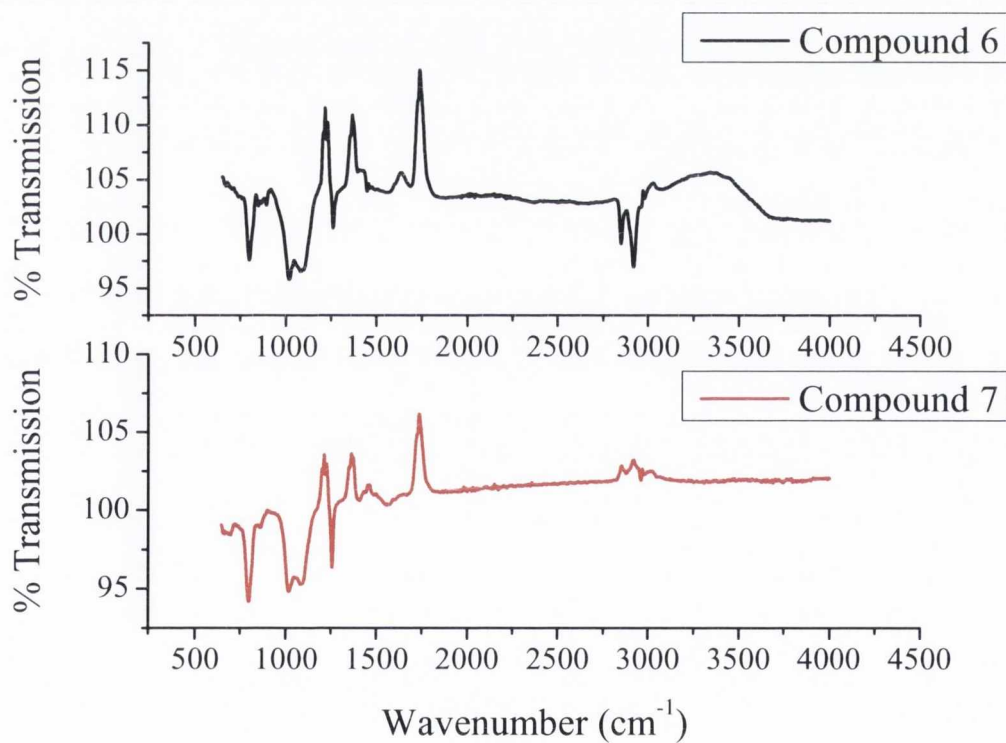


Figure A2.8: FTIR spectrum of Compounds 6 and 7.

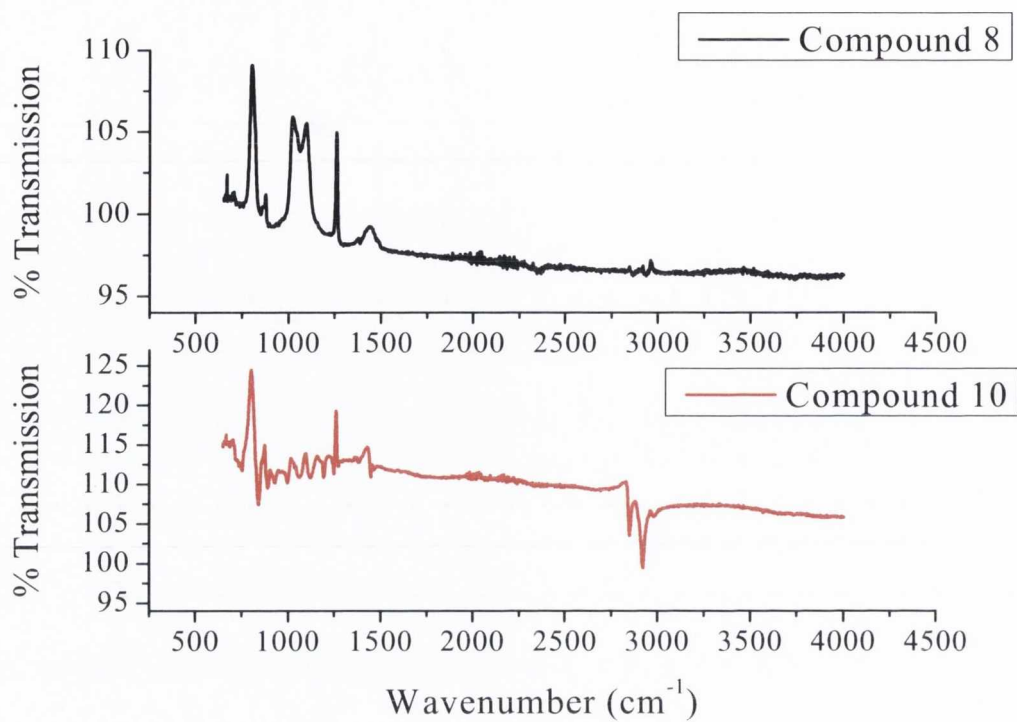


Figure A2.9: FTIR spectrum of **Compounds 8 and 10**.

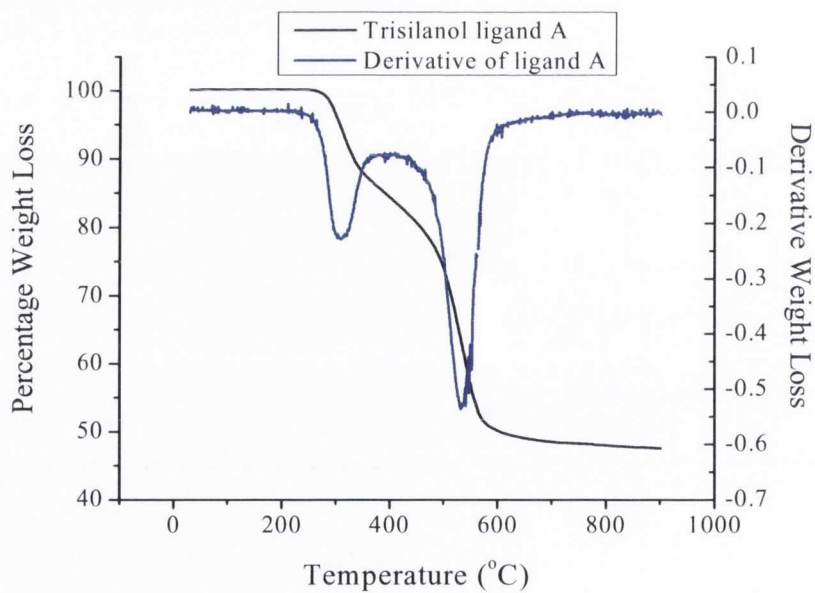


Figure A2.10: Thermal decomposition graph showing the weight loss and derivative curve of trisilanol **Ligand A** $[(c\text{-C}_6\text{H}_{11})_7\text{Si}_7(\text{OH})_3]$.

FTIR spectra of **Compound 4** can be seen in *Figure A2.11*, where it has been compared to the spectrum carried out prior to thermal treatment. The peak $\sim 1100\text{ cm}^{-1}$, observed in both spectra, is due to Si-O stretching and bending vibrations, is expected due to the presence of Si-O bonds in both the untreated **Compound 4** and after subsequent heating. Other peaks seen in the fingerprint region between $1700\text{-}1200\text{ cm}^{-1}$ indicate the presence of hydrocarbon groups,¹ likely to be due to the phenyl substituents present in the compound both before and after heat treatment. The evolution of a broad peak between $3000\text{-}3800\text{ cm}^{-1}$ in the spectrum of the compound after heat treatment can be attributed OH groups caused by hydroxylation of the siloxane compound and the formation of surface silanol bonds. Similar results can be seen in the FTIR spectra of **Compounds 6** and **7** before and after thermal treatment (*Figures A2.12* and *A2.13* respectively).

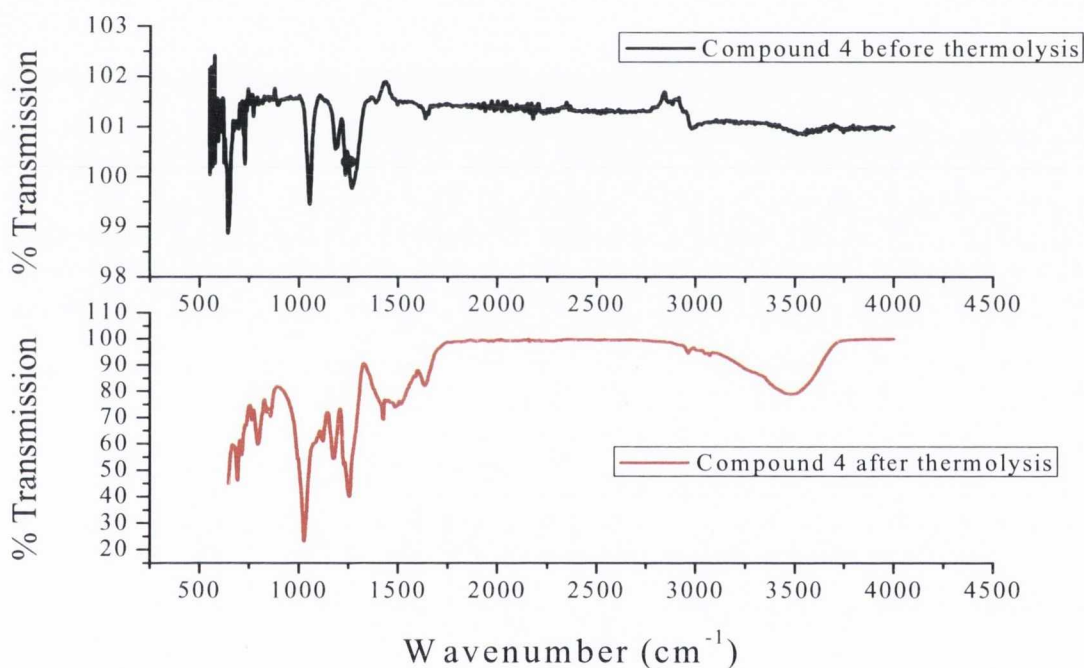


Figure A2.11: FTIR spectra of **Compound 4** before and after thermolysis to $300\text{ }^{\circ}\text{C}$.

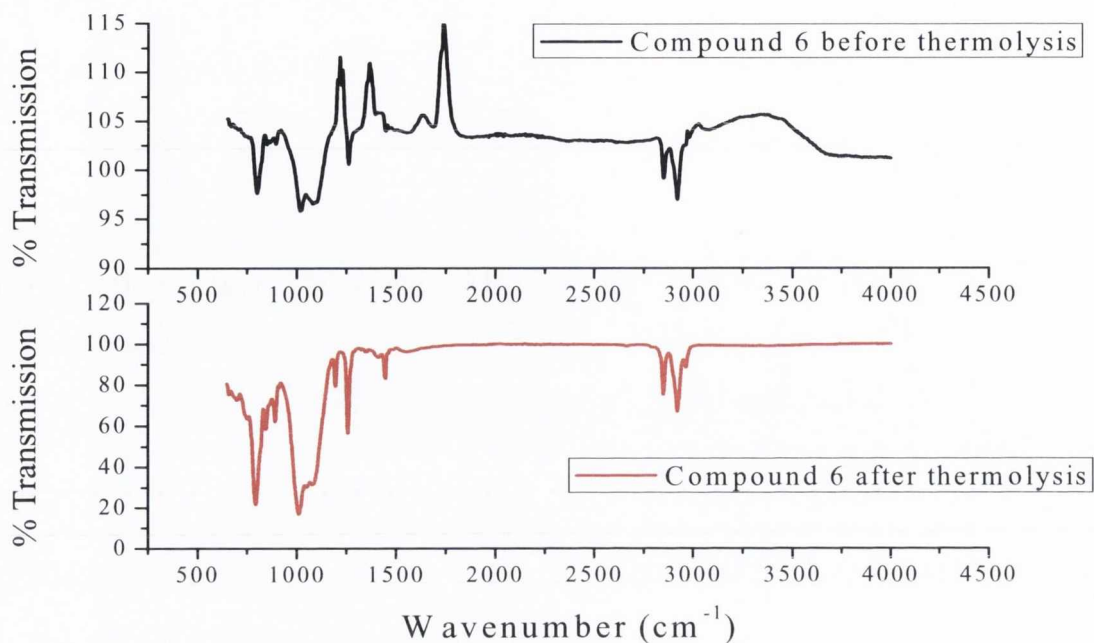


Figure A2.12: FTIR spectra of Compound 6 before and after thermolysis to 350 °C.

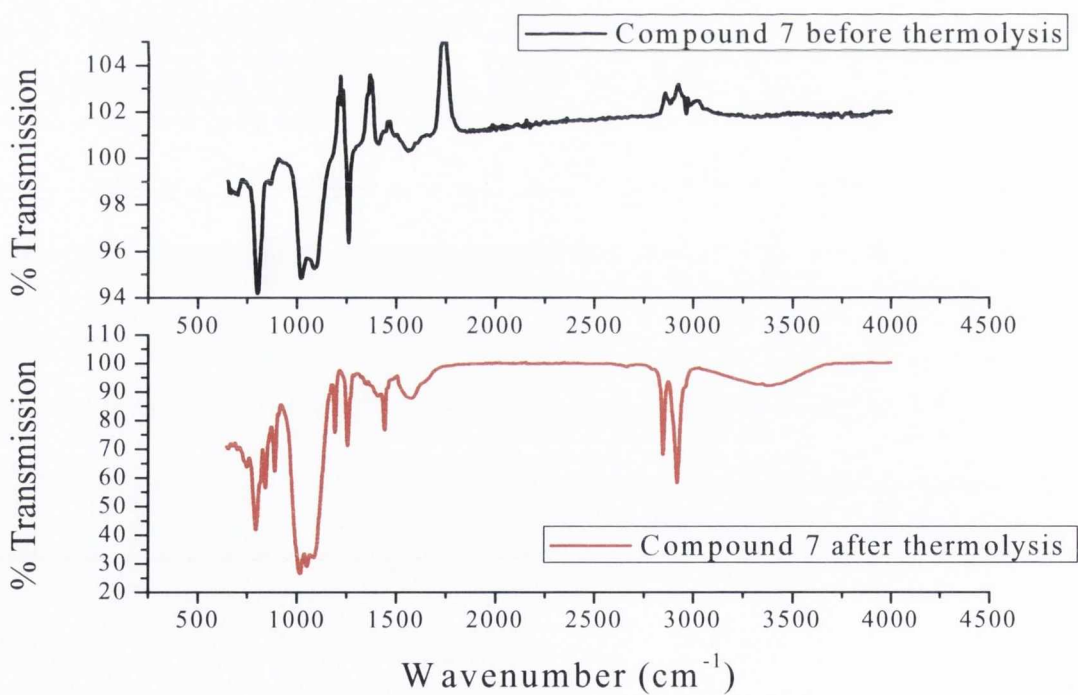


Figure A2.13: FTIR spectra of Compound 7 before and after thermolysis to 300 °C.

Raman spectra of **Compounds 6** and **7** before and after thermal treatment are shown in *Figures A2.14* and *A2.15* respectively. Before thermolysis, both spectra show several sharp peaks between 400 and 800 cm^{-1} which can be assigned to the various symmetric and asymmetric vibrations of Si-O-Si bonds within the compounds.² After thermolysis, these sharp peaks have disappeared and the spectra resemble spectra typical of amorphous nanoparticulate silica. The weak peak at $\sim 350 \text{ cm}^{-1}$ represents the O-bending motion of connected SiO_4^{4-} tetrahedral in the silica matrix. Broad, weak peaks at 480 and 600 cm^{-1} can be assigned to the symmetric oxygen breathing vibrations within the matrix. The peak at about 800 cm^{-1} is assigned to the stretching vibration of Si-O-Si.^{3,4}

The raman spectrum of **Compound 4** (*Figure A2.16*) does not exhibit such a dramatic change after thermolysis as the other two spectra. This could be due to the less bulky geometry of the compound which does not undergo such efficient thermal treatment when compared to the bulky structures of **Compounds 6** and **7** due to the large ligands in their structural configurations. Analysis of the peaks in the spectra of **Compound 4**, however, does allow assignment of similar species. For example, before thermolysis, weak peaks between 400 and 800 cm^{-1} are present and can be assigned to the various symmetric and asymmetric vibrations of Si-O-Si bonds within the compound. After thermolysis, the peak at 350 cm^{-1} representing the O-bending motion of connected SiO_4^{4-} tetrahedral in the silica matrix is present, albeit weak. The peaks at 600 and 800 cm^{-1} are sharper and could represent the breathing and stretching vibrations of Si-O-Si within the matrix.

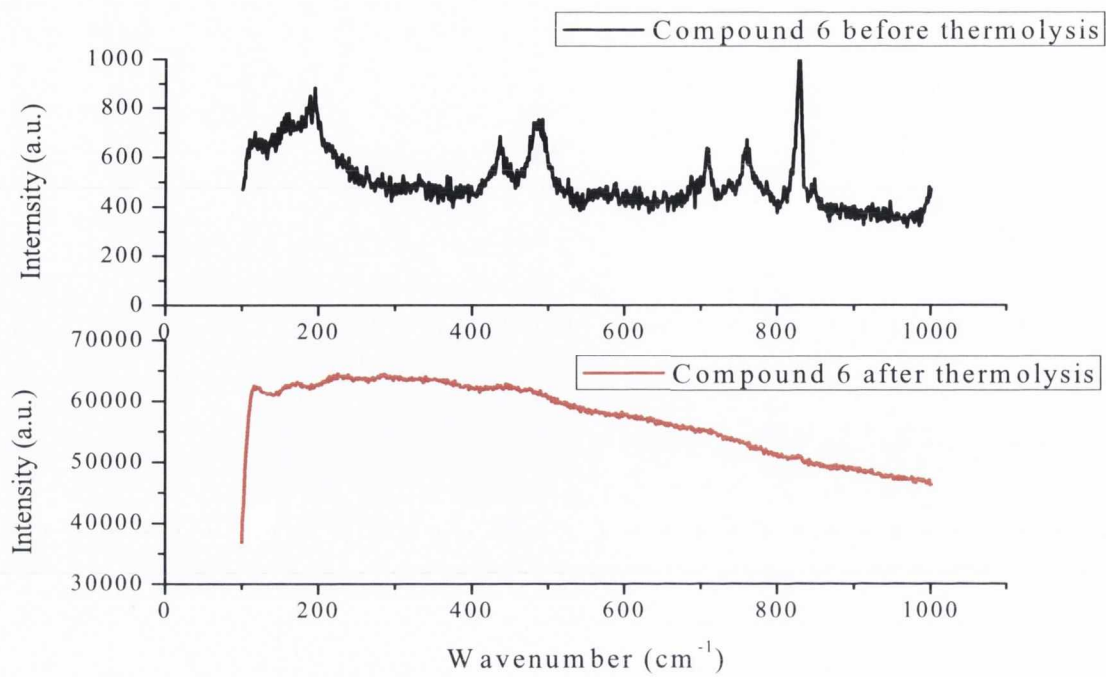


Figure A2.14: Raman spectra of **Compound 6** before and after thermolysis to 350 °C.

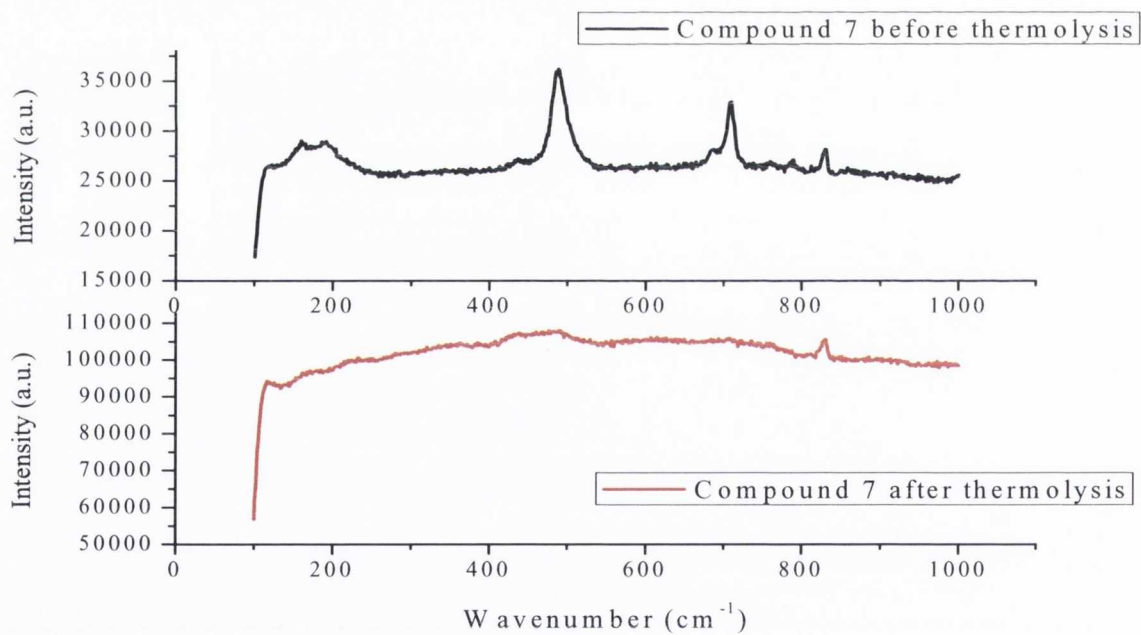


Figure A2.15: Raman spectra of **Compound 7** before and after thermolysis to 300 °C.

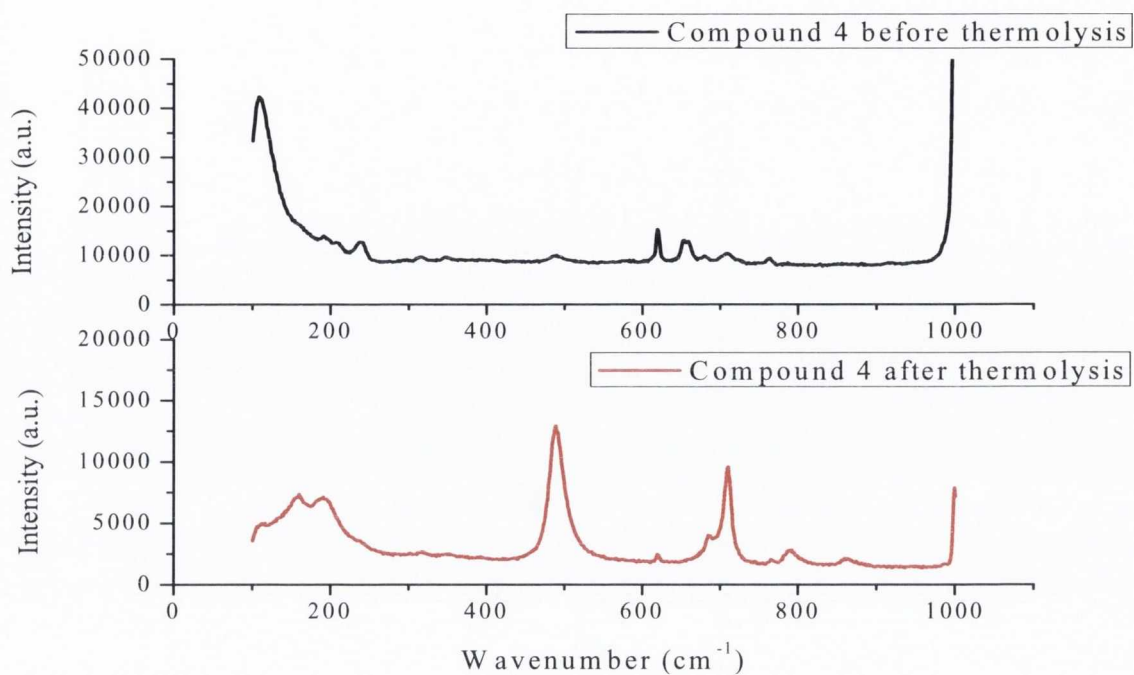


Figure A2.16: Raman spectra of **Compound 4** before and after thermolysis to 300 °C.

Appendix 3

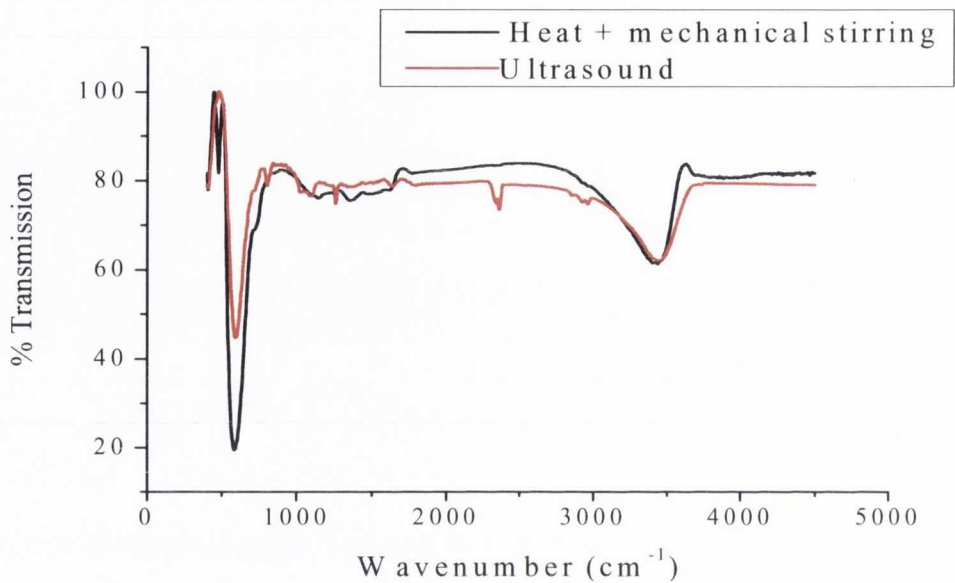


Figure A3.1: FTIR spectra of CoFe₂O₄ nanoparticles prepared by co-precipitation using heat and mechanical stirring (black) and ultrasound treatment (red).

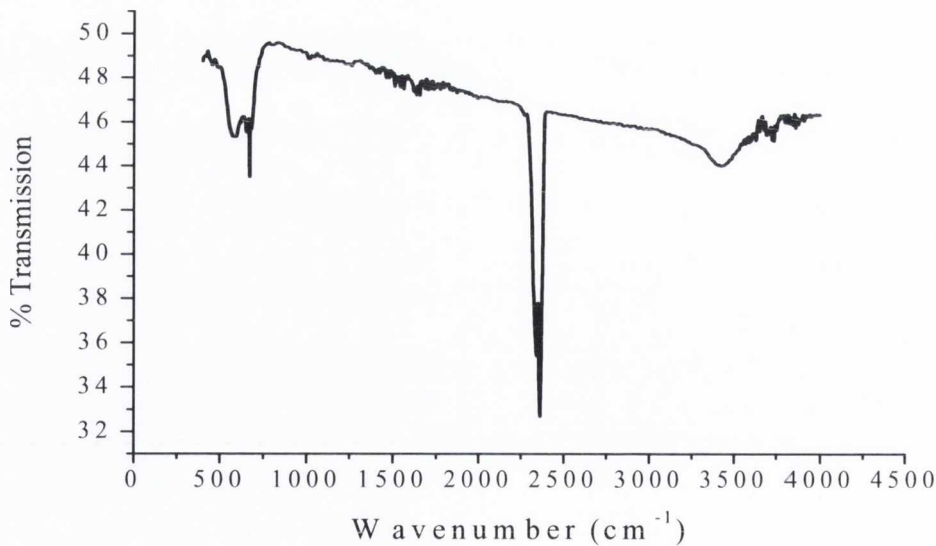


Figure A3.2: FTIR spectra of MnFe₂O₄ nanoparticles prepared by co-precipitation using heat and mechanical stirring.

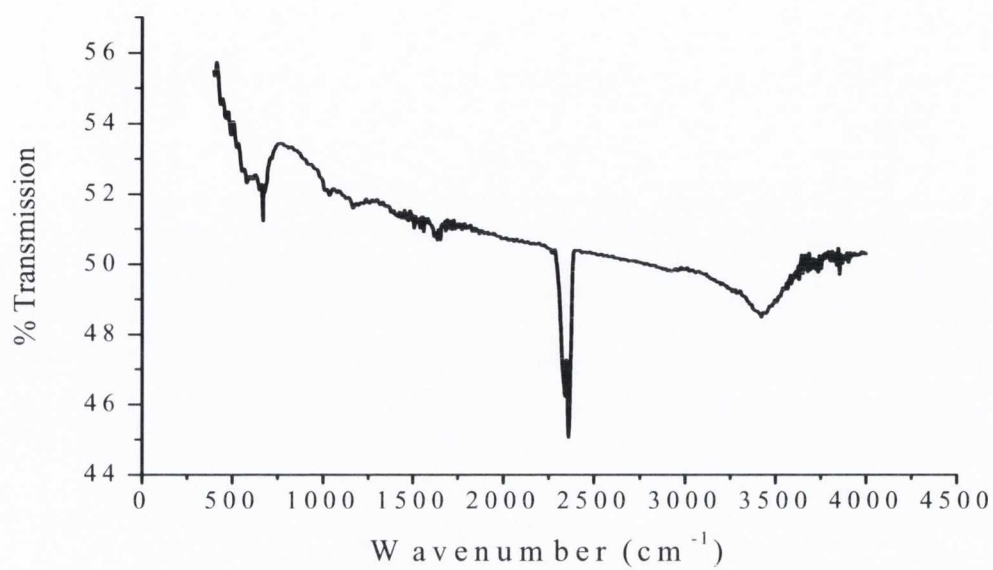


Figure A3.3: FTIR spectra of PSSS-MnFe₂O₄ nanoparticles prepared by co-precipitation.

Appendix 4

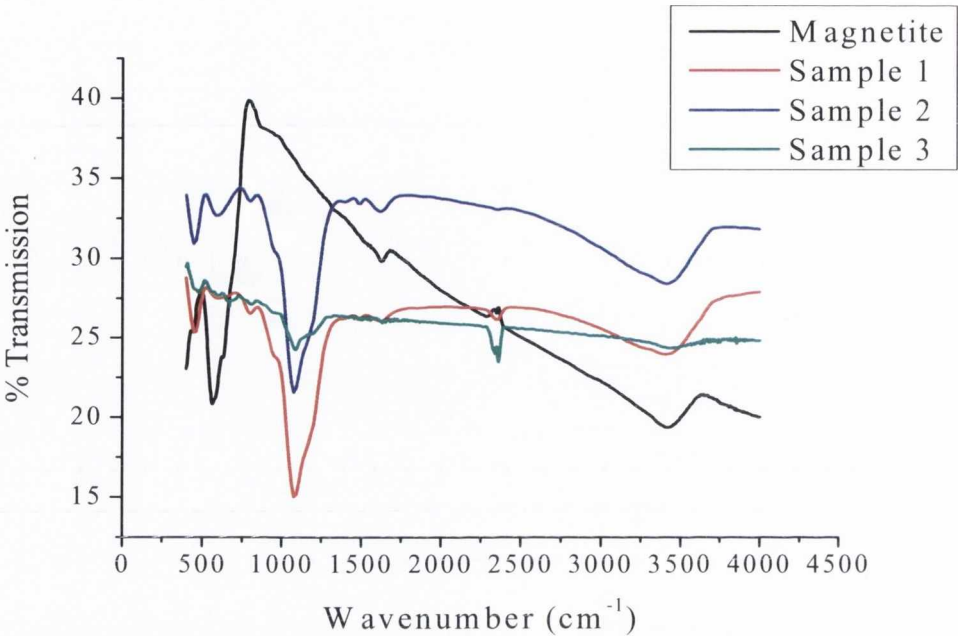


Figure A4.1: FTIR spectra of magnetite and silica coated magnetite nanocomposites, samples 1, 2 and 3, prepared according to Table 6.1, Chapter 6.

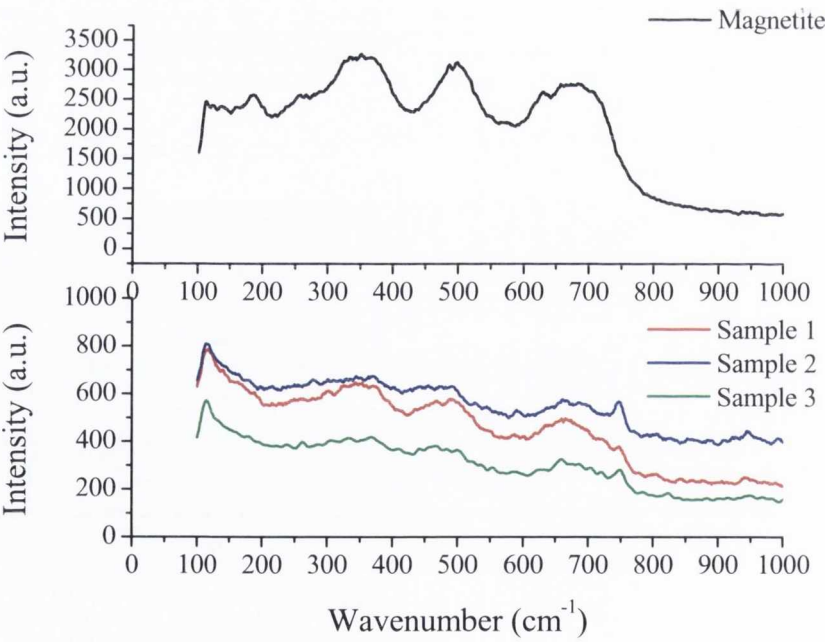


Figure A4.2: Raman spectra of magnetite and silica coated magnetite nanocomposites, samples 1, 2 and 3, prepared according to Table 6.1, Chapter 6.

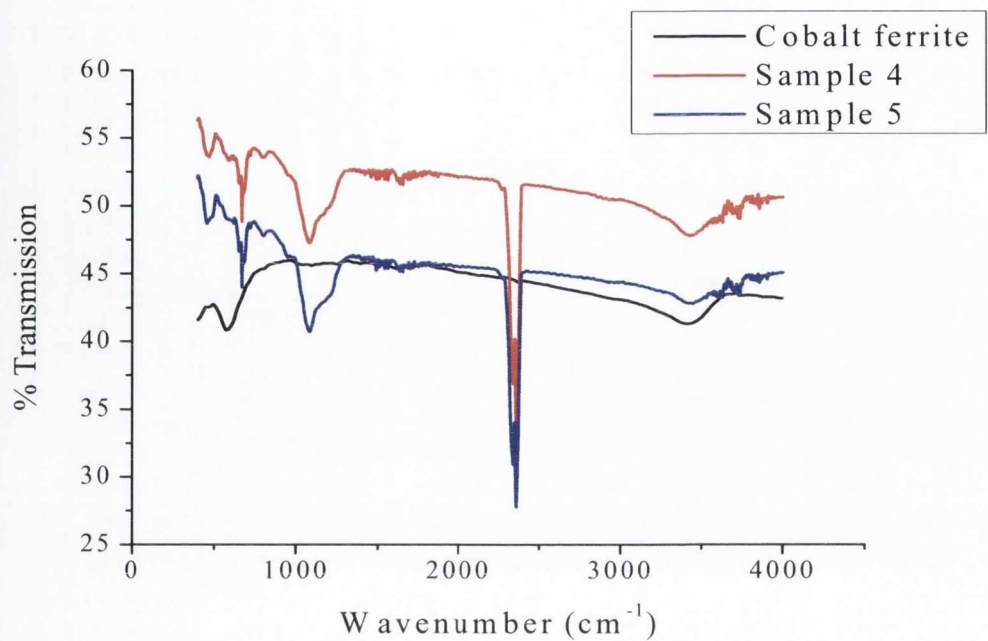


Figure A4.3: FTIR spectra of cobalt ferrite and silica coated cobalt ferrite nanocomposites, samples 4 and 5, prepared according to Table 6.2, Chapter 6.

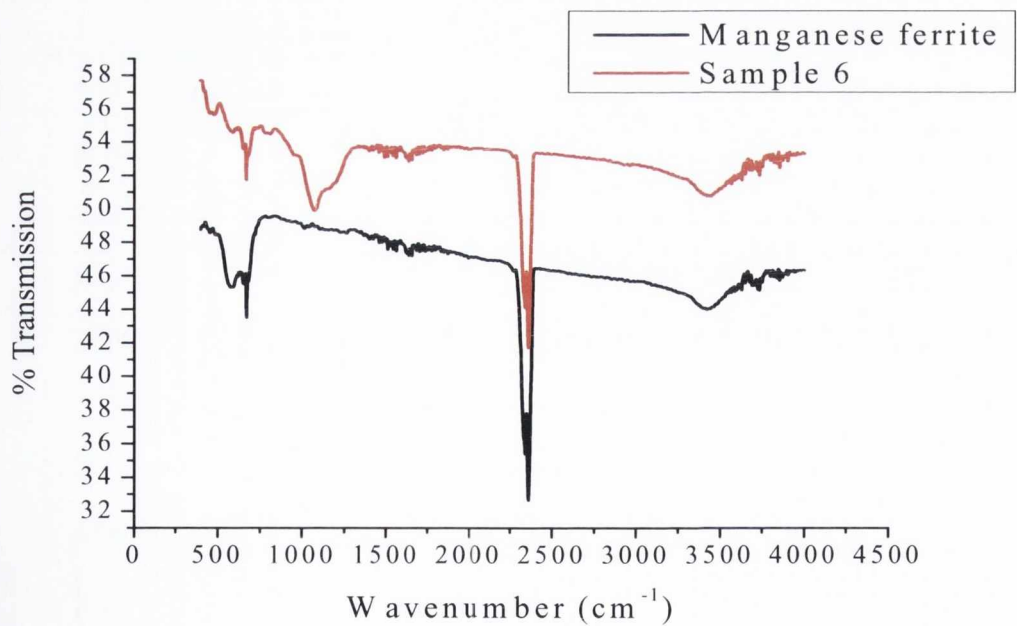


Figure A4.4: FTIR spectra of manganese ferrite and silica coated manganese ferrite nanocomposites, sample 6, prepared according to Table 6.2, Chapter 6.

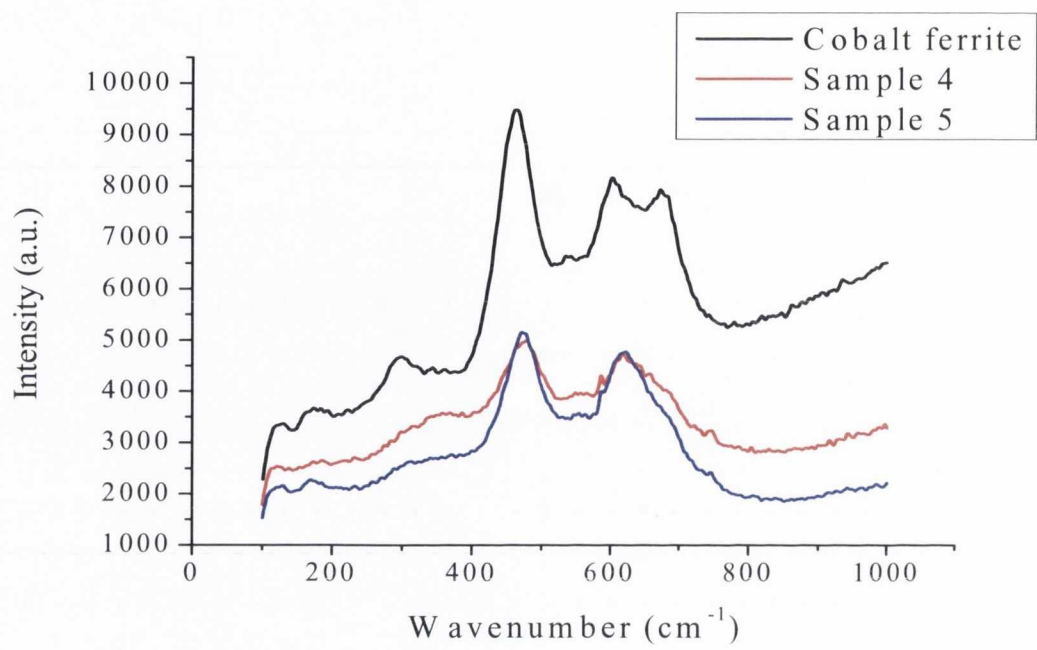


Figure A4.5: Raman spectra of cobalt ferrite and silica coated cobalt ferrite nanocomposites, samples 4 and 5, prepared according to Table 6.2, Chapter 6.

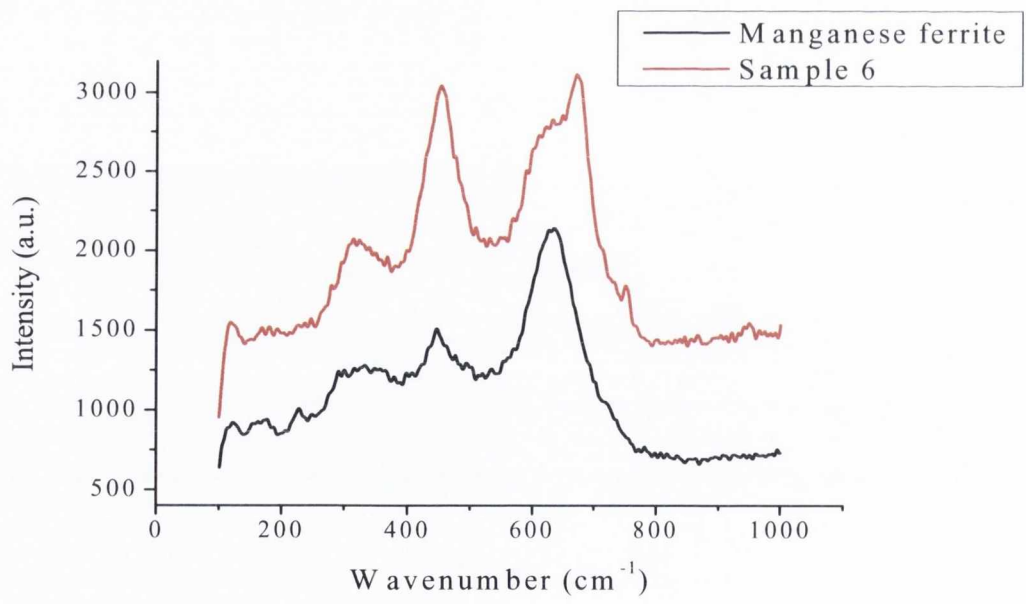


Figure A4.6: Raman spectra of manganese ferrite and silica coated manganese ferrite nanocomposite, sample 6, prepared according to Table 6.2, Chapter 6.

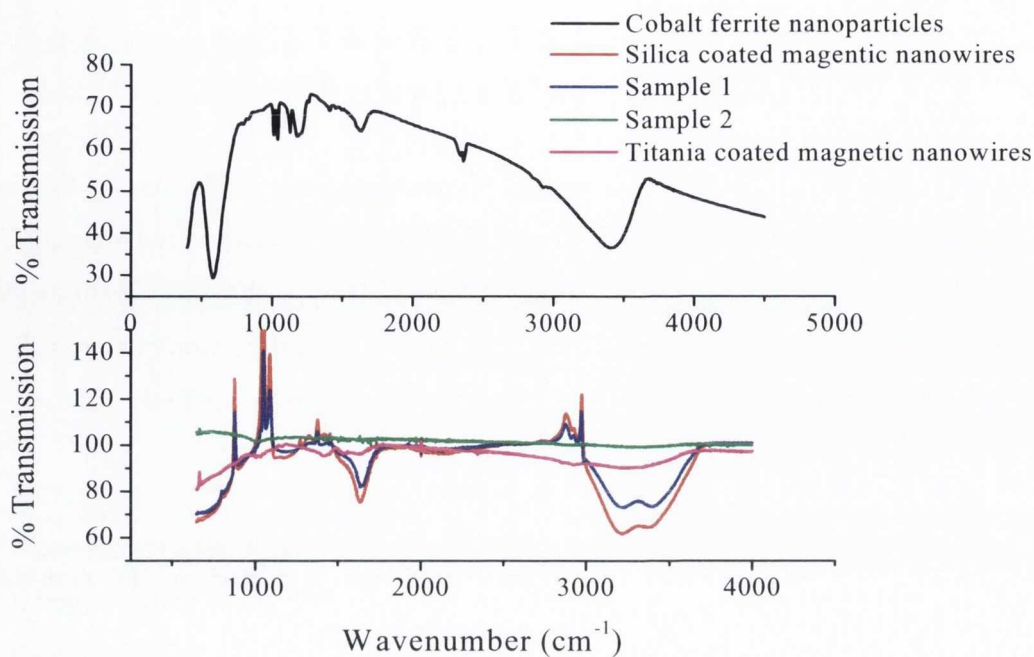


Figure A4.7: FTIR spectra of cobalt ferrite nanoparticles used to prepare the nanowires, silica coated magnetic nanowires, samples 1 and 2 of magnetic nanowires prepared according to Table 6.3, Chapter 6, and titania coated magnetic nanowires.

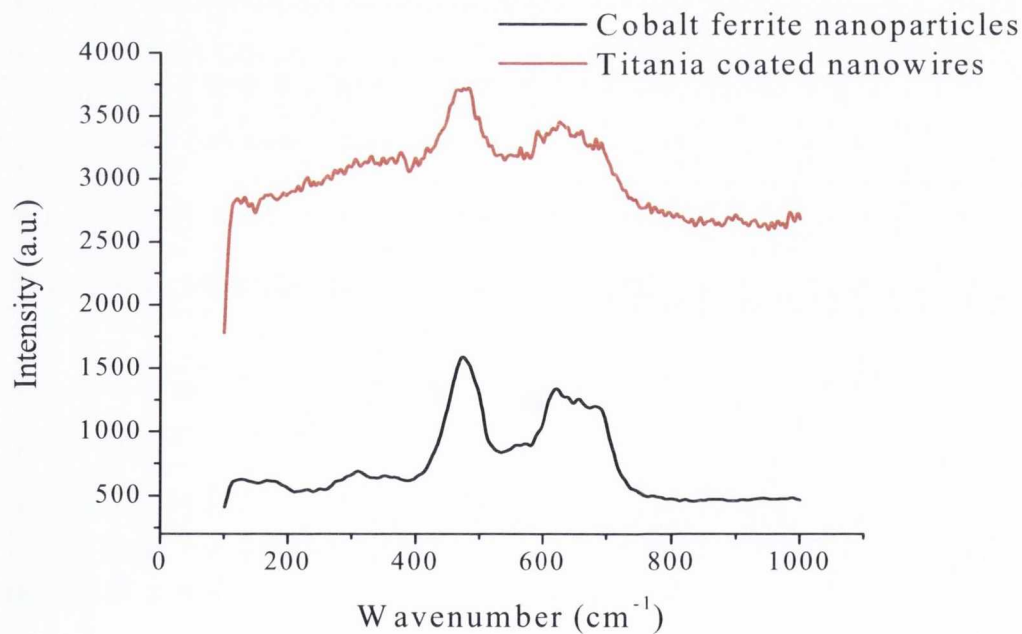


Figure A4.8: Raman spectra of cobalt ferrite nanoparticles used to prepare the nanowires and titania coated magnetic nanowires.

Publications and Patents

Book Chapter

- **Environmentally-safe Polymer-metal Nanocomposites with Most Favorable Distribution of Catalytically Active and Biocide Nanoparticles**

Amanda Alonso, Jorge Macanás, Gemma-Louise Davies, Yurii K. Gun'ko, Maria Muñoz and Dmitri N. Muraviev

Book: "Nanocomposites", ISBN 978-953-308-55-0, Publisher: InTech, 2011.

Publications

- **NMR Relaxation of Water in Nanostructures: Analysis of Ferromagnetic Cobalt-Ferrite Polyelectrolyte Nanocomposites**

Gemma-Louise Davies, Serena A. Corr, Carla Meledandri, Lionel Briode, Dermot F. Brougham and Yurii K. Gun'ko

ChemPhysChem, **2011**, 12, (4), 772.

- **Comparative Flow Cytometric Analysis of Immunofunctionalized Nanoparticle and Nanowire Signatures**

Adriale Prina-Mello, Áine M. Whelan, Ann Atzberger, Joseph E. McCarthy, Fiona Byrne, Gemma-Louise Davies, J. Mike D. Coey, Yuri Volkov and Yurii K. Gun'ko
Small, **2009**, 6, (2), 247.

- **Preparation and Size Optimisation of Silica Nanoparticles using Statistical Analyses**

Gemma-Louise Davies, Antoinette Barry and Yurii K. Gun'ko
Chemical Physics Letters, **2008**, 468, (4-6), 239.

- **Fabrication and Characterisation of Photonic Nanowires**

Joseph McCarthy, Áine M. Whelan, Gemma-Louise Davies, Fiona Byrne, Jennifer Conroy, Yuri Volkov and Yurii K. Gun'ko
Proceedings SPIE, **2008**, 7030, 703019.

- **Synthesis and Characterisation of New Silica and Aluminosilicate Nanoparticles**
Gemma-Louise Davies, Joseph E. McCarthy, Antoinette Barry and Yurii K. Gun'ko
Abstract P22, **2008**, International Conference on Nanoscience and Nanotechnology (ICONN).
- **Literature Article**
Gemma-Louise Davies, Aldo Peschiulli, Isabel Unwin, David Scanlon, Padraig Keane and Padraig Nagle
Irish Chemical News, **2008**, 24, 19.
- **Inflammatory and Fibrogenic Effects of Long Compared to Short Nickel Oxide Nanowires in the Lungs and the Peritoneal Cavity**
Craig Poland, Fiona Byrne, Wan-Seob Cho, Adriele Prina-Mello, Fiona Murphy, Gemma-Louise Davies, Yurii K. Gun'ko, Yuri Volkov, J. Mike D. Coey, Rodger Duffin and Ken Donaldson
Nanotoxicology, **2011**, *Submitted*.
- **Effects of Long-term exposure of Gelatinated and Non-gelatinated Cadmium Telluride Quantum Dots on Differentiated PC12 cells**
Babu R. Prasad, Gillian Mullins, Natalia Nikolskaya, David Connolly, Terry J. Smith, Valerie A. Gérard, Stephen J. Byrne, Gemma-Louise Davies, Yurii K. Gun'ko and Yury Rochev
Nanotoxicology **2011**, *Submitted*.

Patent

- **Magnetic Trans-Phase Formation of Nanomaterials with Surface Coatings YG01-299-01**
Gemma-Louise Davies and Yurii K. Gun'ko,
Patent, **2011**, *Pending*.

Presentations

Presentations

- **Tunable Cobalt Ferrite Based Magnetic Fluids for MR Imaging Applications**, Materials Research Society (MRS) Spring Conference, San Francisco, USA, *9th April 2010*.
- **Nanomaterials for Potential Biomedical Applications**, Karel de Grote University College Visiting Student Tour, Trinity College Dublin, Ireland, *9th November 2009*.
- **New Luminescent Silica Nanoparticles**, COST Meeting, Trinity College Dublin, Ireland, *24-25th September 2009*.
- **Optimisation and Preparation of Novel Luminescent Silica Nanoparticles**, NanoToday 2009 Conference, Singapore, *2-5th August 2009*.
- **New Silicate Materials on the Nanoscale**, Departmental Seminar, Trinity College Dublin, Ireland, *14th May 2009*.

Poster Presentations

- **Strategies for Design of Functional Nanomaterials**, Summer School on Preparative Strategies in Solid State and Materials Chemistry, University of California Santa Barbara (UCSB), USA, *13th August, 2010*.
- **New Silicate-Based Materials on the Nanoscale**, Nanomedicine Seminar and Workshop, Trinity College Dublin, Ireland, *29th June 2009*.
- **New Silica and Aluminosilicate Nanoparticles**, 2008 Symposium on Inorganic Chemistry in Ireland (RSC), Trinity College Dublin, Ireland, *26th September 2008*.
- **Photonic Nanowires – Synthesis and Characterisation**, Symposium on Inorganic Chemistry in Ireland (RSC), Trinity College Dublin, Ireland, *26th September 2008*.
- **Metallasiloxane complexes: Rings and cages**, Foundations of Crystallography, Osaka, Japan, *23-31st August 2008*.
- **Fabrication and Characterisation of Photonic Nanowires**, Optics and Photonics '08, San Diego, USA, *10-14th August 2008*.

- **Synthesis and Characterisation of New Silica and Aluminosilicate Nanoparticles**, International Conference on Nanoscience and Nanotechnology (ICONN), Melbourne, Australia, 25-29th February 2008.
- **Synthesis and Optimisation of Silica Nanoparticles**, IOM Materials for Microelectronics Conference, Trinity College Dublin, Ireland, 17-19th December 2007.