Emulsion droplets as reactors for assembling nanoparticles

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Metadata Record: https://dspace.lboro.ac.uk/2134/36206

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Emulsion Droplets as Reactors for Assembling Nanoparticles

By
Suchanuch Sachdev

A Doctoral Thesis
Submitted in partial fulfilment for the requirements for the award of Doctor of Philosophy of Loughborough University

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Abstract

Materials on the nanoscale have very interesting properties. Hence, they are commonly used for a variety of applications such as drug delivery, bio-imaging and sensing devices. Moreover, coating these particles with other materials forming core@shell or Janus particles can further enhance their properties. However, for the particles to be used in medical and electronic devices, their properties such as size, shape and composition need to be precisely controlled.

In this PhD., an emulsification technique was chosen to investigate the synthesis of nanoparticles; it is a simple process, does not require any harsh chemicals or temperature and is fast. Emulsification occurs when two or more immiscible liquids and surfactants are mixed. Here, emulsion droplets were produced using a microfluidic device which allowed for the creation of uniform droplets. These were employed as templates to synthesise and assemble nanomaterials. The main aim of the Ph.D. was to develop a droplet based synthesis process to generate nanoparticles and then assemble them into core@shell particles. This Ph.D., starts by synthesising Fe$_3$O$_4$ nanoparticles (~ 12 nm) and assembling them into microparticles (~ 1µm – 2µm) using emulsion droplets as microreactors. By tuning the surfactant, droplet size and evaporation rate of the dispersed phase, microparticles of varying shapes and sizes, such as spherical or crumbled shapes, were produced. When these particles are compared with the commercially available particles, the magnetic content of the in-house particles, or sometimes referred to as Loughborough University Enterprises Ltd. (LUEL), are much higher and more uniform, hence resulting in faster separation when used for extraction of analytes. LUEL particles were supplied as part of commercial collaboration.

The use of Pickering emulsions were then explored to create core@shell particles using gold nanoparticles instead of a surfactant to produce gold shells and the addition of pre-synthesised Fe$_3$O$_4$ nanoparticles results in Fe$_3$O$_4$@Au core@shell particles. This is the first time Pickering emulsions were used to produce Fe$_3$O$_4$@Au core@shell particles (~ 1.5 µm) within a microfluidic device. However, the shells were not uniform in thickness. In order to improve the coverage, nanoparticles were synthesised in situ at the droplet interface. By placing the gold chloride (AuCl$_4^-$) in the continuous phase and by varying the concentration of the electron donor in hexane droplet, single crystal
gold nanoparticles and platelets were formed. The reaction is spontaneous at room temperature, creating gold nanoparticles at the interface of the emulsion droplet. The size and shape of the gold nanoparticles were controlled by varying the concentration of the reactants and the size of the droplets. By adding pre-synthesised particles (Fe₃O₄ nanoparticles) to the droplet, Au@Fe₃O₄ core@shell particles were formed with an approximate size of 250 nm.

The same concept of forming core@shell particles using gold nanoparticles was further expanded by using other metal ions; palladium and silver. Unlike gold, palladium and silver only formed spherical nanoparticles, no platelets were observed. The addition of preformed iron oxide nanoparticles to the palladium results in core@shell particles. However, in the case of silver, no core@shell particles were formed. The study of the rate of reaction was conducted to understand the details of the mechanism.

Overall, the process developed in this Ph.D. study allows for the facile synthesis of core@shell particles in a rapid, high throughput reaction. In the future, it is believed it could be scaled up for commercial purposes.
Acknowledgement

I would like to use this opportunity to thank my supervisor, Dr. Mark Platt. I am extremely grateful for his guidance and advice throughout my Ph.D. He always believed in me and gave me words of encouragement even when things did not go as planned. Moreover, he was always accessible for questions and guidance whenever I struggled with anything. I couldn’t have asked for a better supervisor. I also want to thank my second supervisor, Dr. Steven Christie for his guidance. A special thanks to Dr. James O’Mahony for visiting Loughborough University in my first year of Ph.D. and giving advice on the use of microfluidics, his expertise has really helped me throughout my Ph.D.

Doing a Ph.D. is exciting and also stressful at the same time but I am extremely blessed to meet so many supportive and talented individuals during these three years. I would like to thank Dr. Emily Billinge, Dr. Emma Blundell, Laura Mayne, Sarah Hampson, Matthew Healey, Rhushabh Maugi, Marcus Pollard, Boakye Gyimah, Hazim Yusof, Andria Hadjithekl, Kurt Lawson, Jack Woolley, Arnab Guha and Neville Rebelo for all the help, support and fun times. I would like to thank Dr. Caroline Kirk for assisting me with XRD. And all the lab technicians in the Chemistry Department, Dr. Matthew Turner, Dr. David Belcher, Rod Dring and our safety officer Alastair Daley for their countless advice.

I would like to thank, Dr. Zhaoxia Zhou, Dr. Keith Yendall, Scott Doak and Shaun Fowler from the department of materials for training and assisting me with various equipment. I would also like to give a big thank you to Dr. Jagdeep Sagu for proof reading my thesis, helpful suggestions and being a great friend throughout.

Leaving my country and love ones behind to pursue my Ph.D. was a tough decision but it was all worth it in the end. After being in Loughborough for more than three years, it now feels like home to me, I owe it to my flat mates and friends. Thank you for all the love, fun and encouragement.

Lastly, I would like to thank my family. My father, for his constant love for science, has inspired me. My brother, for his endless jokes and encouragement, helped me to stay positive. And lastly the most important person in my life, my mother, who believed and instilled values in me to not just to be good in my field of study but also to use my knowledge for the good of mankind. I would like to dedicate my thesis to my mother, Anita Sachdev.
<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>SDS</td>
<td>Sodium dodecyl sulfate</td>
</tr>
<tr>
<td>LUEL</td>
<td>Loughborough University Enterprise Ltd.</td>
</tr>
<tr>
<td>NPs</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CV</td>
<td>Coefficient of variation</td>
</tr>
<tr>
<td>SPG</td>
<td>Shirasu Porous Glass</td>
</tr>
<tr>
<td>PDMS</td>
<td>Poly(dimethyl siloxane)</td>
</tr>
<tr>
<td>TOAB</td>
<td>Tetraoctylammonium bromide</td>
</tr>
<tr>
<td>CTAB</td>
<td>Cetyl trimethyl ammonium bromide</td>
</tr>
<tr>
<td>PBED</td>
<td>Poly(benzyl ether) dendron</td>
</tr>
<tr>
<td>CMC</td>
<td>Critical micelle concentration</td>
</tr>
<tr>
<td>CPP</td>
<td>Critical packing parameter</td>
</tr>
<tr>
<td>O/W</td>
<td>Oil-in-water</td>
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<tr>
<td>W/O</td>
<td>Water-in-oil</td>
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<tr>
<td>W/O/W</td>
<td>Water-in-oil-in-water</td>
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<tr>
<td>O/W/O</td>
<td>Oil-in-water-in-oil</td>
</tr>
<tr>
<td>SMPs</td>
<td>Superparamagnetic microparticles</td>
</tr>
<tr>
<td>SEM</td>
<td>Scanning electron microscopy</td>
</tr>
<tr>
<td>FEG-SEM</td>
<td>Field emission gun scanning electron microscopy</td>
</tr>
<tr>
<td>TEM</td>
<td>Transmission electron microscopy</td>
</tr>
<tr>
<td>FIB</td>
<td>Focused ion beam</td>
</tr>
<tr>
<td>SAED</td>
<td>Selected area electron diffraction</td>
</tr>
<tr>
<td>TRPS</td>
<td>Tunable resistive pulse sensing</td>
</tr>
<tr>
<td>SQUID</td>
<td>Superconducting quantum interference device</td>
</tr>
<tr>
<td>STEM</td>
<td>Scanning transmission electron microscopy</td>
</tr>
<tr>
<td>EDS</td>
<td>Energy dispersive X-ray spectroscopy</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>DmFc</td>
<td>Decamethylferrocene</td>
</tr>
<tr>
<td>HLB</td>
<td>Hydrophilic lipophilic balance</td>
</tr>
<tr>
<td>UV-Vis</td>
<td>Ultraviolet-visible spectrophotometry</td>
</tr>
<tr>
<td>12-MDA</td>
<td>12-mercaptododecanoic acid</td>
</tr>
<tr>
<td>16-MHDA</td>
<td>16-mercaptophexadecanoic acid</td>
</tr>
<tr>
<td>EELS</td>
<td>Electron energy loss spectroscopy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>RDS</td>
<td>Rate determining step</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full width half maxima</td>
</tr>
<tr>
<td>XRD</td>
<td>X-ray diffraction</td>
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<tr>
<td>PXRD</td>
<td>Powder X-ray diffraction</td>
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Chapter 1. Introduction

1.1. Emulsions

The term “emulsion” was introduced in the 17th century and originates from the Latin word “*mulgere*” which means “milky appearance”.\(^1\) Emulsions are made up of at least two phases, where one is hydrophilic, the other lipophilic.\(^2\) When one phase is dispersed in the other, droplets are formed.\(^2\) To lower the interfacial tension between the two phases and to stabilise the droplets thus to prevent coalescence, an emulsifier is usually added to the system.\(^3\) From both a theoretical and application point of view, emulsions have significant importance.\(^1\) Emulsions can be applied in areas including pharmaceutical\(^4\), cosmetics\(^5\), food\(^6\) and paints\(^7\). Emulsions also have a very important role in nanotechnology as they acts as templates for the synthesis of particles of various size and shapes.\(^8-11\)

There are many ways to generate emulsions, for example, using traditional methods (shaking, stirring, high pressure homogeniser)\(^1\), Couette shear devices\(^12,13,14\), membrane emulsification\(^15\) or microfluidic devices\(^16,17\). Equally, there are many ways to classify emulsions, it can be based on their size such as macro, micro or nano emulsions or it can be based on the number of phases they consist of; single, double or triple emulsions.\(^18\) However, this literature review explores different ways of generating single emulsions (oil-in-water and water-in-oil) which have been used as templates/mini reactors for generating iron oxide or metallic particles/assemblies. Other methods of synthesising particles without the use of emulsion droplets are also mentioned, for example, at the liquid-liquid interface.

1.1.1. Traditional emulsification methods

Traditionally, emulsions were formed by manual shaking, stirring (such as a simple stirrer, vibrator or rotor stator) and high pressure homogeniser.\(^1\) Many times researchers used the term “homogeniser” as a generic term for creating droplets but it could also be referred to as a specific device. According to Becher\(^1\), a homogeniser has a small orifice where mixtures are forced to go through under high pressure to generate emulsions. Based on similar principles, there are different types of homogenisers such as Gaulin homogeniser\(^1\) to more recent examples; ultrasonic homogenisers\(^19\). The emulsion droplets produced by these methods are small in size but typically have broad-size distributions.\(^20,21\) Furthermore, the energy and shear
force required to produce emulsions in these techniques is high\textsuperscript{20}, but in their favour is that these techniques are considered high throughput\textsuperscript{19}. High throughput means high production rate\textsuperscript{19}, although there is no strict definition.

1.1.2. Ultrasonic homogenisers
Several research groups have used homogenisers to generate emulsion droplets which acts as templates for assembling particles. Isojima et al.\textsuperscript{22} first synthesised iron oxide (Fe\textsubscript{3}O\textsubscript{4}) nanoparticles by mixing and heating iron tri(acetylacetonate), 1,2-tetradecanediol, oleyl amine, benzyl ether and oleic acid in the presence of nitrogen. It was then cooled down, purified and redispersed in hexane.\textsuperscript{22} These nanoparticles (~ 7 nm) were mixed with sodium dodecyl sulfate (SDS) using an ultrasonic homogeniser forming emulsion droplets. After the evaporation of the solvent, the nanoparticles were assembled into clusters (~ 150 nm).\textsuperscript{22} The droplets produced were between 800 nm – 1 µm and the clusters were between 150-180 nm.\textsuperscript{22} Superparamagnetic magnetite (Fe\textsubscript{3}O\textsubscript{4}) nanoparticles are used in various applications such as drug delivery, purification and in vivo imaging.\textsuperscript{22} However, the individual nanoparticles may not be useful in certain applications as they do not respond strongly to a magnetic field.\textsuperscript{22} Therefore, in order to keep the superparamagnetic properties (15-20 nm), the nanoparticles are assembled into clusters. This concept is used throughout the thesis (more detail in chapter 3).

Thompson et al.\textsuperscript{23} also used an Ultra Turrax homogeniser to generate Pickering emulsions. Pickering emulsions are emulsions that are stabilised by particles instead of molecular surfactants.\textsuperscript{23} Oil-in-water Pickering emulsions were prepared using poly(glycerol monomethacrylate)-stabilised polystyrene (PGMA\textsubscript{50}-PS) latex particles (230 nm) as the aqueous phase and sun flower oil as the organic phase, these were later used as a platform to produce colloidosomes.\textsuperscript{23} The emulsion droplets produced were polydisperse with a coefficient of variation (CV) of 74% as shown in Figure 1.1.\textsuperscript{23} Coefficient of variation is calculated using the equation 1.1; it is the ratio between standard deviation and mean of the samples (in this case, diameter of emulsion droplets).\textsuperscript{23} CV is usually presented in a form of percentage.
Coefficient of variation (%) = $\frac{\sigma}{\mu} \times 100$  \hspace{1cm} (1.1)

Where,

\[ \sigma = \text{standard deviation} \]
\[ \mu = \text{mean} \]

![Figure 1.1. Droplet size distribution for an oil-in-water emulsion prepared using aqueous solution of PGMA$_{50}$-PS latex particles (230 nm) and sunflower oil, homogenised using an Ultra Turrax homogeniser at the speed of 12000 rpm for 2 min. (B) Optical microscopy image of the generated emulsion (CV = 74%). Reprinted with permission from Langmuir (2011). Copyright 2018 American Chemical Society.](image)

1.1.3. Couette shear device

Over the years, many different emulsification techniques have been developed in order to have more control over the droplet size. Mason and Bibette were the first to present the approach of generating emulsions using a Couette shear mixer.$^{13}$ The device is made up of two cylinders between which is a narrow gap where typically premixed emulsions are pumped across the gap. The inner cylinder rotates and the outer cylinder remains fixed, the force of the rotating cylinder forms uniform droplets as shown in Figure 1.2.$^{12}$ The droplet sizes are mainly controlled by; the viscoelastic medium, speed of rotation and the gap between the two cylinders (narrower gaps produce monodispersed droplets).$^{12}$ The study by Mabille$^{12}$ and Mason$^{13}$ utilized premixed emulsions to achieve monodispersed droplets.$^{12,13}$

Similarly, O’Mahony et al.$^{24}$ also used a Couette type shear device to prepare emulsions. However, the design was modified to eliminate the premixed emulsion step where there are separate inlets for the organic phase and the aqueous phases.$^{24}$ The organic phase consists of a ferrofluid (iron oxide nanoparticles) stabilised by oleic acid in hexane and the aqueous phase consists of 25% dextran (to increase the viscosity)
and 2% SDS in water. When the two phases meet, droplets were formed. Once the solvent evaporates, nanoparticles within each droplet aggregates generating microparticles. Different morphologies of microparticles such as; spherical, dimpled and crumpled shaped, depends on the concentration of the ferrofluid. When the ferrofluid concentration was 1 g/L, the microparticles were spherical (as shown in Figure 1.3A). However, a dimpled and crumpled morphology was observed as the concentration decreased to 0.5 g/L and 0.1 g/L (as shown in Figure 1.3B-C). The cross section transmission electron microscopy (TEM) image in Figure 1.3D shows that even at high concentrations of ferrofluid, there is no internal void, hence during drying it forms a spherical shape. The authors hypothesize that, at lower concentrations of ferrofluid there are hollow cores hence during drying it buckles and collapses forming a dimple and crumpled shaped particle (Figure 1.3 E-F). Moreover, as the concentration of iron oxide decreases, the oleic acid concentration also decreases, reducing the hydrophobicity of the particles. This results in greater affinity for the water-oil interface. Hence, nanoparticles are locked at the interface of the droplets, forming dimpled and crumpled shapes at lower concentrations. These particles have an average diameter of 0.5 µm (maximum diameter of 1.2 µm) and a coefficient of variation of approximately 50%.
Figure 1.2. Schematic diagram of Couette shear device. The premixed emulsion was pushed from the syringe pump to the gap between rotor and stator. At the top of the mixer, sheared emulsion is obtained. ($R$ = inner radius, $\omega$ = angular velocity, $V_{\text{inj}}$ = injection velocity, $H$ = covering height between the inner cylinder (rotor) and outer cylinder (stator)). Reprinted with permission from Langmuir (2000). Copyright 2018 American Chemical Society.
A Couette shear device has higher throughput than membrane and microfluidic emulsification as it can produce up to 2 L/h. However, the emulsions produced are polydisperse and they are harder to make without adding something to increase the viscosity.

1.1.4. Membrane emulsification
Another technique of generating emulsions is referred to as membrane emulsification. Membrane emulsification was first introduced in the late 1980s by Nakashima and Shimizu. They fabricated a glass membrane called Shirasu Porous Glass (SPG) which was used to produce uniform water-in-kerosene and kerosene-in-water emulsions. This method is attractive as it consumes less energy and produces uniform droplets. More recent studies use other types of membrane, such as polymeric, ceramic, metallic and microengineered devices. In membrane emulsification, a dispersed phase is forced through a membrane containing uniform
pores, on the other side is the continuous phase.\textsuperscript{3} The droplet size is controlled by the pores of the membrane.\textsuperscript{3} Both oil-in-water and water-in-oil emulsions can be formed using this method.\textsuperscript{3} The advantage of this technique over conventional homogenisation and the Couette shear device is that it can produce a narrower droplet size distribution and is less energy intensive. However, a drawback is that it is not as high throughput.\textsuperscript{19} Most authors did not report the production rate of their products. However, Yanagishita \textit{et al.}\textsuperscript{15} reported that their membrane emulsification produced emulsion droplets 0.1 µL/min.cm\textsuperscript{-2} for a pore of 220 nm in size, while Mabille\textsuperscript{12} reported that their Couette mixer can produce emulsion droplets approximately 1 L/h to 2 L/h.

Many research groups have used membrane emulsification to synthesise and assemble various types of particles including, iron oxide\textsuperscript{19}, silica\textsuperscript{25,26,27}, Pickering\textsuperscript{23} and natural synthetic particles such as cellulose microbeads\textsuperscript{28}. Various sizes are reported, with a near monodispersed particle distribution. Membrane emulsification has produced particles of a very small size to a very large one (from 0.01 µm to 100 µm). They can be used to produce surfactant stabilised emulsions or Pickering emulsions.

Kakazu \textit{et al.}\textsuperscript{29} synthesized silver nanoparticles (approximately 10 nm) using water-in-oil emulsions produced by membrane emulsification. Emulsion droplets are formed where the dispersed phase consists of silver nitrate in water and the continuous phase consists of tetruglycerol condensed ricinoleate in kerosene. Hydrazine was later added to the emulsions droplets to complete the reaction. A schematic diagram of the process is shown in Figure 1.4. The emulsion droplets had an average size of 210 nm with a coefficient of variation of 20% while silver nanoparticles were reported to have a coefficient of variation between 15-20%.\textsuperscript{29} The particle size is usually much smaller than the emulsions droplets, this could be because the solvent evaporates forming particles or another reaction has taken place. Figure 1.5 shows the size gap between emulsion droplet and particle size.\textsuperscript{29}
Figure 1.4. Schematic diagram for the process of forming droplets using membrane emulsification and the formation of nanoparticle. 1) Shirasu porous glass membrane, 2) Continuous phase (kerosene containing tetracyglycerol condensed ricinoleate), 3) Dispersed phase (aqueous silver nitrate solution), 4) N$_2$ gas, 5) magnetic stirrer and 6) stirring bar. Using the nitrogen gas the dispersed phase (silver nitrate solution) was pushed through the membrane where it meets the continuous phase forming droplets. Hydrazine was added to these droplets, as it reduced silver ions to silver nanoparticles.$^{29}$ Reprinted from Journal of membrane science (2010). Copyright 2018, with permission from Elsevier.
Figure 1.5. Size distribution of water-in-oil microemulsion droplets and nanoparticles measured by Dynamic Laser Scattering (DLS) method. The solid line represents microemulsions and dotted line represent nanoparticles. Reprinted from Journal of membrane science (2010). Copyright 2018, with permission from Elsevier.

Several comparative studies between the two processes have been done. Chang et al.\textsuperscript{19} prepared clusters of magnetic particles where the dispersed phase consists of magnetite nanoparticles (approximately 10 nm) in hexane and the continuous phase consist of SDS in water forming emulsion droplets. The final magnetic clusters had a diameter of approximately 100–300 nm. The average relative variation of the membrane emulsification process was reported to be 6-8% while homogenisation was 22%. The difference in the products uniformity for the two process can be observed in Figure 1.6.

Manga et al.\textsuperscript{30} prepared oil-in-water Pickering emulsions using silica particles for stabilization. Silica particles in sodium chloride solution were the continuous phase while tricaprylin oil was the dispersed phase. The oil phase was pushed through the membrane into the continuous phase as shown in Figure 1.7.\textsuperscript{30} They also conducted the same experiment but using a homogeniser. The coefficient of variation of membrane emulsification was reported to be approximately 30% while homogenization was approximately 75%.\textsuperscript{30}

Thompson et al.\textsuperscript{23} prepared oil-in-water Pickering emulsions using PGMA\textsubscript{50}-PS latexes. Using a stirred-cell membrane, where the aqueous phase consists of PGMA\textsubscript{50}-PS latex and the oil phase consists of sunflower oil, Pickering emulsions were formed. While conventional homogenisation produced droplets with a coefficient of variation of 74%, stirred cell membrane emulsification can reduce the coefficient of

\textsuperscript{9}
variation to 25%. By adding oil-soluble tolylene 2-4-diisocyanate-terminated poly(propylene glycol), it acts as a crosslinker forming colloidosomes. The particle size is approximately 50 µm.

Figure 1.6. Comparison of magnetic clusters generated by a) membrane emulsification b) ultrasonic homogenization. Reprinted with permission from Langmuir (2012). Copyright 2018 American Chemical Society.
Figure 1.7. a) Schematic diagram of the stirred cell membrane emulsification, (b) optical image of the hydrophilic nickel membrane used and (c) oil droplets was push through the membrane into the continuous (aqueous) phase consisting of silica nanoparticles. Reprinted with permission from Langmuir (2017). Copyright 2018 American Chemical Society.

Shang et al. produced magnetic microparticles using premixed emulsions consisting of a ferrofluid in hexane, benzophenone (polymerization initiator) and SDS. This was then pushed through a membrane with uniform pores (2 or 5 µm) forming smaller droplets. Hexane was evaporated forming solid particles and nonylphenoxy propenyl polyethylene alcohol surfactant and acrylic acid monomer were added. It was then exposed to ultraviolet light where polymerization took place, thus generating microparticles. The average diameter of the microparticles is 0.66 ± 0.33 and 0.43 ± 0.20 µm for the pore diameter of 5 and 2 µm, respectively, and coefficient of variance was 45%.

O’Brien et al. generated cellulose microbeads using membrane emulsification. The cellulose beads were formed from water-in-oil emulsions where the dispersed phase consists of microcrystalline cellulose dispersed in 1-ethyl-3-methylimidazolium acetate and dimethyl sulfoxide (30:70) and the continuous phase consists of Span 80 in sunflower oil. Different sizes of microbeads were formed by varying different parameters such as concentration and flow rate. Dragosavac et al. prepared mesoporous spherical silica particles using metal microsieve-type membrane emulsification. The particles produced are near-monodispersed with a size between 30 to 70 µm and it is formed from water-in-oil emulsions, where the aqueous phase is sodium silicate solution acidified using sulphuric acid and the oil phase is kerosene.
containing span-80 as surfactant. The coefficient of variation, of the particles, was approximately 35%. Yuan et al. prepared oil-in-water Pickering emulsions using silica particles for stabilization. Cross-flow membrane emulsification was used, where silica particles in aqueous solution (continuous phase) and polymeric resin in ethyl acetate solution in oil (dispersed phase). The dispersed phase passes through the membrane pores forming oil droplets, these droplets were stabilised by the emulsifier (silica particles) in the continuous phase as shown in Figure 1.8.

Figure 1.8. Schematic representation of a cross-flow membrane emulsification, on the right it shows oil droplet pressured through the membrane and stabilised by nanoparticles in the continuous phase. Reproduced from Soft Matter (2010) with permission of The Royal Society of Chemistry.

A narrower droplet size distribution is achieved by the membrane emulsification technique compared to the traditional emulsification method and the Couette shear device. In addition, the energy consumption is much lower as the droplet size is controlled by the pores of the membrane. However, the rate of production is not as high throughput compared to Couette shear devices.

1.1.5. Microfluidics emulsification

Microfluidics is another technique used to generate particles such as janus, rods, discs and porous particles. The components can be made up of poly(dimethylsiloxane) (PDMS), silicon, ceramic, stainless steel or glass. The most common material for chemists is glass as it enables “optical transparency” and is chemically inert. Silicon materials are also of interest as it can be used in various fabrication methods and also sometimes used as part of the electrical circuits. Microfluidics enables the flow of the
liquids to be controlled and adjusted hence generating very uniform droplets. These droplets usually contain precursors which get solidified in the channel, resulting in monodisperse particles. Monodisperse particles are very crucial especially in the application of drug delivery as it can reduce unwanted side effects and control the encapsulation and kinetics of the drug release more effectively. The technique uses a small amount of liquid (10⁻⁹ to 10⁻¹⁸ litres) and the fluid is easy to control. There are mainly three types of microfluidics for single emulsions; T-junction, flow-focusing and co-flow (Figure 1.9).

1.1.5.1. T-junction

Thorsen et al. were the first to propose the T-junction geometry for the production of droplets. As shown in Figure 1.9A, the dispersed phase is perpendicular to the continuous phase. Upon entering the main channel, the dispersed phase gets pressurized and shears off at the neck of the channel. Droplets formed usually have an oblong shape as droplets are confined by the walls. Dendukuri et al., generated droplets containing 1% SDS (continuous phase) and a polymer in the dispersed phase is photopolymerised in the channel by ultraviolet light forming non-spherical particles; plugs and disks shaped. By reducing the height of the channel from 38 to 16 µm, the droplet’s shape changed from plug to disk shaped before being exposed to UV-light as shown in Figure 1.10.

Figure 1.9. Schematic diagram of microfluidic geometries: A) T-junction B) flow-focusing C) co-flowing. The flow rates of the disperse phase and continuous phase are represented as Q_d and Q_c. Reproduced from ChemPhysChem (2014), with permission of John Wiley and Sons.
Figure 1.10. a) Schematic diagram of the T-junction channel that used to generate plug and disk shaped particles. Reprinted with permission from Langmuir (2005). Copyright 2018 American Chemical Society.

1.1.5.2. Flow-focusing

Anna et al. first introduced flow-focusing for the production of droplets. As shown in Figure 1.9B, the continuous phase (two channel) and the dispersed phase (one channel) meets at the orifice. Hence, there is the consistent breakup of the droplets resulting in a narrow size distribution. With flow-focusing there is greater control of droplets sizes. Droplets formed in this geometry are usually confined at the centre of the microchannel, hence there is less chance of contacting the channel wall and causing wetting of the channel walls. For example, Xu et al. produced drug loaded microparticles by using flow-focusing microfluidic channel made by PDMS. The continuous phase consists of aqueous 1% poly(vinyl alcohol) solution and the disperse phase consists of poly (lactic-co-glycolic acid) in dichloromethane, when the two solutions meet at the junction, droplets are formed. These droplets get collected in a flask which contains Tris buffer with a pH of 8.5. The microparticles produced are ~28 µm in size and they are monosdisperse (coefficient of variation = 3.9%).

1.1.5.3. Co-flowing

Umbanhowar et al. implemented co-flow geometry for the production of droplets. As shown in Figure 1.9C, there are two channels of continuous phase (concentric channels) and the dispersed phase is the inner channel. Jeong et al., generated droplets using co-flow microfluidic channel, where the disperse phase consists of
polymerizable sample fluid and the continuous phase consists of immiscible nonpolymerizable fluid, droplets were formed and becomes solidified by the UV light. Depending on the flow rate, the particles produced were between 70 to 260 µm and the coefficient of variation was less than 2%. Paquet et al.\textsuperscript{33} produced uniform porous superparamagnetic microparticles using a co-flow microfluidics device. The dispersed phase consisted of superparamagnetic nanoparticles in toluene and a copolymer while the continuous phase consists of water, glycerol and poly(vinyl alcohol).\textsuperscript{33} Droplets were produced and collected in SDS solutions. By varying the polarity of the solvent and the critical micelle concentration of SDS, the particles produced are porous the coefficient of variation of the particles are between 2-8 %.\textsuperscript{33} Although the authors did not specifically mention the size of their particles, from their SEM data, the particle size was approximated to be between 80-100 µm.

1.1.5.4. Other types of channels
Apart from the three main types of channels, there are other types of channel that have been adapted and modified for their specific research. For example, Watanabe et al.\textsuperscript{37} produced monodispersed polylactide microcapsules using a Y-shaped microfluidic device using oil-in-water emulsions as the template. The dispersed phase consists of poly(D,L-lactide), ethyl acetate and perfluoroctyl bromide while the continuous phase consists of an aqueous solution containing poly(ethylene glycol)-b-poly(D-L-lactide) which acts as surfactant and results in the formation of droplets\textsuperscript{37}. These droplets were monodispersed and after the diffusion of solvent, a core-shell is formed. Edel et al.\textsuperscript{48} generated cadmium sulfide nanoparticles using a microfluidic device by introducing aqueous cadmium nitrate and sodium sulfide into the channel using a syringe. The design of the channel was developed by Bessoth et al.\textsuperscript{49}, which consists of multichannels. By increasing the flow rates in the channel, polydispersity decreases.\textsuperscript{48} When compared with bulk reactions, the miniaturisation of the microfluidic device enables homogeneity throughout the reaction which reduces coalescence.\textsuperscript{48}

1.1.5.5. Pickering emulsions in microfluidics channel
When water-in-oil, oil-in-water or double emulsions are stabilised by solid particles instead of surfactants, it is called Pickering emulsions.\textsuperscript{50} Similar, to membrane emulsification, microfluidics can generate both oil-in-water and water-in-oil emulsions.
They can also produce both surfactant stabilised emulsions and particle stabilised emulsions.

Microfluidic devices also enable the production of Pickering emulsions which act as templates to produce colloidosomes. Shah et al.\textsuperscript{51} generated Pickering emulsions using a flow focusing microfluidic channel where the dispersed phase consists of aqueous poly(N-isopropylacrylamide) microgels containing glutaraldehyde and the continuous phase consists of a surfactant in silicon oil. Glutaraldehyde was added to enable crosslinking forming colloidosomes. Similarly, Nie et al.\textsuperscript{52} produced oil-in-water Pickering emulsions using a microfluidic device, where the dispersed phase consists of photoinitiator 2,2-dimethoxy-2-phenyl-acetopheneone, poly(divinyl benzene-methacrylic acid) particles and tripropylene glycol diacrylate while the continuous phase consists of NaOH forming emulsions. These emulsions were then exposed to UV-irradiation, photopolymerization results in the formation of supracolloidal microspheres as shown in Figure 1.11. Although the authors did not specifically mention the size of their particles, from the SEM image, the particle size was approximated to be 80 µm.

![Figure 1.11. a) SEM image, Scale bar = 40 µm (b) and confocal fluorescence microscopy of polymer microspheres with poly(divinyl benzene-methacrylic acid) particles as shell, scale bar = 60 µm.\textsuperscript{52} Reprinted with permission from J. Am. Chem. Soc. (2008). Copyright 2018 American Chemical Society.](image_url)

1.1.5.6. Wettability of the microfluidic channel

The microfluidic channels are usually made up of PDMS or glass capillary.\textsuperscript{40} The type of emulsions formed depends on the wettability of the channel.\textsuperscript{40} When a solid (in this case the channel wall) preferred to have contact with one type of liquid over the other, it describes as “wettability”.\textsuperscript{53} For example, to produce oil-in-water emulsions, the
channel walls need to be hydrophilic in order to allow the continuous (aqueous) phase to flow along the channel without wetting it with oil droplet. Polenz et al.\textsuperscript{54} used a microfluidic device to generate oil-in-water or water-in-oil emulsions as a template to produce polyurea microcapsules. To form oil-in-water emulsions, a glass capillary microfluidic channel was treated with 2-[methoxy(polyethylenoxypropyl)]-1 trimethoxysilane to make the surface hydrophilic to avoid wettability with the oil phase on the capillary wall. The dispersed phase consisted of 2,4-toluene diisocyanate in cyclohexane and the continuous phase consisted of aqueous solutions of tetraethylenepentamine.\textsuperscript{54} When the two phases meet they form polyurea microcapsules. To avoid blockages, another continuous phase (SDS) was added which flows in the same direction as the dispersed phase to prevent clogging.\textsuperscript{54} Polyurea microcapsules were also formed by using water-in-oil emulsions as a template. The glass capillary was treated with trimethoxy (octadecyl) silane which makes it hydrophobic.\textsuperscript{54} The dispersed phase consists of aqueous solution of tetraethylenepentamine while the surfactant and continuous phase were Abil EM 90 and of 2,4-toluene diisocyanate in cyclohexane, respectively. The particles produced have a size range between 50 – 100 µm, with a polydispersity between 4 - 6 %.

1.1.6. Summary of ways to make emulsions

By comparing the three methods, we can see that homogenisers and Couette shear devices have the highest throughput but the least uniformity, while microfluidic device produce monodisperse particles they are not as high throughput.\textsuperscript{24} Membrane emulsification lies between the two techniques.\textsuperscript{30} It depends on the applications in which the particles are intended for. For drug controlled delivery, then it’s important to use a highly monodisperse particle distribution. As this has an effect on the kinetics of drug release.\textsuperscript{39} A major challenge in producing particles for commercial applications is the uniformity and limited throughput associated with the production methods. However, microfluidics is ideal for the production of uniform particles with minimal reagents at the research and development stage as it shows promise to be scaled up in the future, for example by increasing the number of output channels.\textsuperscript{55} In this thesis, the particle size distribution that have a coefficient of variation more than or equal to 50% are considered polydisperse, between 15 and 25% are considered near-monodisperse and less than or equal to 15% are considered monodisperse. The summary of each emulsification techniques is shown in Table 1.1.
Table 1.1. Summary of Couette shear device, membrane emulsification and microfluidic techniques

<table>
<thead>
<tr>
<th>Properties</th>
<th>Couette shear device</th>
<th>Membrane emulsification</th>
<th>Microfluidics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Coefficient of variation</td>
<td>≥ 50%</td>
<td>15% ≤ - ≤ 25%</td>
<td>≤ 15%</td>
</tr>
<tr>
<td>2. Particle size distribution</td>
<td>Polydisperse</td>
<td>Near monodispersed</td>
<td>Monodispersed</td>
</tr>
<tr>
<td>4. Particle size</td>
<td>Depends on the viscosity of the fluids and flow rate</td>
<td>Depends on the membrane pore size and flow rate</td>
<td>Depends on the channel’s height and width and flow rate</td>
</tr>
<tr>
<td>5. Other comments</td>
<td>High throughput</td>
<td>Medium throughput</td>
<td>Low throughput but has the potential to scaled up</td>
</tr>
</tbody>
</table>

1.2. Liquid-liquid interface

Due to the nature of emulsion droplets, we now spend some time discussing reactions at liquid-liquid interfaces. When organic and aqueous solutions meet, a bilayer is formed called a liquid-liquid interface. The environment of the liquid-liquid interface is unique due to the discontinuity in physical properties caused by the interface. The contribution made by Marken, Girault, Dryfe, and more recently by Platt and Booth are significant in understanding the concept and applying them to several areas of research. There are various types of reactions that is of relevance to this thesis such as ion transfer, electron transfer and particle adsorption. The mechanism of each technique will be discussed in chapter 2.

The formation of metal nanoparticles at the liquid-liquid interface can be done by applying an external current or without applying any current. However, for the literature review, the focus will be on particle adsorption and electron transfer that leads to particle synthesis processes without applying any external current as it is most relevant.

1.2.1. Particle adsorption

Kumar et al. assembled gold nanoparticles at the liquid-liquid interface. After vigorous shaking of a gold hydrosol (ruby red aqueous phase) and benzene
(colourless organic phase), the aqueous phase becomes colorless and the organic phase is blue in colour. This indicates that there was phase transfer of gold nanoparticles from aqueous to the organic phase. The change in colour from ruby red to blue indicates the presence of gold nanoparticle aggregates. A thin film of gold nanoparticles was also observed at the liquid-liquid interface after 30 minutes.\textsuperscript{73} Similarly, after vigorous shaking of anthracene in hexane (colourless) and gold hydrosol (coloured), a film of gold nanoparticles was observed at the liquid-liquid interface.

Reincke \textit{et al.}\textsuperscript{72} formed gold nanocrystals at the liquid-liquid interface when ethanol was added to the immiscible layer between gold citrate in water and heptane. Figure 1.12 shows the immiscible layer before adding ethanol (left) and after adding ethanol (right).\textsuperscript{72} After the addition of ethanol, gold nanocrystals (blue layer) was formed between water and oil phase. The reason is because ethanol reduces the charge on the surface of gold citrate, this changes the contact angle of gold citrate between the two immiscible liquids to $90^\circ$.\textsuperscript{72} This enables the gold particles to coalesce and form a monolayer.\textsuperscript{72} The TEM image of the gold nanocrystals is shown in Figure 1.13.\textsuperscript{72}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{image1.png}
\caption{Left: two immiscible layers between aqueous gold solution (pink) and heptane (colorless); right: After the addition of ethanol, a gold film (blue) was formed at the interface.\textsuperscript{72} Reproduced from Angew. Chem. Int. Ed. (2004), with permission of John Wiley and Sons.}
\end{figure}
To help assemble nanoparticles at the interface, a ligand is sometimes needed to change the hydrophobic/hydrophilic nature of nanoparticles. Duan et al.\textsuperscript{74} studied the use of ligands to cap nanoparticles at the water and oil interface. Gold citrate in water was capped with the ligand 2,2-dithiobis[1-(2-bromo-2-methyl-propionyloxy)ethane] (DTBE) forming Au@DTBE (Figure 1.14a) and the addition of toluene formed a gold film at the interface (figure 1.14b).\textsuperscript{74} A TEM image of gold nanoparticles formed at the interface between water and toluene is shown in Figure 1.15.\textsuperscript{74} Aqueous silver nanoparticles were also capped with DTBE (Ag@DTBE) and the addition of toluene formed a silver film at the interface. Lee et al.\textsuperscript{75} used 4-aminobenzo-15-crown-5-hydrotetrafluorurate (Ligand L) for the formation of the gold film. After Ligand L was added to the two immiscible liquids; gold hydrosol (wine red aqueous phase) and diethyl ether (colourless organic phase), the aqueous phase becomes colourless and there was a formation of a thin layer of gold which has a blue transmittance.\textsuperscript{75} This indicates that the gold nanoparticles transfer from the aqueous phase to the thin film. A UV-spectrum of the gold film and gold hydrosol (starting material) was recorded. Gold hydrosol has a peak at 525 nm (solid line) but when a gold film formed at the interface, the peak was red-shifted to 730 nm (dashed line) as shown in Figure 1.16.\textsuperscript{75}
Figure 1.14. a) Structure of Au@DTBE b) Photograph of the formation of Au@DtBE nanoparticles at the water/toluene in an Eppendorf tube. Reproduced from Angew. Chem. Int. Ed. (2004), with permission of John Wiley and Sons.

Figure 1.15. TEM image of gold nanoparticles formed at the interface between water and toluene, inset shows high magnification of the particles (scale bar is 25 nm). Reproduced from Angew. Chem. Int. Ed. (2004), with permission of John Wiley and Sons.
1.2.2. Electron transfer at the liquid-liquid interface

Electron transfer at the liquid-liquid interface occurs when one phase consists of an oxidizing agent (for example, metal precursor) and the other phase consists of a reducing agent. When the oxidizing agent is a metal ion, this can lead to the formation of a metal film at the interface which enables particles to grow and assemble in situ without the use of pre-formed particles. Rao et al. synthesized metal nanocrystals in situ, using this technique. A gold film was formed after adding Tetrakishydroxymethylyphosphonium chloride (THPC) to the bilayer containing Au(PPh₃)Cl in toluene (organic phase) and NaOH solution (aqueous phase). A TEM image of gold film formed at the interface is shown in Figure 1.17. The TEM image shows gold nanocrystals with an average diameter of 9 nm (Figure 1.17 inset). Similarly, silver and copper films can be formed with Ag₂(PPh₃)₄Cl₂ and Cu(PPh₃)Cl. Nanocrystalline CdS films can also be formed by adding n-octylamine to cadmium cupferronate (Cd(cup)₂) in toluene (organic phase) which is then added to the Na₂S in water (aqueous phase).

Another study shows that adding surfactants such as tetraoctylammoniumbromide (TOAB) and cetyltrimethylammoniumbromide (CTAB) has an effect on the shape of the nanostructures formed between the liquid-liquid interface. For example, Agarwal et al. used TOAB to transfer AuCl₄⁻ from the aqueous phase to toluene (organic phase). This was followed by the addition of triphenylphosphine (PPh₃) which changes
the colour of the organic layer to colourless. To enable reduction to occur at the interface, hydrazine was added. The SEM image in Figure 1.18 shows the morphology of the gold particles obtained from the liquid-liquid interface; the high-resolution image (top inset) shows that it has a cauliflower-like morphology and an average size of 700 nm (lower inset).
The reports of nanoparticles formed at the liquid-liquid interface mentioned above occurred without the use of any template. Nanoparticles formed in this way have the tendency to form structures that are “ill-defined” or form aggregates.\textsuperscript{57,65} Hence, many studies have used templates at the liquid-liquid interface where the reduction of metals occurred on a solid substrate such as track-etched polyester membranes and γ-alumina.\textsuperscript{57,79} Platt \textit{et al.} \textsuperscript{65} formed palladium particles on a γ-alumina membrane. The membrane was placed between the aqueous phase (tetrachloropalladate in water) and the organic phase (butylferrocene in 1,2-dichloromethane)\textsuperscript{65}. However, using a template could cause defects.\textsuperscript{65} This means that surface of the template may not be consistent, for example it could have grain boundaries present, this may affect the nucleation process of the particles.\textsuperscript{57}

Reactions at the liquid-liquid interface were originally a concept occurred from the interface between two immiscible electrolyte solutions (ITIES), where the two immiscible liquids are electrolyte solutions.\textsuperscript{80} In 1996, Cheng and Schiffrin formed gold particles at the interface between two immiscible electrolyte solutions; tetraoctylammonium tetrachloroaurate (TOAAuCl\textsubscript{4}) in 1,2-dichloroethane and potassium hexacyanoferrate (II) (K\textsubscript{4}Fe(CN)\textsubscript{6}).\textsuperscript{81} To date, the study of ITIES is very popular and is used to generate different types of particles, few examples are shown in Table 1.2.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|p{10cm}|c|}
\hline
Metal & Reducing agent & Experimental method & Reference \\
\hline
Ag & Butylferrocene & Externally polarized pipettes were used to support liquid-liquid interface reactions & 82 \\
\hline
Ag & Decamethylferrocene & Deposition of silver particles by using scanning electrochemical microscopy (SECM) & 83 \\
\hline
Au & Decamethylferrocene & Deposition of gold particles by using organic film modified electrodes & 84 \\
\hline
Pd & Butylferrocene & Spectro-electrochemistry was used to analysed the process involved at the liquid-liquid interface by applying potential difference & 85 \\
\hline
\end{tabular}
\caption{Formation of different types of metals from ITIES reactions\textsuperscript{80} }
\end{table}
1.2.3. Flask to flow-reactor

Over the years, use of liquid-liquid interfaces to conduct reactions to produce nanoparticles has progressed from doing the process in flasks to using microreactors\textsuperscript{86}. In a flask there could be inhomogeneity of metal ions and reducing agent leading to random nucleation which results in particles that are polydispersed.\textsuperscript{86} In addition, due to long mixing, there could be competition for metal ions between the nucleation step and the growth step. To avoid prolonged mixing, a flow reactor was used where mixing happens in a short period of time as the platform is small (micrometer).\textsuperscript{86} Moreover, the technique is highly reproducible and robust which can be scalable.\textsuperscript{86}

Wagner \textit{et al.}\textsuperscript{87} were the first group to generate gold nanoparticles using a microreactor. The microreactor consists of two micromixers, the first micromixer is where ascorbic acid (reducing agent) and gold seeds are mixed and chloroauric acid was added to the second mixer as shown in Figure 1.19.\textsuperscript{86,87} The gold particles obtained are 24 nm in size. The drawback of this method is that there was gold deposition stuck on the wall and the particles were polydispersed. Tsunoyama \textit{et al.}\textsuperscript{88} synthesized polyvinylpyrrolidone (PVP) gold nanoparticles using a micromixer with a multi-parallel channel. Gold precursor (Au and PVP) and aqueous sodium borohydride were mixed via a multichannel as shown in Figure 1.20. The gold nanoparticles generated are 2 nm in size with a 14\% monodispersity. Kohler \textit{et al.}\textsuperscript{89} generated Au/Ag core-shell using two micromixers. The first micromixer consists of ascorbic acid and gold aqueous solution. These two solutions mixed to form gold seeds/nuclei, which passed through silver nitrate in the second mixer forming Au/Ag core-shell, Au and silver particles at the same time.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image.png}
\caption{Microreactor for the synthesis of gold nanoparticles. There are three injection points and one outlet; A) 12 nm gold seeds B) Ascorbic acid, C) HAuCl4 and D) gold nanoparticles.\textsuperscript{87} Reprinted from Chem. Eng. J. (2004). Copyright 2018, with permission from Elsevier.}
\end{figure}
In the early days, use of the liquid-liquid interface to make particles started in a flask, but now, the use of flow reactors to mix two immiscible liquids is becoming popular due to the production of uniform particles within a shorter time period. Wagner et al. synthesized silver nanoparticles using three microreactors. In the first reactor, aqueous silver nitrate was generated followed by mixing it with NaBH₄ (reductant) in the second reactor. And lastly in the third reactor, ligands are added to stabilise the nanoparticles.

The synthesis of metal nanoparticles including metal oxides (nano and micro) particles in a microfluidic channel have been extensively studied, Table 1.3 and 1.4 gives a summary of various approaches that were used.
Table 1.3. Synthesis of different types of metal nanoparticles using microfluidics channel \(^91\)

<table>
<thead>
<tr>
<th>Metal</th>
<th>Size</th>
<th>Conditions</th>
<th>Reactants</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold nanoparticles</td>
<td>0.6 – 0.9 nm</td>
<td>RT</td>
<td>HAuCl(_4) + NaBH(_4) + dodecanethiol</td>
<td>92</td>
</tr>
<tr>
<td>Gold nanoparticles</td>
<td>35 nm</td>
<td>115°C</td>
<td>HAuCl(_4) + Trisodium citrate</td>
<td>93</td>
</tr>
<tr>
<td>Copper nanoparticles</td>
<td>8.9 nm (depending on the flow rate)</td>
<td>RT</td>
<td>CuCl(_2) + lithium hydrotriethylborate (Li[Bet(_3)H]) + 3-(N,N-dimethyldodecylammonia) propane sulfonate (SB12)</td>
<td>94</td>
</tr>
<tr>
<td>Cobalt nanoparticles</td>
<td>3.9 – 4.7 nm</td>
<td>RT</td>
<td>CoCl(_2) + Li[Bet(_3)H] + SB12</td>
<td>95</td>
</tr>
<tr>
<td>Palladium nanoparticles</td>
<td>3.1 nm</td>
<td>140-200°C</td>
<td>Palladium (II) acetate (Pd(OAc)(_2)) + poly(benzyl ether) dendron ligands (PBED)</td>
<td>96</td>
</tr>
<tr>
<td>Silver nanoparticles</td>
<td>15 nm</td>
<td>RT</td>
<td>AgNO(_3) + NaBH(_4)</td>
<td>90</td>
</tr>
</tbody>
</table>
Table 1.4. Synthesis of different types of metal oxides nanoparticles using microfluidics channel\textsuperscript{91}

<table>
<thead>
<tr>
<th>Metal</th>
<th>size</th>
<th>conditions</th>
<th>Reactants</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe\textsubscript{3}O\textsubscript{4}</td>
<td>~ 4 nm</td>
<td>RT</td>
<td>FeCl\textsubscript{2} + FeCl\textsubscript{3} + NH\textsubscript{4}OH</td>
<td>97</td>
</tr>
<tr>
<td>Fe\textsubscript{3}O\textsubscript{4}</td>
<td>~ 4 – 7 nm</td>
<td>RT</td>
<td>FeCl\textsubscript{2} + FeCl\textsubscript{3} + NaOH</td>
<td>98</td>
</tr>
<tr>
<td>γ-Fe\textsubscript{2}O\textsubscript{3}</td>
<td>&lt; 7 nm</td>
<td>RT</td>
<td>FeCl\textsubscript{2} + FeCl\textsubscript{3} + NH\textsubscript{4}OH</td>
<td>99</td>
</tr>
</tbody>
</table>

\textsuperscript{*RT} = Room temperature
1.3. Conclusion
The use of emulsion droplets is extremely useful in the realm of nanoparticle synthesis. There are many ways to generate emulsions such as stirring, shaking, using homogenisers, Couette shear devices, membrane emulsification and microfluidics. Each technique has its own advantages such as homogenisers and Couette shear devices have the highest throughput but least uniformity, while the particles produced by microfluidics have high uniformity but are not as high throughput. As with microfluidics, droplets are produced one at a time. However, when dealing with drug delivery and diagnostics, it is extremely important that the particles are uniform in size. The particle sizes depend on the flow rate, pore’s size or the channel’s height and width. Another widely studied area is the use of liquid-liquid interface to conduct reactions; ion transfer, electron transfer and particle adsorption to produce nanoparticles. Reactions can be conducted in a flask or microchannel. The particles produced are small in size (less than 50 nm).

In my PhD, emulsions droplets were formed using microfluidic device. By varying the concentration and droplet sizes, different morphologies of particles, core@shell and nanosheets were obtained. The combination of emulsion droplets and electrodeposition at the liquid-liquid interface was studied. Different metals particles were obtained by changing the metal ions and its size depends on the nature of the reactions.
1.4. References


Chapter 2. Theory

2.1. Emulsions

A system consisting of two immiscible liquids, where one phase is dispersed in another liquid phase is called an emulsion. The system is stabilised by a component called a surfactant. A surfactant consists of a hydrophilic head and a hydrophobic tail making them amphiphilic molecules, as shown in Figure 2.1A. At the oil-water or air-water interface, the hydrophilic head lies in the water and the hydrophobic tail in the oil or air. This reduces the interfacial tension between the two phases as shown in Figure 2.1B. When surfactant molecules are present at high concentration, it is energetically favourable to form micelles, where the hydrophilic head groups protect the hydrophobic tails as shown in Figure 2.1C.

When the concentration of the surfactant is low, the surfactant molecules preferentially arrange themselves only on the surface (Figure 2.2.1). When the concentration of the surfactant increases, the surface tension reduces as more molecules assemble at the surface. Once the surface is saturated, the addition of more surfactant generates micelles. This point of saturation is called “critical micelle concentration” or CMC. A graph representing surface tension against surfactant concentration (logarithmic scale) is shown in Figure 2.2. Usually when micelles are formed they are spherical in shape as shown in Figure 2.3. This was first proposed by Adam and Hartley, however, later McBain and Debye suggested that it is possible for micelles to take up other shapes such as lamellar and rod shaped.

![Figure 2.1. A) Structure of surfactant B) surfactant lies at the air-water interface C) micelles.](image)
Experts have used several methods such as calculating the surface tension, NMR or fluorescence spectroscopy to measure the values of CMC. Common trends are, longer alkyl chains have lower CMC values, and non-ionic surfactants usually have lower CMC than ionic surfactants as shown in Table 2.1. A low CMC means that a lower concentration of the surfactant is required to reach saturation and form micelles.

**Figure 2.2.** Graph representing surface tension vs. logarithm of surfactant concentration. 1) At low concentration of surfactant, the surface tension was not much affected. 2) Increasing the concentration of the surfactant decreases the surface tension rapidly. 3) At the critical micelle concentration (CMC), the surface is saturated, adding more surfactant does not affect the surface tension.

**Figure 2.3.** Diagram of a spherical micelle for sodium dodecyl sulfate.
Table 2.1. Examples of CMC values used in some surfactants.4

<table>
<thead>
<tr>
<th>Surfactants</th>
<th>CMC values (mol dm⁻³)</th>
<th>Example molecule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anionic surfactants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium octyl-1-sulfate</td>
<td>1.30 × 10⁻¹</td>
<td><img src="image1" alt="Sodium octyl-1-sulfate" /></td>
</tr>
<tr>
<td>Sodium decyl-1-sulfate</td>
<td>3.32 × 10⁻²</td>
<td></td>
</tr>
<tr>
<td>Sodium dodecyl-1- sulfate</td>
<td>8.39 × 10⁻³</td>
<td></td>
</tr>
<tr>
<td>Sodium tetradecyl-1- sulfate</td>
<td>2.05 × 10⁻³</td>
<td></td>
</tr>
<tr>
<td><strong>Cationic surfactants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Octyl trimethyl ammonium bromide</td>
<td>1.30 × 10⁻¹</td>
<td><img src="image2" alt="Octyl trimethyl ammonium bromide" /></td>
</tr>
<tr>
<td>Deceteryl trimethyl ammonium bromide</td>
<td>6.46 × 10⁻²</td>
<td></td>
</tr>
<tr>
<td>Dodecyl trimethyl ammonium bromide</td>
<td>1.56 × 10⁻²</td>
<td></td>
</tr>
<tr>
<td>Hexacetyltrimethyl ammonium bromide</td>
<td>9.20 × 10⁻⁴</td>
<td><img src="image3" alt="Hexacetyltrimethyl ammonium bromide" /></td>
</tr>
<tr>
<td><strong>Nonionic surfactants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Octyl hexaoxyethylene glycol monoether</td>
<td>9.80 × 10⁻³</td>
<td><img src="image4" alt="Octyl hexaoxyethylene glycol monoether" /></td>
</tr>
<tr>
<td>Decyl hexaoxyethylene glycol monoether</td>
<td>9.00 × 10⁻⁴</td>
<td></td>
</tr>
<tr>
<td>Decyl nonaoxyethylene glycol monoether</td>
<td>1.30 × 10⁻³</td>
<td></td>
</tr>
<tr>
<td>Dodecyl hexaoxyethylene glycol monoether</td>
<td>8.70 × 10⁻⁵</td>
<td></td>
</tr>
</tbody>
</table>
2.1.1. Critical packing parameter (CPP)

Experts have also used the concept of critical packing parameter (CPP) to help identify the possible geometry of the micelle.\(^4\) CPP can be calculated using the equation in 2.1.

\[
CPP = \frac{\nu}{l_c a_o}
\]  

(2.1)

Where,

\(\nu\) = volume of the hydrocarbon chain

\(l_c\) = critical chain length

\(a_o\) = optimal surface area per head group

From the above equation, if the critical packing parameter is less than \(\frac{1}{3}\), it forms a spherical shaped. Based on this concept, list of predicted micelle structures were formed, as shown in Table 2.2.

<table>
<thead>
<tr>
<th>Structure of surfactant</th>
<th>Examples</th>
<th>Critical packing parameter</th>
<th>Structure formed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single chained lipids with large head group</td>
<td>SDS in low salt</td>
<td>&lt; 1/3</td>
<td>Spherical micelles</td>
</tr>
<tr>
<td>Single chained lipids with small head groups</td>
<td>SDS and CTAB in high salt</td>
<td>1/3 – 1/2</td>
<td>Cylindrical micelles</td>
</tr>
<tr>
<td>Double chained lipids with large head groups</td>
<td>Phosphatidyl choline</td>
<td>1/2 - 1</td>
<td>Flexible bilayers vesicles</td>
</tr>
<tr>
<td>Double chained lipids with large head groups, anionic lipids in high salt</td>
<td>Phosphatidyl ethanaiamine</td>
<td>~ 1</td>
<td>Planar bilayers</td>
</tr>
<tr>
<td>Double chained lipids with small head-groups, nonionic lipids</td>
<td>Cholesterol</td>
<td>&gt;1</td>
<td>Inverted micelles</td>
</tr>
</tbody>
</table>
2.1.2. Hydrophilic lipophilic balance (HLB)

An alternative way to describe the properties of surfactants is its affinity to polar (hydrophilic) or non-polar (hydrophobic or lipophilic) liquids. A particular number has been given to each surfactant which is called ‘hydrophilic lipophilic balance’ or HLB. The term HLB was proposed by Griffin in 1954, where he suggested a formula to calculate the HLB for non-ionic surfactants. The formula is as shown in equation 2.2.

\[
HLB = \frac{20M_h}{M_h + M_l}
\]  

(2.2)

Where, \(M_h\) = molecular mass of hydrophilic portion of the molecule  
\(M_l\) = molecular mass of lipophilic portion of the molecule

As a result, it has a scale of 0-20; a completely hydrophilic molecule is denoted on the scale as 20, while a completely lipophilic molecule is denoted as 0. Using equation 2.2, the HLB of SDS was calculated to be ~ 8.9.

2.2. Classification of emulsions

There are many ways to classify emulsions. One of the ways is to classify them based on phase; two phase (single emulsion) and three phase (double emulsion).

2.2.1. Single emulsions

Two phase emulsions are formed by two immiscible liquids, the dispersed phase and the continuous phase. The dispersed phase is the inner fluid while the continuous phase is the base fluid. Single emulsions can form oil-in-water (O/W) or water-in-oil (W/O) emulsions. While for oil-in-water emulsions, water is the continuous phase and oil is the dispersed phase as shown in Figure 2.4a. For water-in-oil emulsions, water is the dispersed phase while the oil is the continuous phase as shown in Figure 2.4b.

In the case of a hydrophilic surfactant, the head group occupies more area than the chain, hence the interface curves into the oil phase forming an oil-in-water emulsion (figure 2.4a). While for the lipophilic or hydrophobic surfactant, the area of the chain is larger than the head group and hence a water-in-oil emulsion forms (figure 2.4b). Hence, when forming oil-in-water emulsions, hydrophilic surfactants are used and in water-in-oil emulsions, lipophilic surfactants (non-ionic surfactants) are used.
2.2.2. Double emulsions

In double emulsions, apart from a dispersed and continuous phase, there are droplets inside the dispersed phase.\(^5\) There are mainly two types of double emulsions; water-in-oil-in-water (W/O/W) and oil-in-water-in-oil (O/W/O) emulsions.\(^6\) For W/O/W, the aqueous phase consists of a water-in-oil emulsion as the dispersed phase while for O/W/O, the oil phase consists of an oil-in-water emulsion as the dispersed phase (Figure 2.5).\(^6\)

Usually, they require two types of surfactants to stabilised double emulsions. In the case of O/W/O emulsions, a hydrophilic surfactant stabilises the internal droplet (oil-in-water emulsion) and hydrophobic surfactant stabilise the external droplet (water-in-oil emulsion).\(^6\) While for W/O/W emulsions, a hydrophobic surfactant stabilises the internal droplet (water-in-oil emulsion) and hydrophilic stabilise the external droplet (oil-in-water emulsion).\(^6\)
2.2.3. Janus emulsions
A Janus emulsion is where the surface of the emulsion is divided into two, one of them maybe hydrophobic and the other hydrophilic. This gives them unique chemical and physical properties. They can be used as templates for generating anisotropic particles.

2.2.4. Classification by size
Emulsions can also be classified based on their size, such as macroemulsions, microemulsions and nanoemulsions. The size range of macroemulsions falls between 0.1 – 5 μm. The terminology for emulsions smaller than 0.1 μm is confusing in the literature. Some define micro as 5-50 nm and nano, 20 – 100 nm. According to the IUPAC microemulsions are defined as “dispersion made of water, oil and surfactant(s) that is an isotropic and thermodynamically stable system with dispersed domain diameter varying approximately from 1 to 100 nm, usually 10 to 50 nm”. This is the terminology used in this thesis.

2.2.4.1 Thermodynamics behind emulsions formation
Applying mechanical energy to two immiscible liquids, results in formation of emulsion droplets (from state 1 to state 2) as shown in Figure 2.6.)
The formation of emulsion droplet, increases the interfacial area ($\Delta A = A_2 - A_1$) hence resulting in an increase (or positive) interfacial energy ($\Delta G_i$).\textsuperscript{9,10} It is assumed that the interfacial tension ($\gamma$) is the same for both system 1 and 2.\textsuperscript{4,10} The change in interfacial energy ($\Delta G_i$) composes of interfacial tension and the change in interfacial area as shown in equation 2.3.\textsuperscript{9,10}

$$\Delta G_i = \gamma \Delta A \quad (2.3)$$

The total free energy of the formation of colloidal dispersion for the whole system is composed of the interfacial energy ($G_i$) term and configuration ($-T\Delta S$) term as shown in equation 2.4.

$$\Delta G_{formation} = \Delta G_i - T\Delta S_{config} \quad (2.4)$$

Where,

$\Delta G_i$ = interfacial energy (J)

$T$ = temperature (K)

$\Delta S$ = change in entropy (J/K)

The formation of emulsion droplets (from state 1 to state 2), has a positive surface energy term ($\Delta G_i$) and also positive entropy term ($\Delta S$) as the degree of freedom is higher in an emulsified state.\textsuperscript{9,10} In most situations, $\Delta A\gamma_{12} >> -T\Delta S$.\textsuperscript{4}

Where,

$\Delta A\gamma_{12}$ = surface energy term from system 1 to system 2
Hence, $\Delta G_{\text{formation}}$ is positive which means that the reaction is non-spontaneous. Emulsions are usually considered as thermodynamically unstable.\textsuperscript{9,10} Hence, it has the tendency to breakdown via coalescence.\textsuperscript{9,10}

However, adding a surfactant reduces the interfacial tension, hence reduces surface free energy ($\Delta G_{I}$).\textsuperscript{4,9} Surfactants also act as a film around droplets which can also prevent coalescence.\textsuperscript{9} This could result in kinetic stability due to energy barriers between the two systems (1 and 2) and hence the conversion process is slowed down.\textsuperscript{4,9}

The value for the interfacial tension of a microemulsion is low, hence leading to negative $\Delta G_{\text{formation}}$ which is a spontaneous formation of emulsion droplets.\textsuperscript{9,10} They are usually considered as thermodynamically stable.\textsuperscript{9,10} While, macroemulsions and nanoemulsions are kinetically stable.\textsuperscript{4}

Compared to macroemulsions, nanoemulsions required more surfactants or energy which increases the energy barrier hence resulting more kinetically stable.\textsuperscript{4} Tadros has provided a broad definition of emulsions and related them to thermodynamic and kinetic stability, Table 2.3 summarises them.\textsuperscript{4,11}

In the system used in this thesis, a microfluidic droplet chip produces emulsion droplets; 5 - 30 µm. Hence we are dealing with macroemulsions.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Macroemulsions</th>
<th>Nanoemulsions</th>
<th>Microemulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>0.1 – 5 µm</td>
<td>20 - 100 nm</td>
<td>5 – 50 nm</td>
</tr>
<tr>
<td>Components</td>
<td>Oil, water and surfactant</td>
<td>Oil, water and surfactant</td>
<td>Oil, water and surfactant</td>
</tr>
<tr>
<td>Thermodynamic Stability</td>
<td>$\Delta A_{12} &gt;&gt; -T\Delta S$ Non-spontaneous, thermodynamically unstable</td>
<td>$\Delta A_{12} &gt;&gt; -T\Delta S$ Non-spontaneous, thermodynamically unstable</td>
<td>$\Delta A_{12} &lt; -T\Delta S$ Spontaneous, thermodynamically stable</td>
</tr>
</tbody>
</table>
2.3. Processes of breaking down emulsions
When storing emulsions there may be various breakdown processes that occur, such as creaming, sedimentation, flocculation, Ostwald ripening, coalescence and phase inversion. A schematic diagram of these processes is shown in Figure 2.7.

2.3.1. Creaming and sedimentation
This process occurs when external forces are involved such as gravitational or centrifugal. The system builds up a concentration gradient when the external forces are greater than the thermal motion or Brownian motion of the droplets, this results in bigger droplets moving to the top or bottom of the container. If the density of the droplet is lower than the medium it will move to the top, while a droplet with higher density will move to the bottom.

2.3.2. Flocculation
When droplets aggregate into bigger units without changing its original size it is called flocculation. This happens when the Van der Waals attraction is weak, hence not enough repulsion for the droplets to be apart.

2.3.3. Ostwald Ripening (Disproportionation)
In a system where emulsions are polydispersed, the smaller droplets are more soluble than bigger droplets. Hence, the smaller droplets disappear quicker and their molecules get deposited to the larger droplets. As time passes, the droplet size distribution moves to a larger scale.

2.3.4. Coalescence
Coalescence happens when the film between the droplets get thinner or disrupted hence droplets fuse together into larger ones.

2.3.5. Phase Inversion
This process happens when there is an exchange in phases, for example, oil-in-water emulsion change to water-in-oil emulsion.
2.4. Pickering emulsion

An interesting alternative to using surfactants is to use nanoparticles. These are referred to as Pickering emulsions. When a liquid is dropped on a flat surface, a contact angle forms between the liquid-solid and the liquid-vapor interface (as shown in Figure 2.8). Similarly, a contact angle also forms between a liquid-liquid interface (example, oil-water interface) on a solid. The wetting of a surface is favorable when the contact angle is less than 90°, while it is unfavorable when it is greater than 90°. When the angle is equal to zero there is complete wetting of the liquid, hence droplets become a flat puddle.

Surface tension plays a key role in determining the shape of a liquid droplet. A pure liquid would have other neighboring liquid molecules surrounding it, hence forces acting on it are equally distributed resulting in a balanced net force. However, when a liquid is placed on a solid, the neighboring molecules are no longer liquid resulting in an imbalanced net force which causes the liquid to contract. The contraction of the liquid is called surface tension. In 1805, Thomas Young described the contact angle of the droplet on a solid surface (ideal situation) where there are three interfacial

![Figure 2.7. Schematic diagram of various break down mechanisms in emulsions.](image)
tensions acting on the droplet, these are interfacial tensions between liquid-vapour ($\gamma_{lv}$), solid-vapour ($\gamma_{sv}$) and solid-liquid ($\gamma_{sl}$) as shown in equation 2.5.

$$\gamma_{lv}\cos\theta_y = \gamma_{sv} - \gamma_{sl}$$  \hspace{1cm} (2.5)

Where,

$\theta_y$ = contact angle ($^\circ$)

$\gamma_{lv}$ = interfacial tension between liquid and vapour (N m$^{-1}$)

$\gamma_{sv}$ = interfacial tension between solid and vapour (N m$^{-1}$)

$\gamma_{sl}$ = interfacial tension between solid and liquid (N m$^{-1}$)

This theory is exploited in “Pickering emulsions”. Pickering emulsions are emulsions that are stabilized by solid particles instead of surfactants. They can be either single emulsions water-in-oil, oil-in-water or multiple emulsions.\textsuperscript{13} Pickering emulsions keep the same basic properties as the classical emulsions (surfactant stabilized). Thus it is possible to use a Pickering emulsion instead of a classical emulsion in majority of applications.\textsuperscript{13} However, there are some additional properties that can be achieved when emulsions are stabilized by solid particles, such as the huge resistance to coalescence as the attachment of the particles are irreversible.\textsuperscript{13} Pickering emulsions can be applied to the area of food science such as proteins particles can be used as stabilisers.\textsuperscript{7} Other examples of food emulsions are whipped cream where fat particles are used for stabilisation and ice crystals in ice cream.\textsuperscript{7}

For Pickering emulsions, the important parameter is the contact angle, $\theta$, of the particle relative to the interface.\textsuperscript{7} If the particle is hydrophilic then the $\theta$ measured is usually less than 90$^\circ$ relative to the aqueous phase. This means that more of the particle’s surface area is occupied in the water phase than in the oil phase hence it curves into
the oil-in-water or air-in water emulsion (Figure 2.9a). For hydrophobic particles, $\theta$ is generally more than 90° and therefore more of the particle’s surface area is in oil or air than in the aqueous phase hence it curves into a water-in-oil or water-in-air emulsion (Figure 2.9c). However, when the contact angle is at 90°, particles stay at the interface hence forming liquid-liquid interface system (Figure 2.9b). There are many other differences between using classical emulsions and Pickering emulsions which are summarized in Table 2.4.

Table 2.4. Differences between classical emulsions and Pickering emulsions.

<table>
<thead>
<tr>
<th>No.</th>
<th>Classical emulsion</th>
<th>Pickering emulsion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>The affinity of water or oil of a surfactant can be measured using hydrophilic-lipophilic balance</td>
<td>The important parameter is the contact angle, $\theta$, the particle makes relative to the interface.</td>
</tr>
<tr>
<td>2.</td>
<td>Form micelles which leads to aggregation</td>
<td>Do not form aggregates because there is no micelle but they adsorb to the interface</td>
</tr>
<tr>
<td>3.</td>
<td>In the case of hydrophilic surfactant, oil in water emulsion forms, while for lipophilic surfactant water-in-oil emulsion forms.</td>
<td>If the particle is hydrophilic, this means $\theta$ is less than 90°, hence oil-in-water or air-in-water emulsion forms. If the particle is hydrophobic, this means $\theta$ is more than 90° and hence water in oil or water-in-air emulsion forms.</td>
</tr>
<tr>
<td>4.</td>
<td>Surfactants are amphiphilic molecules which means it contains a hydrophilic head group and hydrophobic tail.</td>
<td>Particles can be surface active from coating</td>
</tr>
<tr>
<td>5.</td>
<td>The adsorption and desorption process occurs very quickly.</td>
<td>Particles are irreversibly adsorbed because they have high energy attached to interface.</td>
</tr>
</tbody>
</table>
When two bulk phases (oil-water or liquid-vapour) come into contact with each other, there is an interfacial tension ($\gamma$). The two bulk phases can be denoted as $\alpha$ and $\beta$. When a spherical particle ($s$) is adsorbed at the interface ($\alpha\beta$) the interfacial tension associated are $s\alpha$, $s\beta$ and $\alpha\beta$. The attachment of the particle to the interface depends on the interfacial tension ($\gamma_{\alpha\beta}$) and contact angle. To remove the spherical particle from the interface, the energy associated is given as shown in equation 2.6 (ignoring gravitational force).

$$E = \pi r^2 \gamma_{\alpha\beta} (1 \pm \cos\theta)^2$$ (2.6)

Where,

$E$ = energy needed to remove the particle from the interface

$r$ = radius of the particle

$\theta$ = contact angle (when $\theta = 90^\circ$, the particle is attached strongest at the interface)

$\gamma_{\alpha\beta}$ = interfacial tension between $\alpha$ and $\beta$ phase (oil and water)

In this case, the Young equation is written as shown in equation 2.7.

$$\gamma_{\text{ow}} \cos \theta = \gamma_{\text{so}} - \gamma_{\text{sw}}$$ (2.7)

Figure 2.9. a) spherical particle at oil-water interface where the contact angle was measured through the aqueous phase, less than $90^\circ$, b) equal to $90^\circ$ and c) greater than $90^\circ$.7
2.5. Liquid-liquid interface

The liquid-liquid interface is a sharp and defect free plane where solid particles are assembled. Several types of reactions can occur at the liquid-liquid interface, either spontaneously or by applying external charged. Here we focused on ion and electron transfer.

2.5.1. Ion transfer

Reactions in this thesis involve two immiscible liquids but they might not be a true definition of the interface between two immiscible electrolytes solutions (ITIES). However, the concept used is similar to ITIES hence its theoretical aspects will be discussed.

The potential difference between the two phases is usually known as the inner potential ($\phi$). It is generally described as the sum of surface potential ($\chi$) and outer potential ($\psi$) as shown in equation 2.8:

$$\phi = \chi + \psi \tag{2.8}$$

At equilibrium the chemical potential is equally distributed between the two phases; organic (O) and aqueous (W) phase as shown in equation 2.9:

$$\mu_i^O = \mu_i^W \tag{2.9}$$

Where,

$$\mu_i^\alpha = \text{chemical potential of the component } i \text{ for phase } \alpha \text{ (} \alpha \text{ = O or W)}$$

When component $i$ is charged, the chemical potential consists of “chemical” and “electrical” energy as shown in equation 2.10:

$$\mu_i^\alpha = \mu_i^\alpha + \mu_i^{\alpha, el} \tag{2.10}$$

Where,

$$\mu_i^\alpha = \text{chemical energy}$$

$$\mu_i^{\alpha, el} = \text{electrical energy}$$

$\mu_i^{\alpha, el}$ can be replaced with $zF\phi$ as shown in equation 2.11.
\[ \mu^{-\alpha}_i = \mu^\alpha_i + zF\phi \]  

(2.11)

Where,

\[ z = \text{charge of the particle} \]

\[ F = \text{Faraday's constant} = 96,500 \text{ c/mol} \]

The potential difference between the two phases for the electrical and chemical component is shown in equation 2.12.\(^{16}\)

\[ \Delta \phi^O_W = \frac{1}{z_iF} \left( \mu^O_i - \mu^W_i \right) \]  

(2.12)

Where,

\[ \Delta \phi^O_W = \phi^W - \phi^O \] (This is called Galvani potential which is the difference between the inner potential of the two phases)\(^{16}\)

When two immiscible liquids are in contact with each other, the ionic components are dissolved more or less in one phase or the other, which could depend on the polarity of the molecule. At equilibrium, the movement of ions are suppressed, which are represented in the form of Nernst equation as shown in equation 2.13.\(^{16}\)

\[ \Delta \phi^W_O = \frac{1}{z_iF} \left( \mu^{O^o}_i - \mu^{W^o}_i \right) + \frac{RT}{z_iF} \ln \frac{\gamma^O_i}{\gamma^W_i} \]  

(2.13)

Where,

\[ \mu^{O^o}_i = \text{standard chemical potential of } i \text{ in phase } \alpha \]

\[ R = \text{gas constant} \]

\[ T = \text{absolute temperature} \]

\[ \gamma^\alpha_i = \text{activity coefficient in phase } \alpha \]

\[ C^\alpha_i = \text{concentration of } i \text{ in phase } \alpha \]

\[ \mu^{O^o}_i - \mu^{W^o}_i = \text{standard molar Gibbs energy of ion } i \text{ from phase } O \text{ to } W \]
Nernst equation can be expressed in different form; another form is shown in equation 2.14.16

$$
\Delta_{O}^{W} \phi = \Delta_{O}^{W} \phi_i^0 + \frac{RT}{z_iF} \ln \frac{y_i^{W}C_i^{W}}{y_i^{O}C_i^{O}}
$$

Where,

$$
\Delta_{O}^{W} \phi_i^0 = \text{standard ion-transfer potential}
$$

The term “standard ion-transfer potential” is a parameter that expresses the “affinity of an ion in the two phases where both solvent are in mutual saturation”.16 The values of standard ionic potential ($\Delta_{O}^{W} \phi_i^0$) can be used to find the inner potential difference between the two phases ($\Delta_{O}^{W} \phi$) for known concentrations of ionic species and activity coefficients in the two phases by using equation 2.14.16

2.5.2. Electron Transfer

When one phase consists of the metal precursor and the other phase consists of a reducing agent, heterogeneous electron transfer can occur as shown in Figure 2.10.17

The organic phase consists of the reducing agent, which denotes electron to the aqueous phase (consists of $M^{n+}$). Equation 2.15 represents the process taking place.18

The subscript (int) denotes the metal deposit at the interface.

\[ \text{Figure 2.10. Schematic representing i) electron transfer ii) metal deposition when the aqueous phase consists of metal ion ($M^{n+}$) and the organic phase consists of the reducing agent} \]

\[ M^{n+} \text{(aq)} + n R_{\text{(org)}} \rightarrow M_{\text{(int)}} + n \text{ Ox} \text{(org)} \quad (2.15) \]

In our case, we used Au(III) and decamethylferrocene (DmFc) as the reducing agent

\[ \text{H}^+ \text{(AuCl}_4\text{)}^– \text{(aq)} + 3\text{DmFc} \text{(org)} \rightarrow \text{Au} \text{(int)} + 3\text{DmFc}^+ \text{(org)} + 3\text{Cl}^- \text{(aq)} + \text{HCl} \text{(aq)} \]

\[ \text{Au}^{3+} + 3\text{e}^- \rightarrow \text{Au} \text{(s)} \]
Principle of charge neutrality suggest that either AuCl\(_4^-\) or DmFc\(^+\) would want to cross the phase boundary as the system would try not to be polarised at the interface. Su et al.\(^{19}\) suggest a mechanism where DmFc diffuses across the phase boundary to the awaiting AuCl\(_4^-\).

From the literature, several mechanism were proposed such as Au(III) is reduce to Au(0) metal directly or Au (III) is reduce to Au(I) and Au (I) can form as an intermediate, undergoing disproportionation reaction to Au(III) and Au(0) (as shown in equation 2.16)\(^{20}\)

\[
3\text{AuCl}_2^- \rightarrow 2\text{Au (s)} + \text{AuCl}_4^- + 2\text{Cl}^- \quad (2.16)
\]

Hence, during the reaction, it is possible that some of DmFc could transfer across the interface, Au (I) could form as an intermediate.

The concentration between the two phase, also relies on the Nernst equation (as shown in equation 2.17).

\[
E = E^{\circ} + \frac{RT}{nF} \ln \frac{C_o}{C_R} \quad (2.17)
\]

Where,

\(E\) = Overall cell potential at equilibrium (mV)

\(E^{\circ}\) = standard electrochemical potential (mV)

\(R\) = Gas constant = 8.31 J/K mol

\(T\) = temperature (298 K)

\(n\) = number of electrons in the valence half reactions

\(F\) = Faraday’s constant

The equation above assumes heterogeneous electron transfer, however it is possible that electron transfer maybe proceeded by ion transfer. This would mean it is not a true heterogeneous process.

2.6. Nucleation Theory

In this work we reduce metal ion creating nanoparticles. The process is controlled by the redox potential at the reaction. The reaction takes place at droplet interface and not in solution.
Under a potential difference, the ions are transferred from the solution to the interface forming “clusters”. Clusters consists of atoms or “growth units”.\textsuperscript{21} This leads to the decrease in Gibbs free energy which is usually a spontaneous reaction as shown in equation 2.18.\textsuperscript{22}

\[ \Delta G(N) = -Nze|\eta| \]  \hspace{1cm} (2.18)

Where,

- \( N \) = number of atoms within a cluster
- \( z \) = charge number
- \( e \) = elementary charge, e
- \( \eta \) = overpotential (overvoltage), V

However, when the clusters are formed, there is an excess energy (\( \Phi N \)) which is related to interface boundaries (cluster/solution and cluster/substrate). This increases the Gibbs energy. Hence, the total change of Gibbs energy for the cluster formation for \( N \) atoms is shown in equation 2.19.\textsuperscript{22}

\[ \Delta G(N) = -Nze|\eta| + \Phi(N) \]  \hspace{1cm} (2.19)

Where,

- \( \Phi = \sum_i \sigma_i A_i \) = minimum surface energy at constant volume
- \( \sigma \) = specific surface energies of crystallographic faces \( i \)
- \( A_i \) = surface areas of crystallographic faces \( i \)

For the formation of small clusters, the second term; \( \Phi(N) \) dominates the first term in equation 2.19 resulting in the increase of Gibbs energy.\textsuperscript{22} While, the formation of large clusters, the first term dominates the second term in equation 2.19 resulting in the decrease of Gibbs energy which gives a negative slope (Figure 2.11).\textsuperscript{22} When the cluster has \( N_{\text{crit}} \) size, it means that Gibbs energy of cluster formation; \( \Delta G(N) \) is at its maximum. \( N_{\text{crit}} \) means “the number of atoms in a critical cluster” or nucleus.\textsuperscript{22} The probability of growing the nucleus or dissolving it in the solution is the same at the maximum condition.\textsuperscript{22}
Instantaneous nucleation occurs when all nuclei are formed at the same time, hence they all grow to a similar size. While, for continuous nucleation; nuclei are formed at different times, hence they grow into different sizes.

2.6.1. Crystal structures
The shape and size of the clusters depends on how the atoms are packed. These clusters grow into crystals which can have different morphology depending on the packing of atoms. The two most common types of packing are hexagonal close-packed and the cubic closed packed structure. Here, an atom is represented as a circular shaped as shown in Figure 2.12. These atoms are stacked in layers. For hexagonal closed packed, the first layer (represent as A) are stacked on top of the second layer (represent as B) as shown in Figure 2.12. This results in a sequence of ABABAB and so on. The atom in the second layer would drop in the gap (or interstices) between the atoms of the layer below. Example of this type of packing are magnesium, zinc and titanium (low-temperature form).

However, for the cubic closed packed structure, the third layer is C (Figure 2.12) where, the atom drops into the interstices C. This results in a sequence of ABCABC and so on. In some textbooks, this type of sequence is referred to as the face centered cubic crystal lattice. Example of this type of packing are gold, silver, aluminium, copper and iron (high temperature form).
In addition, some structures have “stacking defects”, this is a fault in the crystal growth. For example, the stacking of face centered crystal could be interrupted with hexagonal layers resulting in a sequence of ABCABABCA…

![Figure 2.12. Stacking sequences of hexagonal close packed and cubic closed packed.](image)

2.7. Magnetic materials
Magnetic materials can be classified into four types, paramagnets, antiferromagnets, ferrimagnets and ferromagnets. The orientation of magnetic dipole moment in the absence of a magnetic field of each category is shown in Figure 2.13. For paramagnetic materials, the magnetic moments are disordered which results in zero net magnetisation. Similarly, antiferromagnetic materials have no net magnetisation; the reason is due to the antiparallel magnetic dipole moments which cancel each other. In both cases they require a large magnetic field to create a small change in magnetization (M), and after magnetization has been removed they do not retain any magnetization. When magnetization (M) is plotted against magnetic field (H), the slope or susceptibility (χ) of paramagnets and antiferromagnets is small and positive (Figure 2.14). The ratio between M and H is known as the susceptibility (equation 2.20), which determines the how responsive each material is to the magnetic field. Paramagnetic and antiferromagnetic materials are usually found in transition metals.

\[
χ = \frac{M}{H} \tag{2.20}
\]

Where,

\(M = \text{magnetization (emu/cm}^3)\)
H = magnetic field (Oe)

In the case of ferromagnetic and ferrimagnetic materials, they are able to obtain a large net magnetization even with a small external magnetic field as shown in Figure 2.15. It is important to note that the axis scale in this case is different from Figure 2.14. For ferromagnetic, the dipole moments are parallel to each other; while ferrimagnetic materials have dipole magnetic moment that are antiparallel to each other but one is bigger than the other causing a net magnetisation. Above a certain applied field strength, M is saturated, known as saturation of magnetisation. They can retain their magnetisation even after the magnetic field has been removed, this effect is called hysteresis. This makes them permanent magnets. Bulk materials are typically multidomain. When a magnetic field is applied, the domain wall changes and magnetisation stays pinned as shown in Figure 2.16.

In ferromagnetic and ferrimagnetic, the phenomenon called hysteresis occurs. Figure 2.17 shows a hysteresis loop where the axis in this case are magnetic induction, B (units: weber/m² or tesla, T) verses magnetic field strength, H (units: amperes per meter; A/m; 1 Oe = (\frac{1000}{4\pi}) A/m). Starting from the unmagnetised state (origin = 0), the curve keeps increasing in the positive direction until it reaches the point Bs (saturation induction). Reducing the magnetic field (H) to zero, reduces the Bs to Br (residual induction) and to further reduce the induction (B) to zero, a reversed field is required called coercivity (Hc). Reversing the magnetic field could be done by increasing the temperature in order to return to the demagnetised state. By further increasing the reversed H, saturation can be accomplished in the reverse direction. This then forms a hysteresis loop. If magnetization was interrupted, for instance at point ‘a’ then it follows minor hysteresis. Ferromagnetic materials are usually found in metals, while ferrimagnetic materials are usually ionic solids such as magnetite (Fe₃O₄) and maghemite (Fe₂O₃, γ-Fe₂O₃).

The relationship between B, H and M is shown in equation 2.21.

\[ B = H + 4\pi M \] (2.21)
Figure 2.13. Schematic diagram of a) paramagnetic b) antiferromagnetic c) ferromagnetic d) ferrimagnetic dipole moments.

Figure 2.14. Schematic diagram of magnetisation curves for paramagnetic and antiferromagnetic.

Figure 2.15. Schematic diagram of magnetisation curves for ferrimagnetic and ferromagnetic.
2.7.1. Superparamagnetism

Very small ferromagnetic particles (less than 80 nm, material dependent) are called superparamagnetic particles. They have a single domain, so once the magnetic field is removed, the magnetization also rotates back and they do not retain magnetisation. Hence, the hysteresis phenomenon does not occur. However, the magnetic moment is much larger than other paramagnetic materials. The relaxation time ($\tau$) for the particle to flip back (reverse magnetic moments) is shown in equation 2.22. At room temperature, $\Delta E$ is comparable to $k_B T$. By increasing the particle size and reducing the temperature, superparamagnetic property can be ruined; $KV > k_B T$.24
During extraction of the analyte and the washing process, superparamagnetic materials are preferred as they are easily separated using an external magnet and dispersed back in the solution, while using ferromagnetic materials can cause aggregations and disturbs the analyte.

\[
\tau = \tau_0 \exp \frac{\Delta E}{k_B T} 
\]

\[
\Delta E = KV
\]

Where,
\(\tau\) = relaxation time
\(\tau_0\) = order of \(10^{-10}\) to \(10^{-12}\) s (for non-interacting particles)
\(\Delta E\) = energy barrier to moment reversal
\(k_B\) = Boltzmann’s constant (J/K)
\(T\) = temperature
\(K\) = anisotropy energy density
\(V\) = volume of the particle

2.8. Surface Plasmon Resonance

When light is irradiated on a metal particle, it can interact with a specific wavelength of light which causes the electron on the surface of the metal nanoparticle to oscillate as shown in Figure 2.18. The frequency of oscillation is related to the wavelength of light coming in. And only at that wavelength of light that it causes the electrons in the electron cloud on the nanoparticle to oscillate and that causes the colour. At a certain frequency, the amplitude of oscillation attain its maximum – this is known as surface plasmon resonance.\(^{26}\)

The wavelength of surface plasmon resonance depends on the size, type of metal, shape and composition of the particle.\(^{26}\) The surface plasmon resonance is strongest in noble metal nanoparticles such as Au and Ag compared to other types of metal nanoparticles. Hence, gold has optical properties which can be measured using UV-vis spectroscopy.
Figure 2.18. Schematic diagram showing a gold nanoparticle (AuNP) interacts with a wavelength of light causing electron on the surface of the metal to oscillate.
2.9. References


Chapter 3. Assembly of iron oxide nanoparticles within a droplet forming microparticles

3.1. Abstract
Superparamagnetic microparticles (SMPs) are widely used within separation and purification processes, bio-sensing and medical drug targeting. Microparticles that have a high iron content and uniform in size are in high demand as this leads to faster separation of the analyte. Here, Iron Oxide (Fe$_3$O$_4$) nanoparticles approximately 12 nm size were assembled into uniform microparticles (between 1 – 2 µm) using oil-in-water emulsions. A flow focusing microfluidic channel was used to produce emulsion droplets, resulting in uniform particles with high iron oxide content. The diameter of the particles can be varied by changing the concentration of iron oxide or droplet size. In addition, using different surfactants and solvents resulted in a change in shape and size such as spherical and dimpled shapes. To the best of our knowledge this is the first time, iron oxide nanoparticles were assembled into smooth spherical microparticles with a size range between 1-2 µm in a microfluidics channel. The particles produced are monodispersed and have a high magnetic content. These particles were compared with commercially available particles; the results indicate that the in-house or Loughborough University Enterprise Ltd. (LUEL) particles have the highest magnetic content. LUEL particles of size 1µm were supplied as part of commercial collaboration.

3.2. Introduction
3.2.1. Superparamagnetic nanoparticles
Superparamagnetic nanoparticles (Fe$_2$O$_3$ or Fe$_3$O$_4$) are different from bulk iron oxide (ferro or ferrimagnetic materials), as they have superparamagnetic properties. They have a net magnetization only in the presence of an external magnetic field. This makes them suitable for many applications such as bio-imaging, diagnosis, separation and drug delivery as they do not form aggregation in the absence of external magnetic field. Iron oxide nanoparticles are also used in electrochemical sensors due to their attractive properties such as low toxicity, bio compatibility and high electron transfers.
Controlling the size of the particles is very important as it creates particles with uniform properties. Common techniques for preparing nanoparticles are usually co-precipitation, thermal decomposition and laser ablation. Equation 3.1 represents co-precipitation reaction with an alkaline.

\[
\text{Fe}^{2+}_{(aq)} + 2 \text{Fe}^{3+}_{(aq)} + 8\text{OH}^{-}_{(aq)} \rightarrow \text{Fe}_3\text{O}_4(s) + 4\text{H}_2\text{O}(l)
\]

In some cases, the size of the iron oxide nanoparticles needs to be precisely controlled, for example, in applications such as drug delivery and contrast agents in magnetic resonance imaging (MRI). Hence techniques like microfluidics are becoming more demanding as they provide monodisperse particles. In our case, we assembled nanoparticles into microparticles with a size range between 1-2 µm. A bigger particle indicates that it contains more nanoparticles and hence has a stronger magnetic strength, which leads to faster separation of the analyte while retaining the property of superparamagnetism.

3.2.2. Superparamagnetic microparticles

Commercially available SMPs typically consist of aggregates iron oxide nanoparticles (Fe$_2$O$_3$ or Fe$_3$O$_4$) which have various applications in both commercial and medical aspects. Ugelstad et al. first established a method to generate uniform magnetic microparticles. These particles were formed by treating porous polymer particles with an iron salt solution by increasing the pH value or heating. This results in oxidation (Fe$^{2+}$ to Fe$^{3+}$) producing maghemite nanoparticles inside the swollen polymer particles. Later, other techniques were established, Bizdoaca et al. generated core-shell particles by using polystyrene as the core and Fe$_3$O$_4$ as the shell. The process allowed monodispersed particles to be produced but the content of iron oxide was low as it mainly consisted of the polymer core. The magnetisation was measured using a superconducting quantum interference device (SQUID) which was reported to be 20 emu/g. Other techniques of generating magnetic particles include, copolymerization of magnetic cobalt nanoparticles with poly(dimethyl siloxane), polymerization of magnetite into polystyrene beads. Caruso et al. prepared hollow magnetic particles (approximately 650 nm – 1 µm) by coating anionic polystyrene (PS) particles with layers of Fe$_3$O$_4$ nanoparticles and polyelectrolyte solution. Later, the core (PS particle) was removed by calcination resulting in hollow spheres. The magnetisation of the particles was not reported.
Using microemulsions represents an interesting area, as the iron oxide particles can be synthesised without using high temperature. Koo et al. prepared polymeric microcapsules where the polymer shell consists of iron oxide (γ-Fe₂O₃) magnetic nanoparticles by using a double emulsion as a template. Photopolymer NOA 61 and magnetic nanoparticles (in chloroform) was mixed with glycerin using an electronic mixer forming double emulsions which then undergoes UV curing and drying which collapsed the structure into a hemispherical capsule shell with an average size of 12 µm. These particles were reported to be superparamagnetic; SQUID data was shown to be approximately 0.2 emu/g at 300K.

Yang et al. generated hollow superparamagnetic microspheres by using water-in-oil emulsions where the oil phase consists of magnetic nanoparticles, Span 80 in styrene and the aqueous solution consists of NaCl and water solution. The mixture was stirred using ultrasonification. It then underwent irradiation and drying. The size of the particles produced are in the range of approximately 0.2 – 3 µm. The SQUID data was shown to be approximately 30 emu/g for the average particle size of 1.9 µm. The particles produced by these methods require many steps and the particles might not be very uniform. Hence, many research groups have used microfluidic devices.

Particles produced by microfluidic devices are highly uniform in size as it can be easily controlled by flow rates within the microchannel. Moreover, microfluidics can be used as a platform to produce particles of various complex morphologies such as core@shell, janus or double emulsions. Dubinsky et al. synthesised porous polymer particles with the size range of 50 – 100 µm using a photoinitiated microfluidics device. Banderas et al. produced polystyrene particles (size between 5-15 µm) using a flow-focusing microfluidics device, where the dispersed phase (oil phase) consists of polystyrene solution in ethyl acetate or dichloromethane and the aqueous phase is distilled water. Paquet et al. produced uniform porous superparamagnetic microparticles using a co-flow microfluidics device. The particles produced were porous and had a size of approximately 80-100 µm.

In the study presented below superparamagnetic spherical microparticles were produced without adding any polymer which results in higher magnetisation. Droplets were generated using flow focusing microfluidic channel. The dispersed phase consists of Fe₃O₄ nanoparticles in hexane and the continuous phase consists of 2%
SDS. The size of the particles was shown to depend upon the droplet size and the concentration of iron oxide particles. The evaporation rate at the dispersed phase also affects the morphology of the particles. Our work was inspired from O’Mahony et al.\textsuperscript{17}, where iron oxide nanoparticles were assembled into microparticles using emulsion droplets as the template. However, in their work, the microparticles produced are highly polydispersed (coefficient of variation ~ 50%). To improve this, in my PhD, a microfluidic device was used instead of a Couette shear device. The particles obtained are 1-2 μm with a coefficient of variation less than 15%.

3.3. Aims and Objective
The main aim of this study is to produce iron oxide microparticles that are uniform in size. The emulsification technique used was a microfluidic flow focusing channel which enables the production of monodispersed particles. In addition, various parameters such as iron oxide concentration, droplet size and solvent were varied to modify the size and morphology of the particles. A comparison was also done with commercially available particles to shows that LUEL particles have a much higher iron oxide content and separation speed. This work was done with Mark Platt for external collaboration.

3.4. Materials and Methods
3.4.1. Chemical and Reagents
The following chemicals were purchased from Sigma-Aldrich, U.K., and unless stated otherwise the chemicals were used without purification. Sodium dodecyl sulfate (SDS) (436143), sodium octyl sulfate (O4003), sodium decyl sulfate (71443), triton X-100 (X-100), iron(II) chloride tetrahydrate (FeCl\textsubscript{2}·4H\textsubscript{2}O) (220299), iron(III) chloride hexahydrate (FeCl\textsubscript{3}·6H\textsubscript{2}O) (236489), ammonium hydroxide (NH\textsubscript{3}·H\textsubscript{2}O) (338818), oleic acid (364525), perchloric acid (244252) and sodium borohydride (98%) (452882). The following chemicals were purchased from VWR Chemicals, U.K. Hexane (24580.324), Pentane (83632.320), ethanol absolute (20821.330), and toluene (28676.322) were used. Deionized (DI) water with a resistivity of 18.2 MΩ·cm was used throughout.
Table 3.1. Parameters used for the synthesis of iron oxide microparticles at the liquid-liquid interface. P1 and P2 are the organic phase and aqueous phase, respectively.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>P1 (organic)</th>
<th>P2 (aqueous)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Ferrofluid in organic solvent</td>
<td>Surfactant in DI-water</td>
</tr>
</tbody>
</table>

Figure 3.1. a) Schematic of the microfluidic assembly and droplet collection, P1 and P2 represents the organic and aqueous phase, respectively. The droplets flowed through a tube into a collection pot. b) Schematic of the emulsion droplet acting as an interface for the assembling of nanoparticles NP1 (iron oxide) presynthesised and dispersed in the organic phase.

3.4.2. Microfluidics instruments supplier
Microfluidic instruments were supplied by Dolomite Microfluidics Ltd.; 14 μm etch depth Dolomite hydrophilic x-junction “small droplet chip” (Part No. 3200136) and Dolomite Mitos P-Pump basic (Part No. 3200175) were controlled via the Dolomite Mitos Flow Control Centre software Version 2.2.15. The small droplet chip was made from glass and can generate droplets with a diameter of 5-30 μm. The surface of the channel is hydrophilic to produced oil-in-water droplets.

3.4.3. Synthesis of Hydrophobic Nanomagnetic Particles (250 mL) scale
FeCl$_2$·4H$_2$O (12 g) and FeCl$_3$·6H$_2$O (24.5 g) were dissolved in DI water (62.5 mL) in a 250 mL three-neck round-bottom flask. The flask was placed in an ice bath. NH$_3$·H$_2$O (50 mL) was added rapidly with vigorous stirring. The flask was left in the ice bath for 45 min. The solution was rapidly heated to 85 °C for 1 h. Oleic acid (7.5 mL) was then added, and the solution was further heated for another 1 h. The flask was cooled to room temperature, and the black precipitate was transferred to a 150 mL beaker. The black precipitate was washed 3 times with ethanol (50 mL), and each time the black magnetite was collected using a block magnet. The black precipitate was then washed
three times with DI water (50 mL) before washing three times with 20% perchloric acid (50 mL) to dissolve Fe(OH)$_2$ and Fe(OH)$_3$. The black precipitate was again washed three times with DI water (50 mL), followed by three times wash with ethanol (50 mL). Hexane (87.5 mL) was added to the resultant particles to aid dispersion; this was called ferrofluid. Ferrofluid (1 mL) was taken into an Eppendorf tube was allowed to evaporate overnight. The particle concentration was determined by weighing the mass of the material that remained after evaporation.$^{17}$

3.4.4. Creation of Emulsion Droplets
Hexane (P1) and aqueous solution (P2) were connected to the droplet chip as shown in Figure 3.1. P2 was the continuous phase, and the droplets size of P1 was controlled by varying the flow rates of P1:P2. The droplet size was observed through a Celestron LCD digital microscope (Model 44340) and measured by analyzing an image taken on the microscope as shown in Figure 3.1. The droplets were collected in the collection/reaction pot (10 mL glass vial) and left open to the atmosphere for 2–3 h for hexane to evaporate.

3.4.5. Purification of Particles
The sample was placed next to a magnet (GE Healthcare, UK, Magrack) for 2 min. The supernatant was discarded, replaced with DI water (100 μL), and sonicated for 1 min. This process was repeated three times with DI water and twice with acetone. The sample was then redispersed in either water or acetone (100 μL).

3.4.6. Electron Microscopy
3.4.6.1. Scanning electron microscopy
Scanning electron microscopy (SEM) samples were prepared by dropping the suspension onto a conductive copper pad. A table top SEM Hitachi TM3030 was used for imaging particle sizes and distribution, and a field emission gun scanning electron microscopy (FEG-SEM) JEOL 7800F was used for higher resolution imaging of particles. Elemental composition of the particles was measured using the attached energy dispersive X-ray spectroscopy (EDS) to verify the chemistry of the particles. Details of table top SEM and FEG-SEM are shown in Table 3.2.
Table 3.2. Details and features of the Table-top Hitachi TM3030 and FEG-SEM JOEL 7800F

<table>
<thead>
<tr>
<th>System</th>
<th>Table top SEM (Hitachi TM3030)</th>
<th>FEG-SEM (JEOL 7800F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron Source</td>
<td>Tungsten filament</td>
<td>Schottky FEG</td>
</tr>
<tr>
<td>Detectors</td>
<td>Back scattered</td>
<td>Secondary electron detector</td>
</tr>
<tr>
<td>Probe current</td>
<td>Less than 1 nA</td>
<td>Up to 500 nA</td>
</tr>
<tr>
<td>Voltage</td>
<td>5 kV or 15 kV</td>
<td>10 kV – 30 kV</td>
</tr>
</tbody>
</table>

3.4.6.2. Transmission electron microscopy
Transmission electron microscopy (TEM) specimens were prepared by ultrasonicing the suspensions followed by pipetting onto standard holey carbon film supported TEM grids (EM Resolutions Ltd., UK). A Jeol 2000FX TEM equipped with an Oxford Instruments EDS system (INCA350) was used to examine the microstructure and chemical composition of the nanoparticles. The TEM was operated with 200 kV accelerating voltage in conventional bright-field mode. Details of the instrument are shown in Table 3.3. Selected area electron diffraction (SAED) patterns were recorded to identify the crystallinity of the particles.

Table 3.3. Details and features of FEG TEM (FEI Tecnai F20)

<table>
<thead>
<tr>
<th>System</th>
<th>FEG TEM (FEI Tecnai F20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron Source</td>
<td>Schottky FEG</td>
</tr>
<tr>
<td>Detectors</td>
<td>Bright field imaging</td>
</tr>
<tr>
<td>Voltage</td>
<td>200 kV</td>
</tr>
</tbody>
</table>

3.4.7. Superconducting Quantum Interference Device
The magnetic properties of the beads were measured with a superconducting quantum interference device (SQUID) magnetometer (Quantum Design, San Diego, CA, USA) at room temperature as described previously. Measurement were made by Mark Platt.
3.4.8. Sedimentation rates
The samples were vortexed and sonicated. They were then left to stand and were extracted for measurement by Tunable Resistive Pulse Sensing (TRPS)\textsuperscript{30,31}. This process was done by Mark Platt.

3.4.9. Separation Speed
The samples consisting of magnetic particles were vortexed and sonicated. The solution was then placed on a magrack and extracted for measurement by TRPS. This process was done by Mark Platt.

3.5. Results and Discussion
Emulsion droplets were created within a microfluidic chip via a flow focusing strategy; a magnified section of the chip showing the droplet creation is given in Figure 3.1a. The droplet chip had a 14 µm etch depth. The full dimensions of the flow channels are given in Figure 3.2. The size of the droplets were controlled by the chip dimensions as well as the flow rate of the organic solvent (P1) and aqueous phase (P2). As the chip’s dimensions remain constant throughout the experiment, the droplet size is varied by the flow rates of the liquid precursors. Surfactant was added in the aqueous phase to stabilise the droplets.

The droplet diameter that can be created with this chip ranged from 5 to 30 µm. The size range was limited in part due to chip dimensions, the low viscosity of the liquid, and the flow rates that could be applied where the droplets could be clearly imaged on the microscope. The microfluidic chip is optically transparent. This allowed a microscope coupled to a digital high-resolution camera to image and size the droplets. Images of droplet formation are given in Figure 3.3a, b and their size distribution is represented in a histogram in Figure 3.3c, d. The droplets then pass through a short tube into a collection pot. The elution time was around 1-2 min, depending on the flow rate chosen.
Figure 3.2. Dimensions of the flow channel of the chip

a) The size of the chip is 22.5 × 15 × 4 mm (length × width × thickness)
   i) the wide channel cross section is 14 × 500 µm (depth × width)
   ii) the channel cross-section at junction is 14 × 17 µm (depth × width)

b) Image of the chip, it is made from glass with a flow focusing geometry. The surface of the channel is hydrophilic (product no. 3200136) to produce oil-in-water droplets.

c) The image shows the setup of the chip. Images b and c were taken from datasheet from Dolomite Centre Ltd. MAR-000061 v1.4
Figure 3.3 By adjusting the pressure between P1 and P2 (as shown in Figure 3.1), different droplet size can be produced. Example images of droplets where the average size was a) 12 µm ± 0.9 b) 24 µm ± 1.1 c) distribution histogram of image a) and b) respectively.
3.5.1. Fe₃O₄ nanoparticles

The starting materials (Fe₃O₄ nanoparticles) used in the organic phase (P1) were analysed using TEM, SAED and SQUID, as shown in Figure 3.4a, b and c, respectively. These particles have an average size of 12 nm, SAED shows that they are nanocrystals and the SQUID data showed that the nanoparticles had saturation magnetizations of 56 emu/g.

![Figure 3.4.](image)

Figure 3.4. a) TEM image of iron oxide nanomaterials, scale bar = 100 nm b) SAED of iron oxide nanomaterials c) M-H curve data for the feedstock ferrofluid. The data was captured at 298K. The particles have saturation magnetizations of 56 emu/g.

To prove that the nanoparticles are Fe₃O₄, the diameter of each ring of the SAED pattern was measured as shown in Figure 3.5a. Then the radius of each ring and its inverse was calculated (as shown in Table 3.4.). This matches the crystal lattice spacing of the International Centre for Diffraction (ICDD) pdf card of Fe₃O₄ (standard pattern 00-019-0629). Moreover, the 2nd ring of the SAED has the highest intensity which matches with the ICDD card. The indices of the diffraction rings are shown in Figure 3.5b.
Table 3.4. Conversion of measured diameter from SAED diffraction pattern to crystalline lattice spacing

<table>
<thead>
<tr>
<th>Ring no. (innermost)</th>
<th>Measured diameter from ring pattern (nm)</th>
<th>Radius (nm)</th>
<th>Inverse of radius (nm)</th>
<th>Inverse of radius (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{st})</td>
<td>6.78</td>
<td>3.39</td>
<td>0.29</td>
<td>2.9</td>
</tr>
<tr>
<td>2(^{nd})</td>
<td>7.94</td>
<td>3.97</td>
<td>0.25</td>
<td>2.5</td>
</tr>
<tr>
<td>3(^{rd})</td>
<td>9.6</td>
<td>4.8</td>
<td>0.21</td>
<td>2.1</td>
</tr>
<tr>
<td>4(^{th})</td>
<td>11.79</td>
<td>5.895</td>
<td>0.17</td>
<td>1.7</td>
</tr>
<tr>
<td>5(^{th})</td>
<td>12.45</td>
<td>6.225</td>
<td>0.16</td>
<td>1.6</td>
</tr>
<tr>
<td>6(^{th})</td>
<td>13.58</td>
<td>6.79</td>
<td>0.147</td>
<td>1.47</td>
</tr>
</tbody>
</table>
Figure 3.5. a) The diameter of each ring in the SAED pattern b) The indices (hkl) of the diffraction rings

Fe₃O₄ magnetite
Table 3.5. Summary of the droplet size, particle size and coefficient of variation (CV) values

<table>
<thead>
<tr>
<th>Figure no.</th>
<th>Organic phase</th>
<th>Aqueous phase</th>
<th>Droplet size</th>
<th>Particle size</th>
<th>CV of particle size</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6a</td>
<td>4.68 mg/mL ferrofluid in hexane</td>
<td>2% SDS</td>
<td>9.9 µm ± 1.72</td>
<td>1.3 µm ± 0.14</td>
<td>10.94 %</td>
</tr>
<tr>
<td>3.6b</td>
<td>0.52 mg/mL ferrofluid in hexane</td>
<td>2% SDS</td>
<td>12.4 µm ± 1.15</td>
<td>0.8 µm ± 0.08</td>
<td>9.18 %</td>
</tr>
<tr>
<td>3.7a</td>
<td>3.35 mg/mL ferrofluid in hexane</td>
<td>2% SDS</td>
<td>30 µm ± 1</td>
<td>2.9 µm ± 0.13</td>
<td>4.4%</td>
</tr>
<tr>
<td>3.7b</td>
<td>3.35 mg/mL ferrofluid in hexane</td>
<td>2% SDS</td>
<td>11 µm ± 1</td>
<td>1.5 µm ± 0.05</td>
<td>3.1%</td>
</tr>
<tr>
<td>3.9</td>
<td>3.35 mg/mL ferrofluid in pentane</td>
<td>2% SDS</td>
<td>13.4 µm ± 0.8</td>
<td>2 µm ± 0.2</td>
<td>10.73%</td>
</tr>
<tr>
<td>3.10a</td>
<td>2.34 mg/mL ferrofluid in hexane</td>
<td>2% SDS</td>
<td>13.8 µm ± 0.67</td>
<td>1.48 ± 0.11</td>
<td>7.5%</td>
</tr>
<tr>
<td>3.10b</td>
<td>2.34 mg/mL ferrofluid in hexane</td>
<td>4% Sodium octyl sulfate</td>
<td>8.2 µm ± 0.64</td>
<td>1.19 ± 0.04</td>
<td>3.4%</td>
</tr>
<tr>
<td>3.10c</td>
<td>2.34 mg/mL ferrofluid in hexane</td>
<td>2% sodium decyl sulfate</td>
<td>6.58 µm ± 0.99</td>
<td>0.94 ± 0.04</td>
<td>3.8%</td>
</tr>
<tr>
<td>3.10d</td>
<td>2.34 mg/mL ferrofluid in hexane</td>
<td>0.1% triton X-100</td>
<td>11.9 µm ± 1.26</td>
<td>1.92 µm ± 0.18</td>
<td>9.36%</td>
</tr>
</tbody>
</table>

3.5.2. Effect of iron oxide concentration
Using the setup listed as experiment A1 in Table 3.1, where Fe₃O₄ nanoparticles are suspended in hexane as the organic phase (P1) and 2% SDS in the aqueous phase (P2). Figure 3.6a shows an SEM image of the particles produced using a droplet 9.9 µm ± 1.72 in diameter with Fe₃O₄ at the concentration of 4.68 mg/mL. Spherical particles were produced. The size of the droplet was kept constant (approximately 10 µm) and the concentration of ferrofluid was varied. As the concentration of iron oxide was reduced from 4.68 to 0.52 mg/mL, the diameter of the particles reduced from 1.3 to 0.8 µm. The results are shown in Figure 3.6a, b and tabulated in Table 3.5. This is expected, as the concentration of nanoparticles is reduced, each droplet contains fewer iron oxide nanoparticles. Thus, once the hexane has evaporated, the
nanoparticles within each droplet merge and forms microparticles; represented in Figure 3.6c, d.

Figure 3.6. a) SEM image of Fe$_3$O$_4$ microparticles from a droplet size 9.9 µm ± 1.72, Fe$_3$O$_4$ = 4.68 mg/mL b) SEM image of Fe$_3$O$_4$ microparticles from a droplet size 12.4 µm ± 1.15, Fe$_3$O$_4$ = 0.52 mg/mL c) shows high number of nanoparticles in a droplet (corresponds to figure 3.6.a) d) shows lower number of nanoparticles in a droplet (corresponds to figure 3.6.b)

3.5.2.1. Theoretical calculation to predict the particle size
Prior to SEM imaging of the particles, it is possible to estimate the particle size by doing a theoretical calculation. For example, concentration of ferrofluid in hexane is 4.68 mg/mL, each droplet produced in the microfluidics channel has a diameter of 9.9 µm, hence the radius (r) is 4.95 µm.

3.5.2.1.1. Volume of the droplet
Assuming that the droplet produced are spherical in shaped (r = 4.95 µm), it is possible to find out the volume (V) of the droplet using equation 3.2.

\[
V = \frac{4\pi r^3}{3}
\]

\[
= \frac{4\pi(4.95 \, \mu m)^3}{3}
\]
\[ \text{mass} = \text{concentration} \times \text{volume} \]  
\[ = \frac{4.68 \text{ mg}}{1 \text{ mL}} \times 5.08047 \times 10^{-10} \text{ mL} \]  
\[ = 2.377 \times 10^{-9} \text{ mg} \]  
\[ = 2.377 \times 10^{-12} \text{ g} \]

### 3.5.2.1.3. Volume of iron oxide microparticle

The volume of the microparticle can be calculated using the equation 3.4, assuming microparticles are packed into sphere, and using bulk density of Fe$_3$O$_4$.

\[ \text{Volume} = \frac{\text{mass}}{\text{density of iron (III) oxide}} \]  
\[ = \frac{2.377 \times 10^{-12} \text{ g}}{5.24 \text{ g cm}^{-3}} \]  
\[ = 4.536 \times 10^{-13} \text{ cm}^3 \]

### 3.5.2.1.4. Diameter of the solid microparticle

Assuming the microparticle is spherical, it is possible to calculate the diameter of the microparticle by rearranging equation 3.2 into 3.5.

\[ r = \frac{3v}{4\pi} \]  
\[ = \frac{3(4.536 \times 10^{-13} \text{ cm}^3)}{4\pi} \]  
\[ = 4.766 \times 10^{-5} \text{ cm} \]  
\[ \text{Diameter} = 9.532 \times 10^{-5} \text{ cm} \]  
\[ = 0.95 \text{ µm} \]

Hence, when the concentration of iron oxide is 4.68 mg/mL, the estimate size of the microparticle is 0.95 µm, while the actual size is 1.3 µm (see Table 3.5). However, this
calculation is just an estimate, there are other factors that need to be taken into the account. For example, the type of solvent used (evaporation rate) and the viscosity of the surfactant.

3.5.3. Effect of droplet size
When 3.35 mg/mL Fe$_3$O$_4$ nanoparticles in hexane were placed in the organic phase (P1) and 2% SDS in the aqueous phase (P2), using droplet size of 30 µm ± 1, spherical particles were produced. Keeping the concentration of the reactants the same and decreasing the droplet size to 11µm ± 1, the particle size decreased. The data shown in Figure 3.7a-b are SEM images produced from droplet sizes of 30µm ± 1 and 11µm ± 1 in diameter and the sizes of the particles were 2.9 µm ± 0.13 and 1.5 µm ± 0.05, respectively. As the droplet diameter decreased, the particle size also decreased, the reason could be that the emulsion droplet acts as a template for the resultant particle size.

![Figure 3.7. SEM images of microparticles produced using droplet size a) 30 µm ± 1 b) 11µm ± 1 in diameter (hexane: spherical shaped)](image)

3.5.4. Effect of solvent
Keeping the concentration of the reactants the same and changing the solvent from hexane to pentane, the particle morphology changed from spherical to dimpled shape as shown in Figure 3.9. We hypothesise that the reason for the change in morphology is because pentane has a lower boiling point than hexane, so it evaporates quicker. A schematic diagram was proposed to illustrate the assembling of nanoparticles as shown in Figure 3.8.

According to Martin-Banderas et al.\textsuperscript{28} during the evaporation process, the final microparticle morphology is based upon two factors; time needed for the solvent to evaporate from the droplet and the time needed for the solute to diffuse through the droplet. If the drying process is slow, the solute will diffuse throughout the droplet and
accumulated at the center of the droplet, once the solvent evaporates it results in spherical shaped. On the other hand, when the drying process is fast, the solute is accumulated at the front of the droplet and once the solvent evaporates it gets pushed to the surface resulting in dimpled shaped. The particles produced here are bigger than the ones produced by hexane with the same droplet size; hence, we predict that the nanoparticles were locked at the interface of the droplet resulting in dimpled particles as shown in Figure 3.9. In section 3.5.2.1., the theoretical calculation shows the predicted size of the particle based on the droplet size and concentration of the ferrofluid, however it doesn’t take into account the evaporation rate of the solvent. Assuming the rate of evaporation of pentane does not have any effect on the size of the particle, the predicted size of the particle would be approximately 1.15 µm for the droplet size of 13.4 µm. The theoretical calculation of droplet stabilised by pentane is shown in section 3.5.4.1.

3.5.4.1. Theoretical calculation to predict the particle size

The concentration of ferrofluid in pentane is 3.35 mg/mL, each droplet has a diameter of 13.4 µm, and hence the radius (r) is 6.7 µm.

3.5.4.1.1. Volume of the droplet

Assuming that the droplet produced are spherical in shape (r = 6.7 µm), it is possible to find out the volume (V) of the droplet using equation 3.2.

\[
V = \frac{4\pi r^3}{3}
\]

\[
= \frac{4\pi (6.7 \, \mu m)^3}{3}
\]

\[
= 1259.833 \, \mu m^3
\]

\[
= 1.25983 \times 10^{-9} \, mL
\]

3.5.4.1.2. Mass of iron oxide microparticle after evaporation

concentration of ferrofluid = 3.35 mg/mL

mass = concentration \times volume

\[
= \frac{3.35 \, mg}{1 \, mL} \times 1.25983 \times 10^{-9} \, mL
\]

\[
= 4.22033 \times 10^{-9} \, mg
\]
3.5.4.1.3. Volume of iron oxide microparticles

\[
\text{Volume} = \frac{\text{mass}}{\text{density of iron (III) oxide}} = 4.22033 \times 10^{-12} \text{ cm}^3
\]

\[
= \frac{4.22033 \times 10^{-12}}{5.24 \text{ g cm}^{-3}}
\]

\[
= 8.054275 \times 10^{-13} \text{ cm}^3
\]

3.5.4.1.4. Diameter of the solid microparticles

\[
r = \sqrt[3]{\frac{3V}{4\pi}}
\]

\[
= \sqrt[3]{\frac{3(8.054275 \times 10^{-13} \text{ cm}^3)}{4\pi}}
\]

\[
= 1.9228 \times 10^{-13}
\]

\[
= 5.7718 \times 10^{-5} \text{ cm}
\]

Diameter = \(1.15436 \times 10^{-4}\) cm

\[
= 1.154 \mu\text{m}
\]

**Figure 3.8. Schematic of the formation of the microparticle, where NP1 represents Fe₃O₄ nanoparticles**
3.5.5. Effect of changing the surfactant
Using the setup listed as experiment A1 in Table 3.1, Figure 3.10a shows an SEM image of particles produced using SDS to stabilise the droplets. The particles were produced using droplets of 13.8 µm ± 0.67 in diameter with Fe$_3$O$_4$ at 2.34 mg/mL. Keeping the concentration of the reactants the same and changing the surfactant, Figure 3.10a-d are SEM images of Fe$_3$O$_4$ particles produced from surfactant 2% SDS, 4% sodium octyl sulfate, 2% sodium decyl sulfate and 0.1% triton X-100. The morphology of the particles were all spherical except the ones from triton X-100 where it had a crumbled shape. Sodium dodecyl sulfate, sodium octyl sulfate and sodium decyl sulfate are all anionic surfactants but the only difference is the carbon chain length. On the other hand, triton X-100 is a non-ionic surfactant and it has a viscous property. From this, it can be concluded that anionic surfactants are more favourable to use in oil-in-water emulsions than non-ionic surfactants, forming more micelles and aggregates into a spherical shape. As discussed in chapter 2, the CMC of non-ionic surfactant is much lower than ionic-surfactant, hence much lesser surfactant is required to reach the CMC and lesser micelles are formed compared to ionic surfactants. It could also be related to the critical packing parameter (CPP) of the surfactant (discussed in chapter 2). According to the prediction of CPP, SDS mostly forms spherical shaped while triton X-100 is a non-ionic surfactant, forms inverted-micelles which is more suitable to in water-in-oil emulsions.
3.5.6. Effect of critical micelle concentration (CMC)
Many properties of the surfactant changes, when it goes above the CMC. For example, the surface tension reduces rapidly above the CMC. Other properties such as turbidity increases above the CMC. The reason is because above the CMC, molecules or ions forms a larger unit called micelle.\textsuperscript{32} Hence, sodium dodecyl sulfate formed micelles only above the CMC, which is above $8.39 \times 10^{-3}$ mol dm\textsuperscript{-3}.\textsuperscript{32} Keeping the concentration of the reactants the same but reducing the concentration of sodium dodecyl sulfate to be below the CMC, the particles aggregate as shown in Figure 3.11a. Similarly, reducing the concentration of sodium octyl sulfate below the CMC, the particles aggregate as shown in Figure 3.11b. The hypothesis is that at low concentration of CMC there are not enough micelles hence the particles aggregate.
3.5.7. Particle size and CV errors
From Table 3.5., the range of CV values produced are between 3-11%. The variation of the CV could be because of reusing the chip due to its high cost. Even though after cleaning the chip there could still be a slight contamination at the exit channel leading to some samples having a high CV values. While, using a new chip the samples usually have low CV values.

3.5.8. Comparison of magnetisation between LUEL and commercial particles
Information obtained from manufacturers allows the comparison of magnetisation between the in-house or LUEL and commercially available particles (size range 100 nm – 5 µm). Figure 3.12 shows the comparison of magnetisation between different manufacturers. It can be seen that the LUEL particles of 1 µm have the highest magnetisation of 56 emu/g, while the Dyna particles of 1 µm and 2.7 µm have a magnetisation of 17 emu/g and 23 emu/g, respectively, and Spherotech particles of 3 µm have a magnetisation of 24 emu/g. When particles have higher magnetisation it enables faster separation and can extract larger analytes. In terms of applications, if particles take a long time to be extracted from the solution, it affects the detection limit and sensitivity of the assay.

The differences in iron oxide content between LUEL and other companies particles is because of the preparation method. For the preparation of LUEL particles, no additional components (other than iron oxide) were added to the particles. However, other companies could have additional components in their particles such as polymer, hence there could be a lower fraction of iron oxide compared to LUEL particles. Hence, higher magnetisation is observed for LUEL particles compared to other company’s
particles (Figure 3.12). Moreover, LUEL particles also have a higher magnetisation compared to most of the other particles reported in the literatures.

![Magnetisation curves for different commercial particles](image)

*Figure 3.12. Comparison of magnetisation curves for different commercial particles; a) Dynabeads: 17 emu/g for 1 µm, b) Dynabeads: 23 emu/g for 2.7 µm, c) Spherotech: 24 emu/g for 3 µm and in-house or LUEL particles: 56 emu/g for 1 µm.*

3.5.9 Comparison of sedimentation rates and separation speed between LUEL and Dyna particles
This comparison study was done between LUEL and Dyna particles as part of an external collaboration. The LUEL and Dyna particles that were used have a mean size of 1.04 ± 0.04 µm and 1.06 ± 0.01 µm, respectively.

3.5.9.1 Sedimentation rates

The study of sedimentation rates is not very common in the literature; however we consider it important to study the rates in order to compare the mass of iron oxide content. Using the method described in section 3.4.8, for both LUEL and Dyna particles, the solution that contained LUEL particles was found to settle to the bottom of the beaker faster than Dyna particles. After 15 and 30 minutes, the concentration of LUEL particles reduced to 25% and 22%, respectively, while the concentration of Dyna particles reduced to 34% and 31%, respectively. Hence, it can be concluded that there is a high mass of iron content in LUEL than in Dyna particles.
3.5.9.2. Separation Speed
Using the method described in section 3.4.9., the solutions containing LUEL and Dyna particles were placed on the magrack and the magnetic particles moved towards the magnet. The remaining particles were extracted as shown in Figure 3.13a. The extracted solution was measured using TRPS. This process was repeated for different concentrations (4 x 10^9, 4 x 10^8, 4 x 10^7 and 4 x 10^6 particles/mL) for both LUEL and Dyna particles. Almost all concentrations of LUEL particles were removed from the solution within 30 minutes. The extraction time for each concentration is shown in Figure 3.13b. For Dyna particles at high concentrations (>4 x10^9 particles/mL), particles were removed within 30 seconds and at lower concentrations (<4x10^9 particles/mL), more than 90% still remained in the solution. The extraction time for each concentration is shown in Figure 3.13c. The speed of extraction depends on the susceptibility of the particle, volume of the particle, solution viscosity and applied magnetic field, as described in equation 3.6. Faster sedimentation and separation is very desirable as this enables the extraction of larger analytes within a minimum time.

\[ \vec{F} = \frac{V \Delta \chi}{\mu_0} (\vec{B}, \nabla) \vec{B} \]  

(3.6)

Where,

F = Force (N)

V = volume of particle (m^3)

\( \mu_0 \) = permeability of a vacuum (TmA^-1)

B = applied magnetic field (T)

B. \( \nabla \) = magnetic gradient (Tm^-1)

\( \Delta \chi \) = difference in magnetic susceptibility between particle and surrounding medium
Figure 3.13. a) The magrack was used to separate particles from the solution, at different time intervals the remaining solution was extracted and measured; b) separation efficiencies for LUEL beads; c) separation efficiencies for Dyna beads
3.6. Conclusions
Monodispersed superparamagnetic microparticles were successfully generated using a flow focusing microfluidic channel. These particles have a size ranged between 1-2 μm and the CV below 11%. When these particles were compared with commercial particles, they have higher magnetisation. Highly uniform and magnetic particles are in demand for both commercial and medical aspects as it enables faster separation of analytes from the solution and allows particles to move at the same speed which results in higher sensitivity.

By increasing the concentration of ferrofluid and droplet size, bigger spherical particles were obtained. When the solvent was changed from hexane to pentane, the particles have a dimpled morphology. A series of surfactants were used such as sodium octyl sulfate, sodium decyl sulfate, sodium dodecyl sulfate and triton X-100. All surfactants formed spherical morphologies except for triton X-100. These particles provide a platform for forming core@shell particles which will be discussed in future chapters.
3.7. References


Chapter 4. Synthesis and Assembly of Gold and Iron Oxide particles within an Emulsion droplet; facile production of Core@Shell particles

4.1. Abstract
This chapter report a method for synthesising and assembling nanomaterials between two immiscible liquids using an emulsion droplet as a template. This results in a simple strategy for producing gold shells (Au shells) or \( \text{Fe}_3\text{O}_4 \)@Au core@shell particles, where @ represents “in”. Mercaptododecanoic acid stabilised Au nanoparticles were added to the aqueous continuous phase, to stabilise hexane emulsion droplets formed within a microfluidic chip. This created Pickering emulsions and the diameters of Au Pickering emulsions could be controlled by varying the flow rates. Evaporation of the hexane produced gold shell particles. The addition of a second nanoparticle, \( \text{Fe}_3\text{O}_4 \) (average diameter of 12 nm), into the organic phase produced \( \text{Fe}_3\text{O}_4 \)@Au core@shell particles. The diameter of the resultant material was determined by the concentration of the \( \text{Fe}_3\text{O}_4 \). This chapter provides the first demonstration of Pickering emulsions within a microfluidics chip for the production of \( \text{Fe}_3\text{O}_4 \)@Au core@shell particles, and it is believed that this could be a versatile platform for the large scale production of core@shell particles. The work here was published in Colloid and Interface Science Communications in 2017, pg. 14-18.

4.2. Introduction
The use of solid particles acting as stabilizers between two immiscible liquids was first founded by Ramsden\(^1\) and Pickering\(^2\) in 1903 and 1907. Pickering emulsions are basically adsorption of solid particles at the interface (oil-water).\(^3\) When droplets are coated by particles its rigid and hence resists coalescence.\(^3\) These types of droplets resembled an egg shell.\(^3\) There is adhesion energy that holds these particles to the oil-water interface (detail in section 2.4).\(^3\) Due to its stability, Pickering emulsions can be used in various applications in cosmetic, food and pharmaceutical purposes.\(^4\) Frelichowska et al.\(^5\) compared the transfer rate of a hydrophilic drug (caffeine) through the skin from Pickering emulsions and surfactant based emulsions. The results showed faster permeability through the Pickering emulsions than surfactant based
emulsions.\textsuperscript{5} The reason was because of the stronger adhesion of particle based coating than surfactant based coating.\textsuperscript{3,5}

Moreover, some surfactants maybe harmful for the environment hence solid particles are better alternatives.\textsuperscript{4} Different types of particles can be used as emulsion stabilisers, for example, polystyrene, silica, metal sulfate, iron oxide and clay particles.\textsuperscript{6} In some cases, particles made from natural materials are also used for stabilisation such as naturally occurring spore particles\textsuperscript{7}, bacterial cellulose nanocrystals\textsuperscript{8} and water-insoluble proteins\textsuperscript{9}. Before these particles can be used to form Pickering emulsions they are usually modified in order to be surface active. For example, Zhou \textit{et al.}\textsuperscript{10} functionalised Fe\textsubscript{3}O\textsubscript{4} nanoparticles with carboxylic acid while Du \textit{et al.}\textsuperscript{11} functionalised gold nanoparticles by grafting them with mercaptoundecyltetra (ethylene glycol).

The use of nanomaterials instead of surfactant has additional benefits or nanomaterials. For example, gold nanoparticles are used in electronic, and optical devices\textsuperscript{12}, catalysts\textsuperscript{13} and biosensors\textsuperscript{14}. Similarly, superparamagnetic Fe\textsubscript{3}O\textsubscript{4} nanoparticles can be used in magnetic resonance imagining (MRI) and drug delivery\textsuperscript{15}. Yamanaka \textit{et al.}\textsuperscript{14} used a homogeniser to generate water-in-oil Pickering emulsions where gold nanoparticles coated with 15-mercaptopentadecanoic acid (MPDA) were used for stabilisation. The emulsions produced were stable over a long period (approximately 12 months). The resultant particles were aggregates of gold.\textsuperscript{14} Zhou \textit{et al.}\textsuperscript{15} prepared Pickering oil-in-water emulsions using silane coated Fe\textsubscript{3}O\textsubscript{4} nanoparticles as the emulsifier.

The combination of iron oxide as a core and gold as a shell is a very interesting area of study as may result in a magnetically responsive core with a shell which exhibits plasmonic behaviour.\textsuperscript{16} However, no literature has reported the synthesis of Pickering emulsions within a microfluidic channel to generate Fe\textsubscript{3}O\textsubscript{4}@Au core@shell particles. Hence, we present the first demonstration of Pickering emulsions within a microfluidic chip for the production of Fe\textsubscript{3}O\textsubscript{4}@Au particles, where the core size can be controlled by the concentration of iron oxide (NP1) in the organic phase as shown in Figure 4.1. While, the shell was formed by assembling gold nanoparticles (NP2) at the interface of the droplet (Figure 4.1.). The technique has the advantages of not requiring long reaction times, surfactants or templates to produce the asymmetric materials.
4.3. Aims and Objective
The main aim of this study is to generate gold shells and Fe$_3$O$_4$@Au core@shell particles. Gold nanoparticles (AuNPs) were used as surfactants to assemble gold shells and the addition of iron oxide nanoparticles formed Fe$_3$O$_4$@Au core@shell particles within a flow-focusing microfluidic device.

4.4. Materials and Methods
4.4.1. Chemicals and Reagents
The following chemicals are from Sigma Aldrich, U.K. and unless stated the chemicals were used without purification. Sodium dodecyl sulfate (SDS) (436143), Iron (II) chloride tetrahydrate (FeCl$_2$·4H$_2$O) (220299), Iron (III) chloride hexahydrate (FeCl$_3$·6H$_2$O) (236489), ammonium hydroxide (NH$_3$·H$_2$O) (338818), oleic acid (364525), perchloric acid (244252), Gold (III) chloride trihydrate (≥49%) (G4022), Tetraoctylammonium bromide (98%) (294136), 12-mercaptododecanoic acid (12-MDA) (675067), 16-mercaptohexadecanoic acid (16-MHDA) (448303), sodium borohydride (NaBH$_4$) (98%) (452882), sodium hydroxide (NaOH) (795429). The following chemicals are from VWR chemicals, U.K. and unless stated the chemicals were used without purification. Hexane (24,580.324), ethanol absolute (20,821.330), toluene (28,676.322), were used. Deionized (DI) water was collected from Millipore water purification system having 18 Ω cm conductance) was used throughout.

Figure 4.1. a) Schematic of liquid-liquid interface with i) nanoparticles NP1 and NP2 presynthesised and dispersed in the organic and aqueous phase respectively. ii) Particle at a Pickering emulsion interface. iii) Core@shell Pickering emulsion. b) Schematic of the microfluidic assembly and droplet collection. P1, P2 represents the organic and aqueous phase respectively. The droplets flowed through a tube 5 cm long into a collection vial.
Table 4.1. Parameter for experiments using Pickering emulsions (B1, B2). P1, P2 is the organic phase, and aqueous phase respectively.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Classification</th>
<th>P1 (organic)</th>
<th>P2 (aqueous)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>Pickering emulsion (Au Shell)</td>
<td>hexane</td>
<td>5 mg/mL MDA-Au particles</td>
</tr>
<tr>
<td>B2</td>
<td>Fe$_3$O$_4$@Au (core@shell)</td>
<td>3 mg/mL ferrofluid in hexane</td>
<td>5 mg/mL MDA-Au particles</td>
</tr>
</tbody>
</table>

4.4.2 Synthesis of hydrophobic nanomagnetic particles, the setup of microfluidic set up and analysis is described in chapter 3

4.4.3. Synthesis of gold nanoparticles coated with 12-mercaptododecanoic acid in toluene.

Gold nanoparticles were prepared by a previously reported technique$^{17}$, HAuCl$_4$ (0.05 M, 4 mL) was mixed with 11 mL of 0.05 M tetraoctylammonium bromide in toluene (0.05 M, 11 mL) in a vial. The mixture was left stirring for a minimum of 2 h, the organic phase was then transferred to another vial and 12-mercaptododecanoic acid (1200μL) was added to it followed by freshly prepared NaBH$_4$ (0.4 M, 25 mL) with vigorous stirring. Colour change from orange to deep brown indicates completion of the reaction. The mixture was left stirring for a minimum of 3 h. The organic phase was separated from the mixture and transferred to a clean vial. The organic phase (500 μL) of the AuNP solution was transferred to an Eppendorf tube allowing the solvent to be evaporated to dryness. Ethanol (1500 μL) was then added to the precipitate, followed by 2 drops of NaOH (5 M). The Eppendorf tube was vortexed to disperse the pellet and then kept in the freezer for 16 h following a centrifuged process at 12000 rpm for 5 min. The supernatant was removed and washed twice with ethanol (1000 μL) followed by DI-water (100 μL). At this point, the particles had dispersed into the aqueous solution and it appeared brown.

4.4.4. NanoDrop UV-Vis Spectrophotometer

The instrument was calibrated by first running it with a blank (DI-water), and then the sample was pipetted on the pedestal. The pedestal adjusts itself to achieve the optimum path length (0.05-1 mm). The measurement was then taken and recorded.

4.5. Results and Discussion

4.5.1. Gold nanoparticles

In our previous chapter (experiment A1 in Table 3.1), we have shown that using oil-in-water emulsions as templates, iron oxide nanoparticles were assembled into
microparticles. By varying the concentration of Fe$_3$O$_4$ or the droplet size, the resultant microparticle diameter can be varied. To replace the SDS with a nanoparticle, the flow rates of P1 and P2 were adjusted to give emulsion droplets. 12-mercaptododecanoic acid (12-MDA), stabilised particles were synthesised as described in section 4.4.3. A TEM image and SAED pattern are shown in Figure 4.2a, b which illustrates their size is approximately 2nm, however, no crystalline structure was detected, this could be due to instrument limitation. Gold peak was observed on the EDS spectrum (Figure 4.3). These particles have been previously shown to sit at the toluene-water interface.$^{14}$

![Figure 4.2. a) TEM of aggregates of 12-MDA-Au particles used for Pickering emulsion b) SAED pattern of Au particles](image)

Figure 4.2. a) TEM of aggregates of 12-MDA-Au particles used for Pickering emulsion b) SAED pattern of Au particles
4.5.2. Gold shells

To test the ability of these particles to stabilise droplets, the gold nanoparticles were added to P2 at 5 mg/mL, in the absence of SDS or any Fe₃O₄ within P1, the flow rates of P1 and P2 adjusted to give emulsion droplets of 7.7 μm ± 0.73, experiment B1 in Table 4.1. It is important to note that in this setup no SDS or other surfactants are present, and that the droplets formed at the junction are stabilised by the AuNPs themselves. In the control experiment, where no SDS and no gold nanoparticles are present, no droplets were formed and a jetting regime is maintained across all P1:P2 flow ratios.

Forming droplets shows that the AuNPs are surface active and that their absorbance onto the interface is rapid. The resultant emulsion droplets were then collected allowing hexane to evaporate, before imaging. SEM of Au shells are shown in Figure 4.4a and its EDS analysis shown in Figure 4.5. The average particle size obtained was 2.3 μm ± 0.56. Given the droplets were initially 7.7 μm ± 0.73 in size, it demonstrates that the sizes of the initial droplets created in the microfluidic device are not maintained. This may be due to either the surface coverage of the AuNPs on the droplets surface, being less than 1, and that the hexane is evaporating quicker than the AuNPs can form a full shell. More likely given the stabilising ligand (12-MDA), maybe a contributing factor and AuNPs are being transferred into the hexane layer as the droplet shrinks.

Analysis of the Au shells using TEM, Figure 4.4b, shows particles of differing morphologies under the electron beam. Smaller particles seemed to be more stable.
and maintained their spherical shape during observation, while larger particles, inset of Figure 4.4b, collapsed under the electron beam. This indicates that particles are not stable under the 200 kV beam used in TEM. Analysis of particles using SEM with an operating voltage not more than 20 kV does not cause the particles to change. The stability of the particles in biological solutions, or under applied forces still needs to be investigated. The different sizes of particles are then thought to be the result of this internalisation process at different stages.

Figure 4.4. a) Pickering Emulsions created from 12-MDA stabilised AuNPs, scale bar = 5 µm. b) TEM image of particles in part a, insert is a larger Au shell particle, scale bar for both = 100 nm.
4.5.3. Fe$_3$O$_4$@Au core@shell particles

For experiment B2 as shown in Table 4.1, the core and shell concepts, demonstrated in A1 (previous chapter) and B1 were combined together, and shown schematically in Figure 4.1aiii, to create an iron oxide core and AuNP Pickering emulsion shell. The SEM images of the particles are shown in Figure 4.6a. The flow ratios for the fluids created emulsion droplets 8.8 μm ± 0.9 in size, and the resultant particles were measured to be 1.5 μm ± 0.07 in size through analysis of the SEM images. This is comparable in size to the results obtained from chapter 3, suggesting the iron oxide core determines the eventual microparticle size. Some smaller particles were also observed under the SEM as shown in Figure 4.6a – white box labelled 1, elemental analysis of the stub and particles, labelled 1 and 2 respectively in Figure 4.6a are given in Figure 4.7. A clear Au signal was observed on the microparticles (area 2 and EDS spectrum in Figure 4.7b), whereas only Cu signal (SEM stub material) was observed in area 1 (EDS spectrum in Figure 4.7a). It may be that these smaller particles are a cluster of AuNPs and that their signal is swamped by the Cu making it difficult to detect. Upon closer inspection using high resolution FEG-SEM, the surface of the microparticles appears rough as shown in Figure 4.6b and suggests that the Au shell phase separates or forms clumps on the surface of the particle further analysis via
TEM confirms this as shown in Figure 4.6c. The TEM image (Figure 4.6c insert) does appear to show a layer of Au particles across the surface of the Fe$_3$O$_4$ microparticles. It was then possible to produce Fe$_3$O$_4$@Au core@shell particles via the Pickering emulsion, however the resultant microparticles may not have a uniform coating of AuNPs on their surface.

Figure 4.6. a) SEM image of Fe$_3$O$_4$@Au core@shell particles, scale bar 5 μm. b) High resolution SEM image of Au@Fe$_3$O$_4$ core@shell particles, scale bar 1 μm. c) TEM image of Fe$_3$O$_4$@Au core@shell particles, scale bar 200 nm, insert - magnified section of the microparticle surface.
4.5.4. UV-measurement
The optical properties of gold are always very interesting. Hence, UV measurements were taken for 12-MDA gold particles and the pickering emulsion created from it. The measured UV spectra is shown in Figure 4.8a. However, the spectra didn’t give us any peak. The reason could be that the particles were really small or it was obscured by the ligand used. However, the result from EDS analysis (figure 4.3 and 4.5) shows that both samples contain gold. According to Isaac et al.\textsuperscript{18} the ligand used have an effect
on the optical properties of the gold nanoparticles and can destroy the optical
properties of the nanoparticles. Similar experiments were conducted for 16-
mercaptohexadecanoic acid (16-MHDA) stabilised gold nanoparticles and the
pickering emulsion created from it. Figure 4.8b shows a bump at 500 nm. This
corresponds to the measurement reported in the literature, where it shows a peak at
520 nm using 15-mercaptopentadecanoic acid as the ligand\textsuperscript{14}.

\textbf{Figure 4.8.} a) Absorbance spectra for 12-MDA stabilised AuNPs and Pickering emulsions
created from 12-MDA stabilised particles b) Absorbance spectra for 16-MHDA stabilised
AuNPs and Pickering emulsions created from 16-MHDA
4.6. Conclusions
A method for the rapid assembly of nanomaterials between two immiscible liquid using an emulsion droplet as a template is presented. By placing the nanomaterials either outside/inside on both sides of the emulsion droplet, a shell/core or core@shell particle can be produced. In the absence of a core (inner particle), the Au shell was found to be unstable under the TEM beam, but appeared to form stable, micron sized particles when viewed under the SEM. Further studies are needed to show the stability of the shells under any external force, which may limit their applications, but the facile nature of the process opens up rapid and cost effective methods of materials synthesis. To the best of our knowledge, this is the first demonstration of Pickering emulsions within a microfluidics chip for the production of Fe$_3$O$_4$@Au core@shell particles. The technique has the advantages of not requiring long reaction times, surfactants or templates to produce the asymmetric materials.
4.7. References


Chapter 5. Synthesis of Gold Nanoparticles using the interface of an emulsion droplet

5.1. Abstract
A facile and rapid method for synthesising single crystal gold spherical or platelet (non-spherical) particles is reported in this chapter. The reaction takes place at the interface of two immiscible liquids where decamethylferrocene (DmFc) in hexane was the reducing agent and the aqueous phase was gold chloride (AuCl$_4^-$). The reaction is spontaneous at room temperature, leading to the creation of gold nanoparticles, (AuNPs). A flow focusing microfluidic chip was used to create emulsion droplets allowing reactions to take place as they act as microreactors. The technique allows the number of droplets, their diameter and even the concentration of reactants in both phases to be controlled. The size and shape of the AuNP is dependent upon the concentration of the reactants and the size of the droplets. By adjusting the reaction parameters the synthesised nanoparticles vary from nanometre to micrometre sized spheres or platelets. The surfactant used to stabilise the emulsion was also shown to influence the particle shape. Finally, the addition of other nanoparticles within the droplet allows for core@shell particles to be readily formed. It is believed that this technique can act as a platform for large scale production of core@shell particles. The work here was published in Langmuir in 2017, vol. 33, pg. 5464-5472.

5.2. Introduction
There are generally two main approaches to synthesise metal nanoparticles; “top down” and “bottom up” approaches. The top-down approach starts from bulk material and the size is reduced to nanomaterials by methods such as high-energy ball milling, electron-beam lithographic method or laser-based ablation. While, the bottom up approach, starts from ions in the solution which assembled to generate nanoparticles such as chemical reduction, microemulsions and interfacial synthesis. The focus here is more on the bottom-up approach.

Michael Faraday was the first scientist to synthesise gold nanoparticles where he used phosphorus disulfide to reduce tetrachloroaurate solution. In 1951, Turkevich synthesised gold nanoparticles in situ by reducing HAuCl$_4$ using the citrate stabilised method. Trisodium citrate dihydrate solution was added to the boiled HAuCl$_4$
solution under mechanical stirring. A red wine coloured colloidal suspension was obtained after several minutes and the size of the gold nanoparticles is approximately 20 nm. The first time gold nanoparticles were synthesised by in-situ using alkanethiol as stabiliser was in 1994, which is called “two-phase Brust-Schirifin method”. This method receives great success due to several reasons such as, the reaction was conducted in ambient temperature, gold nanoparticles are small (less than 5 nm in size) and monodispersed, stable and easily functionalised. The mechanism was investigated by many research groups. Later, other stabilisers were used such as polymers, dendrimers and surfactants.

Gold nanoparticles (AuNPs) of various morphologies are in great demand as they have many applications in catalysis, biosensing and therapeutics. Anisotropic particles, especially gold nanosheets and core@shell particles have gained particular attention as they possess enhanced optical properties for the treatment of tumours, enhanced Raman detection and optical sensors. Gold nano platelets on multilayer graphene can act as a photocatalyst for water splitting into oxygen and hydrogen which contributes to the advancement of renewable fuels. Synthetic strategies leading to highly anisotropic particles can require high temperatures, templates or polymer and molecular capping agents, however, recently there is an emerging trend to produce nanomaterials using “green” chemistries. Continuous microfluidic flow reactors are a powerful tool for synthesizing materials. The translation of batch chemistries onto continuous flow platforms represents an area of increased research as they offer reduced production costs, controlled and reproducible reaction parameters and scalable synthesis strategies. A common strategy for synthesising nanomaterials within these reactors is to use emulsion droplets. Such systems have been used to create a range of materials including particles of high aspect ratios. Experimental variables explored for these systems include surfactants, solvents and droplets sizes. These have all been found to influence the products. An extensive review on the subject was reported by Ganguli et al. and have been extensively applied to the production of AuNPs. Other techniques for AuNP synthesis include single and two phase liquid-liquid systems. The interface between two immiscible liquids offers a defect free, reproducible substrate to grow and assemble metals. This interface allows the material to be easily recovered, as the majority of the newly created particles remain
The assembly of nanomaterials at the liquid-liquid interface is spontaneous due to the favourable stabilisation of the interfacial free energy and was first discovered by Ramsden\textsuperscript{40} and Pickering\textsuperscript{41}.

The interface between two immiscible electrolyte solutions (ITIES) combines the defect free liquid-liquid interface, with the benefits of electrochemical strategies, allowing a degree of control over the growth and assembly of the material through the applied potential or template.\textsuperscript{27,35,37,42–51} Alternative chemical based strategies for liquid-liquid reactions are also reported\textsuperscript{39,46,51}, such reactions place with reducing agent in one phase (for example, organic) and a metal precursor in the second phase (for example, aqueous) as shown in (Figure 5.1Di) and a wide range of synthetic strategies at these interfaces have been reported\textsuperscript{32,33,52,53}.

In this chapter, a strategy for producing Au nanomaterials and Au@Fe$_3$O$_4$ core@shell particles using a simple chemical reaction at the interface of an emulsion droplet is presented. Each droplet acts as a microreactor, and the size and shape of the nanoparticle (NP) is then determined by the concentration of the reactants, surfactant and the concentration of the droplets. By changing the reaction parameters, either spherical single crystal AuNPs, single crystal micron sized Au platelets are produced. While, the same reaction was conducted at a large free standing interface produces only spherical AuNPs. Finally, to create Au@Fe$_3$O$_4$ particles, pre-formed Fe$_3$O$_4$ nanoparticle (NP1) were added in the organic phase (Figure 5.1). This could be a versatile platform for the large scale production of core@shell particles, which is later expanded to other metals (Chapter 6).

5.3. Aim and Objective

The main aim of this study is to combine emulsion droplets with the liquid-liquid interface to create gold particles and core@shell. In chapter 4, Fe$_3$O$_4$@Au core@shell particles were obtained but the shell was not fully covered, hence in this study particles are grown in situ using emulsion droplets as reactors. The reaction between decamethylferrocene and gold chloride results in gold spherical or platelet (non-spherical) particles. In addition, adding iron oxide nanoparticles results in the formation of Au@Fe$_3$O$_4$ core@shell particles unlike chapter 4 which formed Fe$_3$O$_4$@Au core@shell particles.
5.4. Materials and methods

5.4.1. Chemicals and reagents
The following chemicals were purchased from Sigma Aldrich, U.K. and unless stated the chemicals were used without purification. Sodium dodecyl sulfate (SDS) (436143), Iron (II) chloride tetrahydrate (FeCl₂·4H₂O) (220299), Iron (III) chloride hexahydrate (FeCl₃·6H₂O) (236489), ammonium hydroxide (NH₃·H₂O) (338818), oleic acid (364525), perchloric acid (244252), gold (III) chloride trihydrate (≥ 49%) (G4022), tetraoctylammonium bromide (98%) (294136), 12-mercaptododecanoic acid (12-MDA) (675067), bis(pentamethylyclopentadienyl) iron (II) (97%) (378542), sodium borohydride (98%) (452882), cetyltrimethylammoniumbromide (CTAB) (H9151), hydrochloric acid (HCl) (258148). The following chemicals were purchased from VWR chemicals, U.K. Hexane (24580.324), ethanol absolute (20821.330), toluene (28676.322), were used. Deionized (DI) water with a resistivity of 18.2 MΩ·cm was used throughout.

5.4.2. The microfluidic setup and analysis is described in chapter 3

5.4.3. Powder X-ray Diffraction
Samples were prepared for analysis by Powder X-ray Diffraction (PXRD) from suspensions. The suspensions were dropped onto silicon substrates and the liquid allowed to evaporate before being placed into Perspex sample holders. The sample holders were loaded onto a Bruker D8 Advance Powder X ray Diffractometer set up in reflection geometry with Cu Kα₁ radiation (1.54056 Å), selected from a Ge 111 monochromator and a LYNXEYE™ 1D detector. Data were collected over the 2θ range 30 80° 2θ with a step size of 0.007° and a count time of 2 s per step.

5.4.4. Thickness of the Au nanoplates
Thickness of the Au nanoplates was measured by two methods: 1) electron energy loss spectroscopy (EELS) attached to a FEI Tecnai F20 G2 S-Twin field emission gun (FEG) TEM; 2) cross section SEM. The Tecnai F20 FEGTEM was operated at 200kV and equipped with a Gatan ENFINA EELS spectrometer. EELS is the analysis of the energy distribution of electrons that have come through the specimen including elastic scattered electrons (zero-loss energy) and inelastic scattered electrons (low-loss and core-loss energy).
Figure 5.1. Schematic of the microfluidic assembly and droplet collection. A) P1, P2 represents the organic and aqueous phase respectively. B) The chip allows the droplets to be imaged via an optical microscope. C) The droplets flowed through a tube approximately 5 cm long into a collection vial. D) i) Schematic of the reaction taking place at the liquid-liquid interface, \( n \) molecules of reductant, \( nR \), are oxidised via the metal salt, \( M^{n+} \), to create \( n \) moles of oxidised reagent, \( nO \). ii) Product of the reaction adsorbed at the interface. Nanoparticle, NP1 or NP2 are presynthesised and dispersed in the organic or aqueous phase respectively.

Table 5.1. Parameters for experiments at the liquid-liquid interface (C1, C2). P1 and P2 is the organic phase, and aqueous phase respectively.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Classification</th>
<th>P1 (hexanes)</th>
<th>P2 (aqueous)</th>
<th>Reaction pot</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Au synthesis</td>
<td>DmFc (1-10 mM)</td>
<td>2%(wt/wt) SDS</td>
<td>AuCl_4^- (5-10 mM)</td>
</tr>
<tr>
<td>C2</td>
<td>Au@Fe_3O_4 (core@shell)</td>
<td>DmFc (1-10 mM)</td>
<td>3mg/mL Ferrofluid</td>
<td>2%(wt/wt) SDS</td>
</tr>
</tbody>
</table>

5.5. Results and Discussion

The concept is that, each droplet acts as a microreactor and this setup was used in the previous study (chapter 4) to assemble presynthesised AuNP on the surface of the hexane droplets.\(^{54}\) The AuNPs were added to the aqueous phase, NP2 (Figure 5.1D) stabilising the droplets even in the absence of any other surfactant, i.e. a Pickering emulsion is formed. This process created a gold shell on top of iron oxide nanoparticles added to the hexane phase, NP1 (Figure 5.1D) creating core@shell particles. However, in this Pickering emulsion setup the gold shell was thin and nonuniform in its coverage. Thus, to advance their application herein, the hypothesis was to create and control the thickness of the gold shell, growing the gold particles through a chemical reaction, similar to growing a fresh layer of Au skin. A similar mechanism
and process has been used with large free standing liquid-liquid interfaces creating a dense uniform layer of approximately 20 nm, spherical particles. The work reported here was inspired by Dryfe et al., where a liquid-liquid reaction takes place between tetrachloropalladate and DmFc with and without templates forming palladium nanoparticles. The particles formed without templates were reported to have ill-defined structures. Adapting from this, gold chloride was used as the oxidizing agent (metal precursor) and DmFc as the reducing agent, a reaction scheme is shown in Figure 5.1D.

A control experiment was performed to confirm if Au particles can spontaneously form at a free standing DmFc in Hexane/SDS/AuCl₄⁻ in water interface. The resultant AuNPs are shown in Figure 5.2a. The reaction can be represented in equation 5.1. TEM analysis shows that the particles observed via SEM are clusters of small approximately 70 nm AuNPs (Figure 5.2b). There could also be a possibility of ion transfer across the phase boundary as discussed earlier in chapter 2.

\[
H^+ (\text{AuCl}_4^-)_{(aq)} + 3\text{DmFc} \text{ (org)} \rightarrow \text{Au} \text{(int)} + 3\text{DmFc}^+ \text{ (org)} + 3\text{Cl}^- \text{ (aq)} + \text{HCl} \text{ (aq)} \quad (5.1)
\]

The same reaction was then performed at the interface of an emulsion droplet in the microfluidic device. To achieve this, the chip was filled until a steady stream of droplets was created, with DmFc in hexane (organic phase) and 2% SDS (aqueous phase). This was done to ensure no air bubbles are trapped in the device. Once a steady droplet stream had been created, e.g. Figure 5.1A, the aqueous solution was changed to include the AuCl₄⁻ salt. Upon reinitiating the droplet stream it quickly became disrupted as the chip outlet became blocked or obstructed with debris, resulting in the droplets being trapped, coalescing and obstructing the flow of liquid. This observation was repeated several times on numerous chips and always resulted in a deposit on the chip surface that disrupted droplet production until it had been removed through washing with 5M HCl. Once the chip had been washed in HCl for several hours, it was able to be reused to produce droplets, but quickly became blocked again upon the addition of the AuCl₄⁻ salt. It was assumed that the deposit was gold particles, and that the Au material was synthesised within seconds, causing the emulsion droplets to become unstable before exiting the chip. To avoid this problem, the droplets were first made in the presence of SDS before being dropped into the collection pot containing AuCl₄⁻ as described in experiment C1, Table 5.1. The exit tube from the chip was always submerged at the bottom of the solution to aid
dispersion and at least 5 mL of the HAuCl₄ solution was used. This was to try and ensure the gold was always in excess. During the reaction the collection pot changed from a yellow to green colour over a period of several minutes depending on the concentration of DmFc. After forming droplets for ~ 2 hours the pumps were switched off and the reaction pot was left for a minimum of 1 hour to allow the reaction to take place and hexane to evaporate. Following this the solution was centrifuged to collect the AuNP as described above.

![Figure 5.2. Free standing liquid-liquid interface particle with [AuCl₄⁻] = 5 mM and [DmFc] = 5 mM. a) SEM (Scale bar = 10 µm) and b) TEM (Scale bar= 200 nm) (click to enlarge)](image-url)
Table 5.2. Summary of the size of droplets, particles, total no. of particles and platelets of all the reactions mentioned in the chapter. * = stirring

<table>
<thead>
<tr>
<th>Figure no.</th>
<th>P1 (Organic phase)/P2 (Aqueous Phase)</th>
<th>Droplet size/ µm</th>
<th>spherical particle size</th>
<th>no. of spherical particles</th>
<th>no. of platelets particles</th>
<th>Collection Pot (AuCl₄⁻)/mM</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3a</td>
<td>5 mM DmFc/2% SDS</td>
<td>22 ± 0.9</td>
<td>450 nm ± 124.1</td>
<td>108</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5.3b</td>
<td>5 mM DmFc/2% SDS</td>
<td>15.1 ± 0.7</td>
<td>410 nm ± 128.1</td>
<td>86</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>5.3c</td>
<td>5 mM DmFc/2% SDS</td>
<td>13.4 ± 1.6</td>
<td>250 nm ± 69.3</td>
<td>76</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>5.3d</td>
<td>5 mM DmFc/2% SDS</td>
<td>9.1 ± 1</td>
<td>243 nm ± 65.6</td>
<td>55</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>5.3e</td>
<td>5 mM DmFc/2% SDS</td>
<td>7 ± 1</td>
<td>230 nm ± 55</td>
<td>39</td>
<td>35</td>
<td>5</td>
</tr>
<tr>
<td>5.4a</td>
<td>5 mM DmFc/2% SDS</td>
<td>11.4 ± 1.1</td>
<td>260 nm ± 65.5</td>
<td>53</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>5.4b</td>
<td>5 mM DmFc/2% SDS</td>
<td>12 ± 1</td>
<td>331 nm ± 76.5</td>
<td>51</td>
<td>13</td>
<td>5 *</td>
</tr>
<tr>
<td>5.4c</td>
<td>5 mM DmFc/2% SDS</td>
<td>12 ± 1</td>
<td>220 nm ± 85.9</td>
<td>48</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5.5a</td>
<td>10 mM DmFc/2% SDS</td>
<td>11 ± 1.4</td>
<td>194 nm ± 66.6</td>
<td>93</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>5.5b</td>
<td>5 mM DmFc/2% SDS</td>
<td>10 ± 1</td>
<td>240 nm ± 52.5</td>
<td>55</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>5.5c</td>
<td>1 mM DmFc/2% SDS</td>
<td>12 ± 1</td>
<td>454 nm ± 101.6</td>
<td>28</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>5.8a</td>
<td>5 mM DmFc/MDA-gold particles</td>
<td>11.5 ± 2.2</td>
<td>301 nm ± 49.5</td>
<td>100</td>
<td>34</td>
<td>5</td>
</tr>
<tr>
<td>5.8b</td>
<td>5 mM DmFc/2% CTAB:2% SDS (1:1)</td>
<td>11.7 ± 1.8</td>
<td>77 nm ± 26.4</td>
<td>25</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>5.12a</td>
<td>5 mM DmFc/3mg/mL ferrofluid</td>
<td>11.3 ± 1.17</td>
<td>286 nm ± 75</td>
<td>37</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>5.12b</td>
<td>50 mM with 3mg/mL ferrofluid</td>
<td>10.7 ± 0.81</td>
<td>264 nm ± 77.6</td>
<td>100</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>5.12c</td>
<td>10 mM with 3mg/mL ferrofluid</td>
<td>11.46 ± 1.4</td>
<td>280 nm ± 81.4</td>
<td>100</td>
<td>14</td>
<td>10</td>
</tr>
</tbody>
</table>
5.5.1. Effects of droplet size

Figure 5.3, shows an SEM image of the particles produced using droplets 22 ± 0.9 µm in diameter, with both the AuCl$_4^-$ and DmFc at 5 mM. Spherical particles were produced; they were much smaller than the initial droplet. Given that each DmFc molecule can only donate one electron, three mole equivalents of DmFc are required for each Au (III) ion. When placed in equivalent concentrations, the reaction would be limited by the DmFc. Keeping the concentration of the reactants the same and changing the droplet size should then result in different sized, or fewer, Au particles. The data shown in figure 5.3 a-e are SEM images of Au particles produced for droplet sizes of 22 ± 0.9, 15 ± 0.76, 13 ± 1.6, 9 ± 1 and 7 ± 1 µm in diameter. The sizes of the spherical particles were 450 ± 124.1, 410 ± 128.1 and 250 ± 69.3 nm for droplet sizes of 22, 15 and 13 µm, respectively, as shown in Figures 5.3 a-c. The data, including droplet size and number of counted particles, are summarised in Table 5.2. As the droplet diameter was decreased Au platelets were observed within the SEM images. This trend continued and as the droplet size was further reduced the number of platelets increased (Figure 5.3f). The average size and number of each particle taken from multiple SEM images is given in Table 5.2.

It was interesting and unexpected to see the appearance of gold platelets, and attempts were made to understand the parameters that influenced their formation. The decrease in droplet size affects two parameters. First the total number of droplets created and secondly, the total surface area for the reaction to take place. The volume of hexane used to make the 22 and 7 micron droplets was similar: approximately 1 mL over 30 minutes. Therefore, as the volume remains constant, the number of droplets and the total surface area of all the droplets increases by approximately 31 and 3.1 times respectively, as the diameter decreases from 22 to 7 microns (see detail calculation in section 5.5.1.1.). Hence, as the number of droplets and total surface area increases it leads to faster depletion of AuCl$_4^-$ around the droplets, resulting in more number of platelets (highest in droplets with diameter of 7 µm).

To test the effects of AuCl$_4^-$ concentration on particle morphology two experiments were performed. The first was increasing the AuCl$_4^-$ concentration to 10 mM, and in a second experiment a stirrer bar was placed into the reaction pot to help further disperse the droplets. Neither of these had any effect on the number of platelets and
the size of the spheres remained similar see Table 5.2 and Figure 5.4a-b. Lowering the AuCl$_4^-$ concentration to 1 mM resulted in the loss of the platelets (Figure 5.4c).

Figure 5.3. SEM of Au particle created under the conditions [AuCl$_4^-$] = 5 mM and [DmFc] = 5 mM. Droplet size a) 22 µm ± 0.9. b) 15.11 µm ± 0.76 c) 13.4 µm ± 1.6 d) 9.1 µm ± 1 e) 7 µm ± 1. Scale Bar = 1 µm f) Graph that shows the effect of droplet size on the number of spheres and platelet particles, Blue – spheres and Red - platelets.
Figure 5.4. SEM images a) [AuCl$_4^-$] = 10 mM and [DmFc] = 5 mM b) A stir bar was added to the pot to help disperse droplets [AuCl$_4^-$] = 5 mM and [DmFc] = 5 mM c) [AuCl$_4^-$] = 1 mM and [DmFc] = 5 mM SEM (Scale bar = 5 µm)

5.5.1.1. Calculation of number of droplets used and total surface area (a);
When the diameter of the droplet is 22 µm and radius is 11 µm

\[ V = \frac{4\pi r^3}{3} \]

\[ = 5.5 \times 10^{-15} \text{ m}^3 \]

\[ a = 4\pi r^2 \]

\[ = 1.52 \times 10^{-9} \text{ m}^2 \]

Number of droplets = \( \frac{\text{volume used to make droplets}}{\text{volume used to make 22 µm}} \)

\[ = 1.8 \times 10^8 \]

Total surface area = surface area \times \text{number of droplets}

\[ = 0.274 \text{ m}^2 \]

When the diameter of the droplet is 7 µm and radius is 3.5 µm

volume of the droplet = \( 1.79 \times 10^{-16} \text{ m}^3 \)

Surface area = \( 1.54 \times 10^{-10} \text{ m}^2 \)

Number of droplets = \( \frac{\text{volume used to make droplets}}{\text{volume used to make 7 µm}} \)

\[ = 5.59 \times 10^9 \]

Total surface area = 0.86 m$^2$
5.5.1.2. Ratio of number of droplets from 22µm to 7 µm (volume remain constant)

\[
\text{Ratio of droplets} = \frac{\text{number of droplets from 7µm}}{\text{number of droplets from 22 µm}}
\]

\[
= \frac{5.59 \times 10^9}{1.8 \times 10^8}
\]

\[
= 31
\]

5.5.1.3. Ratio of surface area from 22µm to 7 µm (volume remain constant)

\[
\text{Ratio of surface area} = \frac{\text{total surface area of droplets from 7 µm}}{\text{total surface area of droplets from 22 µm}}
\]

\[
= \frac{0.86 \text{ m}^2}{0.274 \text{ m}^2}
\]

\[
= 3.1
\]

5.5.2. Effects of DmFc concentration

The size of the droplet was kept constant (~ 12 µm, approximately half way in the size range created in this setup), and the concentration of DmFc was then varied. As the concentration of DmFc was reduced from 10, 5 to 1 mM it was expected that the resultant spherical AuNP diameter would also decrease, given the total number of e\(^-\) are reduced (see theoretical calculation in section 5.5.2.1). The results are shown in Figures 5.5a-c, and tabulated in Table 5.2. In contrast, larger spherical particles were formed; in addition, the number of platelets also increased as the concentration of DmFc decreased (Figure 5.5b) leading to large Au platelets (>2 µm) as shown in Figure 5.5c. This may be due to the number of nucleation events decreasing as the concentration of DmFc is lowered, allowing fewer nuclei to grow to larger particles.

The TEM images of the different shaped particles from Figure 5.5b are given in 5.5d, e and the SAED pattern for the platelet is shown in Figure 5.6a-b. The diffraction pattern shows the particles to be single crystals. When a material is crystalline its SAED pattern gives a sharp peak or has a spot pattern. The spot pattern matches to a single crystal face centered cubic, gold. Figure 5.6c shows the UV-Vis analysis of the spherical and platelet materials, as the concentration of DmFc was reduced from 10 to 1 mM. As the concentration of DmFc reduces, the particle size increases (as shown in Table 5.2), however from the UV-spectrum there was no shift in the peak, all the peaks were observed at approximately 300 nm. Hence, from the spectrum it could be inferred that the particles have very weak optical properties. However, further work needs to be done to have conclusive detail of their optical properties.
Hence, from the above experiments, it was observed that there are three main parameters that affect the increase in the presence of platelets: decreasing the concentration of DmFc, smaller droplet size and high AuCl₄⁻ concentration.

5.5.2.1. Theoretical calculation for the predicted size of gold particles
For example, if droplet diameter = 10µm, radius = 5 µm

5.5.2.1.1. Droplet volume
\[ v = \frac{4\pi r^3}{3} \]
\[ = 5.235 \times 10^{-16} \text{ m}^3 \]
\[ = 5.235 \times 10^{-13} \text{ dm}^3 \]

5.5.2.1.2. moles in each droplet
Concentration of DmFc = 0.005 M
\[ = 0.005 \text{ mol dm}^{-3} \]
Moles = concentration \times volume
\[ = 2.6175 \times 10^{-15} \text{ mol} \]

5.5.2.1.3. molecules per droplet
Molecules per droplet = Avogadro’s number \times moles
\[ = 6.022 \times 10^{23} \text{ mol}^{-1} \times 2.62 \times 10^{-15} \text{ mol} \]
\[ = 1.58 \times 10^8 \]

5.5.2.1.4. Moles of gold produced
1 droplet of DmFc denotes 3 electrons
\[ = \frac{1.58 \times 10^9}{3} \]
\[ = 5.27 \times 10^8 \]
moles of gold produced
\[ = \frac{5.27 \times 10^8}{6.022 \times 10^{23} \text{ mol}^{-1}} \]
\[ = 8.74 \times 10^{-16} \text{ mol} \]

5.5.2.1.5. mass of gold produced
Molar mass of gold = 197 g
Mass = mole \times molar mass
\[ = \frac{197 \text{ g}}{1 \text{ mol}} \times 8.74 \times 10^{-16} \]
\[ = 1.722 \times 10^{-13} \]
5.5.2.1.6. Volume of gold produced

\[
\text{volume} = \frac{\text{mass}}{\text{density}}
\]

\[= 9.062 \times 10^{-15} \text{ cm}^3\]

5.5.2.1.7. Radius of the particle

\[
\text{Radius} = \frac{3}{\sqrt{4\pi}} \sqrt[3]{\frac{3V}{4\pi}}
\]

\[= 1.29 \times 10^{-5} \text{ cm} \]

\[= 0.129 \mu\text{m}\]

Diameter of the particle = 0.129 µm × 2 = 0.258 µm = 258 nm

Hence theoretically, for a lower concentration, the particle size will be smaller but not in our case, where higher DmFc concentration the smaller the particle size and lower DmFc concentration gives bigger particle size. The reason could be that the probability to get 3e\(^{-}\) together to form one gold is less when the DmFc concentration is lowered, so it transfers 1e\(^{-}\) to the already formed metal, so it grows into bigger particles or platelets. Hence, at lower DmFc concentration, bigger particles are formed and also more platelets were observed.

Figure 5.5. a) SEM image of Au particles, from a droplet size 11 µm ± 1.4, [AuCl\(_4\)] = 10 mM and [DmFc] = 10 mM, b) SEM image of Au, from a droplet size 10 µm ± 1, [AuCl\(_4\)] = 5 mM and [DmFc] = 5 mM. c) SEM image of Au particles, from a droplet size 12 µm ± 1, [AuCl\(_4\)] = 5 mM and [DmFc] = 1 mM. Scale bars 1 µm. d - e) TEM of particles in figure b, scale bar 500 nm f) Graph that shows the effect of concentration of DmFc to the number of gold particles and platelets, Blue – spheres and Red – platelets.
Figure 5.6. (a) SAED pattern of the AuNP platelet shown in figure 5.5e. (b) The pattern is fully indexed to a single crystal Au [111] orientation. The major spots with higher intensity can be attributed to the {220} Bragg reflections and the weaker spots corresponding to $1/3(422)$ and $2/3(422)$ are forbidden reflections. The forbidden spots appearing have been well-documented as a result of surface defects of very flat shape single crystal Au.$^{57,58}$ (c) UV-Vis absorbance spectrum of AuNP produced by varying the DmFc concentration. The initial AuCl$_4^-$ salt solution (Black dashed line)
5.5.3. X-ray Diffraction (XRD) analysis
XRD analysis of the materials are shown in Figure 5.7. All the XRD data exhibit preferred orientation along the <111> direction, highlighted by the enhanced intensities of the 111 and 222 reflections. This is especially pronounced in the data shown for the samples in Figures 5.3e and 5.5c. As Au has a face centred cubic structure, this suggests its growth direction is along <111> which is common for face centred cubic materials and fits with the hexagonal platelet morphology, as observed in the SEM images (Figures 5.3e and 5.5c respectively). The data from the sample corresponding to the image in Figure 5.5a has greater peak widths, which suggests a smaller crystallite size and the peak shapes are also anisotropic, with a high angle tail (most pronounced for the reflection at 44.4° (2θ)). This could indicate the presence of different crystallite sizes, with sharper peaks superimposed on broader peaks. The SEM images in Figures 5.5b and 5.5c suggest the presence of large platelets and smaller spherical particles, which correlate with the XRD data.

Figure 5.7. XRD analysis of samples from figures 5.3 and 5.5, with offset to show the diffraction peaks.

5.5.4. Mechanism of gold particles and platelets
The growth of an Au particle across the interface as illustrated in Figure 5.1D would require an interfacial reaction. Both the metal (AuCl₄⁻) in the aqueous phase and reducing agent (DmFc) in organic phase react at the interface to form the nanoparticle. It is however unclear if the nucleation of the particles takes place at the liquid-liquid
interface, or as discussed elsewhere if the low solubility of the DmFc in hexane allows it to transfer to the aqueous phase before reacting to form nuclei. Upon the formation of the nuclei it would then be energetically favourable for the nuclei to become adsorbed at the interface. Once fixed it can act as a conduit for electrons i.e. once created the particles growth could be autocatalytic as the electrons from the diffusing DmFc can be tunnelled across the metallic particle to a waiting AuCl$_4^-$ ion in the aqueous phase. DmFc has been shown to enhance electron transfer rates at AuNP functionalised liquid-liquid interfaces. Such interfaces have also been shown to reduce O$_2$ forming H$_2$O$_2$, and the fermi level established across the interface is determined by the ratio of the DmFc/DmFc$^+$. In this circumstance the nucleation of new particles may be slowed as the concentration of DmFc is depleted.

In the current setup the droplets are stabilised by SDS, and in some synthetic strategies SDS has been shown to produce asymmetric AuNPs$^{64,65}$. In the examples here, we have a high throughput, room temperature synthesis strategy for producing platelets. To ascertain the influence of SDS on the particle morphology, it was removed and droplets were created and stabilised in the presence of small gold nanoparticles, NP2 (Figure 5.1D). These Pickering emulsions have been previously shown to form a gold layer on the outside of the droplets, stabilising the emulsion without the need for surfactant.$^{54}$ The AuNPs formed from the Pickering emulsion experiment are shown in Figure 5.8a. It is not clear if the Pickering particles acted as seeds to produce the cubic and platelet particles, and certainly not all of these initial Pickering particles are adsorbed into the growing phases as evident by their presence in the SEM. In the absence of the SDS, more cubic particles are produced as well as some platelets, which indicate that while SDS may play some role in templating the material it is not the only effect. Mixtures of CTAB and SDS were also used as alternative surfactants and the particles are shown in Figure 5.8b and summarised in Table 5.2. The platelets are no longer observed and only spherical particles remain. CTAB is known to have a strong influence on the growth of Au particles, although only spherical ones are observed here. Future work may allow the addition of specific surfactants to the reaction pot to produce a more uniform and controlled particle morphology. It is clear that while the surfactant has some influence on the resultant shape it is not be the only factor.
The growth of the NP will require the AuCl$_4^-$ salt to diffuse to the particles surface (D1), and as DmFc is consumed by the growing particle its diffusion towards (D2), and away from the particle (D3). The electron transfer rate will also affect the particle growth. The mechanism for the production of Au platelets or spherical particles is determined by which process is the rate determining step (RDS). The proposed scheme of the mechanism is shown in Figure 5.9. Since each DmFc molecule can only donate one electron, therefore three mole equivalents of DmFc are required for each Au (III) ion. Hence, at low concentration of DmFc the probability to get 3e$^-$ together to form 1 Au is reduced. Our hypothesis is that when DmFc doesn’t have 3e$^-$ to form new particles, instead it transfers 1e$^-$ to the already formed particles, so it grows into platelets and bigger particles. Similarly, as the surface area of the droplet increases (smaller size of the droplet) the rate of DmFc to DmFc$^+$ increases. This could lead to a lot of cations on one side and a lot of anions on the other side. This could slow the reaction, forming more platelets.

Our hypothesis only takes into account a single step reduction of Au(III) to gold metal. From the literature Au(I) might be an important aspect in the mechanism of the growth of the particles. The reaction could form Au(I) and then Au(I) could disproportionate on the preformed metal surface forming more metallic gold. However further work needs to be done.

In most of the experiments we have the AuCl$_4^-$ at a high and consistent concentration; when it is lowered the particles tend towards a spherical morphology. The concentration of DmFc is a variable with a more pronounced effect on the shape. By lowering its concentration, more platelets are produced. Oxidation of the DmFc causes the fermi level, and electron transfer rate, across the interface to decrease. Thus for spherical particles a low concentration of AuCl$_4^-$ and high concentration of DmFc is required, and for platelets a high concentration of AuCl$_4^-$ and low DmFc concentration is preferred. Interestingly if the concentration of the reactants remains constant and the droplets diameter decreased, data shown in Figure 5.3e, the rapid conversion of the DmFc to DmFc$^+$ lowers the potential energy much faster and this slow growth leads to enlarged platelets.
5.5.5. Thickness of platelets
Gold nanosheets have significant importance in various applications such as nanodevices and other electrochemistry related areas. Li et al. reported that large gold nanosheets that are single crystal and have very flat surfaces are desirable in sensor devices for treating tumors and also as a substrate. Huang et al. reported that ultrathin films exhibit unique properties. Kida synthesized gold nanosheets that have a thickness of 150 nm. Sanyal et al. synthesized gold nanosheets that have thickness between the range of 30 – 300 nm. Kim et al., synthesized gold nanosheets that have a thickness of 100 nm.
The thickness of platelets produced in this work was determined to be $36 \pm 7$ nm using cross-section SEM and EELS (Figure 5.10 and 5.11 respectively). Using EELS, the thickness can be worked out with an accuracy of $\sim \pm 20\%$.

*Figure 5.10. Cross-section SEM images to measure the thickness of platelets (Scale bar = 10 µm)*
Figure 5.11. a) Scanning transmission electron microscopy (STEM) bright field image b) EELS line scan profile of which the location is indicated by the line on the image. The scan started from the vacuum through the plate, passing the vacuum again and end on the carbon. Each point an EEL spectrum was recorded. c) a typical spectrum featuring the zero loss and low loss range of the transmitted electrons. d) The data points are converted to thickness. The thickness of the plate is calculated to be $\sim 36 \pm 7$ nm. The average mean free path ($\lambda$) value for 200kV electron in Au was taken to be 80nm. $^{59,60}$
5.5.6. Au@Fe₃O₄ core@shell particles

Finally, the setup was investigated to determine if core shell particles could be created. Fe₃O₄ nanoparticles were added to the hexane droplets with the DmFc. The resultant particles are shown in Figure 5.12a. Some platelets were produced alongside the spherical particles, although the number of platelets were higher with the addition of the Fe₃O₄. As described above, we hypothesise that platelets are formed when the diffusion of the DmFc to the particle is the RDS. The addition of the Fe₃O₄ particles to the organic phase would act to slow the diffusion of the DmFc towards and away from the interface. In an attempt to reduce the number of platelets, the concentration of DmFc was increased to 50 mM and while this had the desired effect, some platelets are still visible as shown in Figure 5.12b. All the particles imaged in Figure 5.12 were separated from solution and washed using a handheld magnet, and although not visible under the SEM the AuNPs must have either encapsulated or adsorbed some Fe₃O₄ particles on their surface. The reason could be that once the hexane evaporated, the particles attached itself to the gold surface, as they are hydrophobic they prefer not to be in the aqueous phase. TEM analysis of the particles (Figure 5.12c) shows how each AuNP is surrounded by the Fe₃O₄ NPs, EDS spectrum for Au and Fe₃O₄ is given in Figure 5.13.
Figure 5.12. SEM Images of Au@Fe₃O₄ particles produced using a) Droplets size 11.3 μm ± 1.17 [AuCl₄] = 10 mM and [DmFc] = 5 mM. Scale bar = 5 μm. b) Droplets size 10.7 ± 0.81 μm, [AuCl₄] = 10 mM and [DmFc] = 50 mM. Scale bar = 5 μm. c) TEM of particles produced droplets size 11.46 ± 1.4 μm, [AuCl₄] = 10 mM and [DmFc] = 10 mM. Scale bar = 50 nm. d) Graph that shows the effect of the concentration of ferrofluid in DmFc.
Figure 5.13. EDS spectrum for the sample in figure 5.12b a) Au peak b) Fe and O peak
5.6. Conclusions
A method for synthesising and assembling nanomaterials at the liquid-liquid interface of an emulsion droplet was presented. In an attempt to adorn each droplet with an Au nanoparticle skin, an interfacial reaction between DmFc in hexane and AuCl$_4^-$ within the aqueous phase, was employed to synthesise the Au nanoparticles on the droplets interface. In contrast to the same reaction at a large free standing interface which produces smaller spherical AuNPs, each droplet acted as a microreactor where the final size and shape of the NP was determined by the concentration of the DmFc or the size of the droplet. By changing the reaction parameters either spherical single crystal AuNPs or single crystal micron sized Au platelets can be produced. This could be a versatile platform for the large scale production of core@shell particles. The technique has the advantages of not requiring long reaction times, temperatures or templates to produce the asymmetric materials.
5.7. References


60. Iakoubovskii, K.; Mitsuishi, K. Elastic scattering of 200keV electrons in elemental solids: Experimental observation of atomic-number-dependent


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Chapter 6. Spherical and wrinkle shaped Fe$_3$O$_4$@Pd core@shell particles via microfluidics channel single step approach

6.1. Abstract

The synthesis of core@shell particles typically requires several steps, high temperature, supporting templates or harsh chemicals. A single step approach of producing core@shell particles, using palladium nanoparticles (PdNPs) and iron oxide (Fe$_3$O$_4$) microparticles as an example is reported. The microparticles produced are either spherical or wrinkle shaped, depending on the concentration of iron oxide and the rate at which Pd is created. These particles have the potential to function as catalysts as they are easily recoverable by an external magnet. The technique was attempted to be expanded to silver nanoparticles (AgNPs), this was less successful although it was shown how droplets can be used to make AgNPs. To the best of our knowledge, this is the first time wrinkled Fe$_3$O$_4$@Pd core@shell particles were synthesised using emulsion droplets as templates via microfluidic device.

6.2. Introduction

Metallic nanoparticles have been widely studied for several decades.¹ Catalysis, electronics, photography, optics, biological and sensing, surface enhanced Raman scattering (SERS) and information storage are some of the applications of metal nanoparticles.¹ The shape and structure of the metal nanoparticles determines its properties.¹ For instance, hollow Pd nanospheres due to their high surface area are used as catalysts.²

Bi-metallic nanoparticles further expand the use of metal nanoparticles. They are currently used in many applications due to their unique properties, for example, core-shell Au-Pd nanoparticles exhibit powerful activity for hydrogenation than plain palladium nanoparticles.³ The combination of iron oxide and palladium is an interesting area. These core-shell particles promise excellent catalytic activity and can be recovered by a magnet.⁴ Hence, many research groups have come up with different techniques of making iron oxide-palladium core-shell particles. Kumar et al.⁵ embedded Pd nanoparticles onto carbon@Fe$_3$O$_4$ by first synthesising carbon@Fe$_3$O$_4$ using Fe$_3$O$_4$ in the presence of glucose under hydrothermal conditions and then
deposited Pd nanoparticles. Tuo et al. used microorganisms (Shewanella oneidensis MR-1) to synthesise Pd/Fe3O4. Le et al. synthesised magnetic fibrous core-shell, Pd/Fe3O4@SiO2@KCC-1 by first functionalizing Fe3O4@SiO2@KCC-1 with amino groups which behave as anchors for palladium nanoparticles to be well distributed.

Silver nanoparticles are another interesting area, their antimicrobial properties allow them to be used in drug treatment for burns, dental equipments and sun screen lotions. There are many ways to synthesise silver nanoparticles, such as, the seeded growth or at the liquid-liquid interface.

Flow reactors are increasing in popularity due to the fact that the particle morphology can be controlled, it is reproducible and parameters are scalable. Santana et al. used droplet based reactors to synthesise Au@Pd core@shell particles, where the Pd shell was grown on Au seeds. Abou Hassan et al. synthesise goethite, Fe2O3@SiO2 core/shell and iron oxide nanoparticles using a coaxial flow reactor. Baber et al. synthesised silver nanoparticles in a coaxial flow channel by using silver nitrate and trisodium citrate solution in the inner stream and sodium borohydride (reducing agent) in the outer stream.

As reported in previous chapters, a flow focusing droplet chip was used to create emulsion droplets, in a flow-focusing microfluidic chip. The diameter of the droplets was controlled via the dimensions of the droplet chip and the flow rate between hexane (P1) and the aqueous phase (P2). Using the same concept, we hoped to form palladium particles, silver particles and core@shell particles by changing our collection pot to (PdCl4)2 and AgNO3, described in Table 6.1.

6.3. Aim and Objective

The aim of this chapter was to expand the concept used in Chapter 5 to other metal ions; palladium and silver ions. The addition of iron oxide nanoparticles allowed the formation of Fe3O4@Pd core@shell, but was shown not to work for silver. By varying the concentration of Fe3O4, different core@shell morphologies were observed from spherical to wrinkled shaped. It is believed that these core@shell has the potential properties to be used as catalysts or in other medical devices. The reactions occurring at the interface between the organic phase (DmFc) and the aqueous phase (palladium ions or silver ions) can be described as shown in equation 6.1 and 6.2.
\[
(PdCl_4)^2^-_{(aq)} + 2DmFc_{(org)} \rightarrow Pd_{(int)} + 2DmFc^{+}_{(org)} + 4Cl^-_{(aq)} 
\]
(6.1)

\[
AgNO_3_{(aq)} + DmFc_{(org)} \rightarrow Ag_{(int)} + DmFc^{+}_{(org)} + NO_3^-_{(aq)} 
\]
(6.2)

Table 6.1. Parameters for experiments at the liquid-liquid Interface (D1, D2, E1, E2)

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Classification</th>
<th>P1 (hexanes)</th>
<th>P2 (aqueous)</th>
<th>Reaction pot</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>PdNP synthesis</td>
<td>DmFc (1-10 mM)</td>
<td>2% (wt/wt) SDS</td>
<td>(PdCl_4)^2^- (5mM)</td>
</tr>
<tr>
<td>D2</td>
<td>Fe_3O_4@Pd (core@shell)</td>
<td>Fe_3O_4 (3-0.3 mg/mL) in DmFc (5 mM)</td>
<td>2% (wt/wt) SDS</td>
<td>(PdCl_4)^2^- (5mM)</td>
</tr>
<tr>
<td>E1</td>
<td>AgNP synthesis</td>
<td>DmFc (5 mM)</td>
<td>2% (wt/wt) SDS</td>
<td>AgNO_3 (10mM)</td>
</tr>
<tr>
<td>E2</td>
<td>Fe_3O_4@Ag (core@shell)</td>
<td>Fe_3O_4 (3mg/mL) in DmFc (5 mM)</td>
<td>2% (wt/wt) SDS</td>
<td>AgNO_3 (10 mM)</td>
</tr>
</tbody>
</table>

6.4. Materials and Methods

6.4.1. Chemical and Reagents
The following chemicals were purchased from Sigma-Aldrich, U.K., and unless stated otherwise the chemicals were used without purification. Sodium dodecyl sulfate (SDS) (436143), iron(II) chloride tetrahydrate (FeCl_2·4H_2O) (220299), iron(III) chloride hexahydrate (FeCl_3·6H_2O) (236489), ammonium hydroxide (NH_3·H_2O) (338818), oleic acid (364525), perchloric acid (244252), sodium tetrachloropalladate (II) (205818), bis(pentamethylcyclopentadienyl) iron(II) (97%) (378542), Potassium ferricyanide (K_3Fe(CN)_6) (244023), silver nitrate (99%) (204390) and sodium borohydride (98%) (452882). The following chemicals were purchased from VWR Chemicals, U.K. Hexane (24580.324), ethanol absolute (20821.330), and toluene (28676.322) were used. Deionized (DI) water with a resistivity of 18.2 MΩ·cm was used throughout.
6.4.2. The microfluidic setup and analysis is described in chapter 3

6.4.3. Focused Ion Beam
A focused ion beam (FIB) instrument is almost identical to a SEM, but uses a beam of ions rather than electrons. The focused ion beam can directly "mill" the specimen surface, via the sputtering process. A FIB becomes even more powerful when it is combined with a SEM as in the FEI DualBeam system. In a DualBeam, the electron and ion beams intersect at a 52° angle at a coincident point near the sample surface, allowing immediate, high resolution SEM imaging of the FIB-milled surface. Such systems combine the benefits of both the SEM and FIB and provide complementary imaging and beam chemistry capabilities. A FEI Nova 600 nanolab dual beam (FIB and SEM) equipped with EDS for chemical analysis was employed to cross section the Fe₃O₄@Pd core@shell particles.

6.4.4. UV-Vis Spectrophotometer
The instrument was calibrated by first running it with a blank (DmFc in hexane). From this, the absorbance maxima (λ_max) was obtained. Experiments at a free standing liquid/liquid interface were conducted for DmFc in hexane/SDS/metal ions in water, the top layer (DmFc) was placed in a cuvette for different time intervals.

6.5. Results and Discussion
The first experiment was to test if Pd has a spontaneous reaction with DmFc by conducting the experiment at a free standing DmFc in hexane/SDS/(PdCl₄)²⁻ in water interface. After the addition of DmFc to (PdCl₄)²⁻, a brownish film formed at the interface and the top solution was a tinge of green (indicating the formation DmFc⁺). The same reaction was then conducted at the interface of an emulsion droplet in the microfluidic device as described in experiment D1. Droplets continued to form for 2 hours, after which the collection pot was left for 1 hour to allow the hexane to evaporate. This was followed by centrifugation to collect palladium particles.¹⁷

6.5.1. Palladium nanoparticles
Using the setup listed as experiment D1 in Table 6.1, the size of the droplet was 8.52 µm ± 1 and the concentration of DmFc was 5 mM. The results shown in Figure 6.1a show that all were forming clusters of nanoparticles and some were breaking into fragments. It wasn’t clear if individual nanoparticles were forming, hence further analysis was done using TEM. Figure 6.1b shows a TEM image of palladium particles.
that gives a clearer indication that each cluster of particles consists of individual nanoparticles. The size of palladium nanoparticles was 4.69 nm ± 1.19. The histogram of the particle size is shown in Figure 6.1c. Its SAED pattern is shown in Figure 6.2a, indicating that these palladium nanoparticles are single crystal and its EDS spectrum is shown in Figure 6.2b. The hypothesis is that many palladium particles are formed on the emulsion surface and once the hexane evaporates, it forms clusters of particles.
Figure 6.1. a) SEM image of Pd particles, from a droplet size 8.52 µm ± 1, (PdCl$_4$)$_2$ = 5 mM and [DmFc] = 10 mM, scale bar = 1 µm b) TEM image c) histogram of the size distribution of palladium nanoparticles, average size is 4.7 nm ± 1.2.
6.5.2. Silver nanoparticles.
Again using the droplets, the formation of silver nanoparticles were studied by using the setup listed as experiment E1 in Table 6.1. Silver nanoparticles were formed by using 5 mM of DmFc with the droplet size of 10.6 μm ± 0.98. SEM and TEM images of the silver particles are shown in Figure 6.3a-b. The results are very similar to the
palladium nanoparticles, clusters of nanoparticles are formed, but here the silver nanoparticles are slightly bigger with an average particle size of 11.94 nm ± 2.73. Compared to palladium, silver nanoparticles are not as uniform. Its SAED pattern is shown in Figure 6.4a, indicating that these silver nanoparticles are single crystal and its EDS spectrum is shown in Figure 6.4b.

Figure 6.3. a) SEM image, scale bar = 2 µm b) TEM image of Ag particles, from a droplet size 10.68 µm ± 0.98, AgNO₃ = 10 mM and [DmFc] = 5 mM
Figure 6.4. a) SAED pattern b) EDS spectrum of Ag nanoparticles
6.5.3. Rate of reaction
The hypothesis was that many palladium and silver nanoparticles are formed on the emulsion surface and once the hexane evaporates, it forms clusters of particles. Here, only spherical particles were observed unlike gold particles where spherical particles and platelets were seen (Chapter 5). To gain a better understanding of the mechanism, the rate of reaction of three metals; gold, palladium and silver were studied. The rate of reaction was determined using UV-VIS spectroscopy measuring the rate of DmFc consumption. This was done by forming a free standing liquid-liquid interface between DmFc in hexane/SDS/metal ions in water where the absorbance of DmFc was measured at 0, 2, 5 and 10 min intervals at a wavelength of 424 nm. This wavelength was chosen as it shows maximum absorption ($\lambda_{\text{max}}$) when running a UV spectrum scan through DmFc. The data collected for the measured absorbance versus each time interval is shown in Table 6.2 and the plotted graph is shown in Figure 6.5. Potassium ferricyanide was used as the control.

Table 6.2. Measured absorbance verses time interval

<table>
<thead>
<tr>
<th>time</th>
<th>Au</th>
<th>Ag</th>
<th>Pd</th>
<th>Fe (Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.643</td>
<td>0.643</td>
<td>0.643</td>
<td>0.643</td>
</tr>
<tr>
<td>2</td>
<td>0.643</td>
<td>0.424</td>
<td>0.624</td>
<td>0.57</td>
</tr>
<tr>
<td>5</td>
<td>0.633</td>
<td>0.388</td>
<td>0.542</td>
<td>0.512</td>
</tr>
<tr>
<td>10</td>
<td>0.6</td>
<td>0.367</td>
<td>0.513</td>
<td>0.32</td>
</tr>
</tbody>
</table>
From Figure 6.5, it is observed that as time increases the absorbance of DmFc decreases. This indicates that during the reaction, DmFc diffuses to the metal ions forming an interface of nanoparticles, hence over a period of time the interface becomes more green in colour as well as forming a thicker layer of nanoparticles at the interface.

From the result, it could be inferred that the formation of nuclei in palladium and silver is much faster, which we attribute to the nuclei forming instantaneously. While, for gold, the formation of nuclei are much slower, resulting in the formation of nuclei at different time, therefore some form spherical particles while others form platelets.

The standard electrode potential ($E^\circ$) of AuCl$_4^-$ and PdCl$_4^-$ were found in the literature to be 0.591 V and 1.002 V.\textsuperscript{18,19} While most standard potentials are measured in water, the standard potential of AgNO$_3$ is widely reported in acetonitrile.\textsuperscript{20} The standard potential of AgNO$_3$ in acetonitrile was reported to be 0.503 V and its potential was calculated to be higher in water by 0.162 V. Hence, the $E^\circ$ of AgNO$_3$ in water is approximately 0.665 V.

From equation 6.3 to 6.5, gold has the highest standard electrode chemical potential which means the reaction should be the easiest to occur. This contradicts the observed rate of reaction.
6.5.4. Effects of DmFc concentration on Pd particles

In chapter 5, it was shown that the concentration of DmFc has an effect on the nanoparticle size and morphology. As a comparison, a study was done on the effect of DmFc on palladium particles. Using the setup listed as experiment D1 in Table 6.1, the size of the droplet was kept constant (~8 µm) and the concentration of DmFc was varied from 10 to 5 to 1 mM. The results shown in Figure 6.6a-c, The SEM images shows that the particles have similar morphology in all the three concentration which indicates that the effects of DmFc is not prominent on the size and morphology of the particles. The reason could be that the formation of the nuclei occurs at the same time, and that the instantaneous nucleation leads only to small spherical particles.
Figure 6.6. a) SEM image of Pd particles, from a droplet size 8.14 µm ± 1.24, \((\text{PdCl}_4)^2= 5 \text{ mM and } [\text{DmFc}]= 10 \text{ mM}\), b) SEM image of Pd, from a droplet size 8.52 µm ± 1, \((\text{PdCl}_4)^2= 5 \text{ mM and } [\text{DmFc}]= 5 \text{ mM}\), c) SEM image of Pd particles, from a droplet size 8.67 µm ± 1.13, \((\text{PdCl}_4)^2= 5 \text{ mM and } [\text{DmFc}]= 1 \text{ mM}\). Scale bars 1 µm

6.5.5. Effects of droplet size on Pd particles

Figure 6.7 shows an SEM images of particles produced using droplets 13µm ± 1.87. Increasing the droplet size from 8 µm to 13 µm, doesn’t change the morphology of the particles.
6.5.6. Formation of Au-Pd particles

An experiment was design to see if a Pickering emulsion could be used to create core@shell; Au@Pd particles. 12-mercaptododecanoic acid (12-MDA) was used as the surfactant instead of 2% SDS. These Pickering emulsions have been used in previous chapters to stabilised droplets. In chapter 4, it was used to create a gold skin on the outside of the droplet and adding iron oxide to it formed a core@shell particle. In chapter 5, it was used instead of SDS in the presence of DmFc in hexane and aqueous gold salt forming gold platelets and cubic particles. Therefore, it is interesting to see the influence it has on palladium particles.

In this experiment, 12-mercaptododecanoic acid (12-MDA) was used to stabilise DmFc in hexane droplets which were created in the microfluidic chip. These droplets were then collected in a pot containing (PdCl4)2-. Figure 6.8a, shows a TEM image of Au-Pd particles. It shows a big black particle (labelled 1) surrounded by lots of fluffy particles (labelled 2), the EDS spectrum (figure 6.8b) indicates that it consists of both Au and Pd elements. Particles labelled 1, have a size of approximately 7 nm and particles labelled 2 have an average size of 2.47nm ± 0.34 (same size to the gold particles used to form Pickering emulsion in chapter 4). From the observation, there is a formation of Pd particles without the use of SDS. In the future, this could be used for the formation of core@shell; Au@Pd particles.

Figure 6.7. SEM image of Pd particles, from droplet size, 13 µm ± 1.87, (PdCl4)2- = 5 mM and [DmFc] = 5 mM, Scale bar = 5 µm
6.5.7. Adding iron oxide to Pd nanoparticles

Using the setup listed as experiment D2 in Table 6.1, iron oxide nanoparticles were added to the DmFc droplets in hexane. The size of the droplet was kept constant (∼12 µm) and the concentration of iron oxide in the DmFc droplets was varied from 3 to 1 to 0.3 mg/mL (the concentration of DmFc was the same throughout; 5mM). The morphology of the particles changed from spherical to wrinkled shaped as shown in Figure 6.9a-c. Focused Ion Beam (FIB) was used on these particles as shown in Figure 6.9d-f. EDS spectrum and EDS mapping indicates that the white spot are palladium and the rest of the inside is iron oxide as shown in Figure 6.10, Figure 6.11 and Figure 6.12 for Fe₃O₄@Pd core@shell particles for the concentration of Fe₃O₄ of 3, 1 and 0.3 mg/mL respectively.

Figure 6.8. a) TEM image of Pd particles produced using pickering emulsion, from droplet size, 23µm ± 1.53, (PdCl₄)²⁻ = 5 mM and [DmFc] = 5 mM, b) EDS spectrum of Au-Pd particles.
Increasing the concentration of iron oxide will change the mass transport of the other molecules within the droplet. This change is hypothesised to be the reason the shells change their appearance. At a high concentration of iron oxide, the movement of DmFc to the interface will be slower, thus as DmFc is reacted at the interface its concentration decreases and as a result the growth of more palladium nanoparticles is reduced. This results in the formation of Pd@Fe₃O₄ core@shell particles where fewer palladium particles were formed inside the particles, as shown in Figure 6.9d, e. The holes inside the particles shows that the DmFc has been washed out (Figure 6.9d,e). In contrast at lower concentrations of iron oxide i.e. 0.3 mg/mL, DmFc can diffuses quicker through the droplet forming newer palladium particles at a very fast rate resulting in the formation of Fe₃O₄@Pd core@shell particles where palladium forms a skin, on the outside of the particle, as shown in Figure 6.9f. When the hexane evaporates it collapses and forms a wrinkle shaped particle. Here, we do not see any holes but rather a smoother skin on the inside (Figure 6.9f). This is a very interesting observation, as by simply reducing the concentration of Fe₃O₄, the core@shell particles gets inverted from Pd@Fe₃O₄ to Fe₃O₄@Pd core@shell particles. The reason for this could be due to the rate of reduction, high concentration of iron oxide particles lead to slow reduction.

To understand the mechanism better, a control experiment was set up where only iron oxide in hexane was stabilised using 2% SDS. The size of the droplet was kept constant and the concentration of iron oxide was varied from 3 to 1 to 0.3 mg/mL. As shown in figure 6.13a-c, particles formed spherical shape regardless of the iron oxide concentration, hence the wrinkled morphology was due to the formation of a palladium skin. We also FIB plain iron oxide particles as shown in Figure 6.13d and no holes were observed, hence it is hypothesised that the holes are due to entrapped DmFc.

Another control experiment was set up, where 3.35 mg/mL iron oxide in 5mM DmFc in hexane was stabilised using 2% SDS and gets collected in 50mM of potassium ferricyanide (K₃Fe(CN)₆). As shown in figure 6.14, particles formed holes in it and fragments, hence it is proven that the holes were due to DmFc. A scheme of the formation of palladium nanoparticles and Fe₃O₄@Pd core@shell were proposed as shown in Figure 6.15a-c.
Figure 6.9. a) SEM of Pd@Fe₃O₄ core@shell particles from a droplet size 11.7 µm ± 1.28, (PdCl₄)²⁻ = 5 mM and 3.35 mg/mL ferrofluid in [DmFc] = 5 mM, b) SEM of Pd@Fe₃O₄ core@shell particles from a droplet size 12.4 µm ± 1.58, (PdCl₄)²⁻ = 5 mM and 1 mg/mL ferrofluid in DmFc c) SEM of Fe₃O₄@Pd core@shell particles from a droplet size 12.01 µm ± 1.6, (PdCl₄)²⁻ = 5 mM and 0.3 mg/mL ferrofluid in DmFc. Scale Bar = 1 µm, d) FIB of particles in figure a, scale bar 0.5 µm, e) FIB particles in figure b, scale bar 0.5 µm, f) FIB particles in figure c, scale bar 250 nm.
Figure 6.10. EDS spectrum of Pd@Fe₃O₄ core@shell particles, \((\text{PdCl}_4)^{2-} = 5 \text{ mM}\) and 3.35 mg/mL ferrofluid in \([\text{DmFc}] = 5 \text{ mM}\). a) EDS spot 1; Pd peak, b) EDS spot 2; Fe and O peak.
Figure 6.11. EDS mapping of Pd@Fe₃O₄ core@shell particles, (PdCl₄)²⁻ = 5 mM and 1 mg/mL ferrofluid in [DmFc] = 5 mM. a) SEM image of the Pd@Fe₃O₄ core@shell, mapping of element; b) Fe c) O d) Pd

Figure 6.12. EDS mapping of Fe₃O₄@Pd core@shell, (PdCl₄)²⁻ = 5 mM and 0.3 mg/mL ferrofluid in [DmFc] = 5 mM. a) SEM image of the Fe₃O₄@Pd core@shell, mapping of element; b) Fe c) O d) Pd
Figure 6.13. Different concentration of Fe$_3$O$_4$ with 2% SDS a) 3.35 mg/mL b) 1 mg/mL c) 0.3 mg/mL, scale bar = 5 µm d) FIB image of plain Fe$_3$O$_4$, scale bar = 250 nm

Figure 6.14. SEM of Fe$_3$O$_4$ particles (Control Experiment) from a droplet size 21.35 µm ± 2.34, K$_3$Fe(CN)$_6$ = 50 mM and 3.35 mg/mL ferrofluid in [DmFc] = 5 mM, scale bar = 5 µm
6.5.8. Adding iron oxide to silver nanoparticles
Using the setup listed as experiment E2 in Table 6.1, where iron oxide nanoparticles were added to DmFc in hexane droplets. Figure 6.16a shows an SEM image of silver-iron oxide particles which were polydispersed. In order to get a better understanding of the mechanism the particles were FIB as shown in Figure 6.16b and measured an EDS mapping on it, but here, no silver was detected (Figure 6.16c-f). The reason could be that silver forms really quickly (fast nucleation rate) and because of its big crystal size, it drifts off and doesn’t sit at the interface unlike palladium. To prove our hypothesis, the remaining supernatant solution (particles that didn’t settle during our centrifugation) were analysed. Both silver and Fe₃O₄ were observed in the TEM image, SAED pattern and EDS spectrum as shown in Figure 6.17a-c. From analysis, the sizes (25.5 nm ± 6.5) of the particles are much bigger as silver and iron oxide form
aggregates on the TEM grid. The supernatant particles are highly polydispersed due to the combination of iron oxide and silver particles.

Figure 6.16. a) SEM image of Ag-Fe₃O₄ nanoparticles from a droplet size 8.82 μm ± 0.91, [AgNO₃] = 10 mM and [DmFc] = 5 mM; scale bar = 2 μm. b) FIB image of particles in a); scale bar = 250 nm. c-f) EDX mapping of elements Fe, O, Ag and Pt respectively.
Figure 6.17. a) TEM image b) SAED pattern c) EDS of supernatant solution silver particles
6.6. Conclusion
The method of using emulsion droplets as reactors to grow particles in situ has proven to be a versatile platform for generating nanoparticles. By changing the metal ions, different morphologies were observed. For example, in our previous work (chapter 5), gold forms spherical particles and platelets, while using the same method but changing the metal ions to palladium and silver, only a spherical morphology was observed no platelets. The rate of reaction was studied between gold, palladium and silver, results show that silver is the fastest and gold is the slowest. This could infer that the reaction of silver is so quick that it drifts back to the bulk aqueous phase hence silver is not found in the particles. While for gold, the reaction is slow hence fewer nuclei are formed which enables the growth of platelets or nanosheets. Moreover, gold might not be as interfacial as palladium, hence the formation of nuclei might be drifted from the interface.

The addition of iron oxide to palladium ions formed core@shells particles. The concentration of Fe₃O₄ had an effect on the morphology of the particle. At high concentrations it formed spherical shaped particles, while at low concentrations it formed wrinkled shaped particles. The addition of iron oxide to silver ions were not as successful in forming core@shells. However, it is believed that this process could be used as a platform for forming anisotropic particles with other types of metal ions.
6.7. References


Chapter 7. Conclusion and Future Work

7.1. Conclusion
This PhD study was able to obtain three main findings using emulsion droplets for synthesis and assembling nanoparticles. These are generating core, shell and core@shell particles. A microfluidic device was chosen as it provides uniform droplets. Different materials such as Fe₃O₄, Au, Pd and Ag were explored in this thesis.

The work in this PhD started by first synthesising Fe₃O₄ nanoparticles, which would then go on to be used as the core in core@shell particles later in the thesis. In order to control Fe₃O₄ particles size and morphology, different parameters were varied such as the concentration of iron oxide nanoparticles (precursor), droplet size and different surfactants were used. This resulted in various morphologies such as spherical, dimpled and crumpled shaped. When compared with commercial particles (less than 5 µm), the LUEL particles had the highest magnetisation.

The use of Pickering emulsions was then explored, gold nanoparticles were synthesised and assembled into gold shell particles. The assembling of gold nanoparticles and iron oxide nanoparticles allows the first demonstration of Fe₃O₄@Au core@shell particles via a microfluidics device without the use of surfactants. However, the core@shell was not fully covered. The study was then further developed by combining the use of emulsion droplets with the liquid-liquid interface, where particles grow in situ. When using gold ions, gold spherical particles, platelets and nanosheets were observed. However, the products ratio can be tuned between the spherical particles, platelets and nanosheets by varying the concentration of DmFc and droplet sizes, as this has an effect on the rate of nucleation. Using the same technique, presynthesised iron oxide nanoparticles were added to gold ions, forming Au@Fe₃O₄ core@shell particles.

Lastly, the work was expanded to using Pd and Ag ions. The nanoparticles obtained for both Pd and Ag nanoparticles were only spherical in shape. Adding iron oxide to palladium ions formed Fe₃O₄@Pd core@shell particles. By tuning the concentration of iron oxide and DmFc the morphology of core@shell particles were varied such as spherical and wrinkled shaped morphologies. However, when iron oxide nanoparticles were added to silver ions they did not form any core@shell particles.
Even though all three metal ions were formed using the same methodology they all formed completely different morphologies. Hence, the rate of reaction was studied for each metal ion by conducting experiments at a free standing liquid-liquid interface with DmFc in order to understand the difference in morphology. Gold was the slowest and silver was the fastest, which relates to its nucleation rate. For gold, each nuclei are formed at different times, hence resulting in spherical particles and platelets. While, for silver and palladium, all the nuclei are formed at the same time. Hence, only spherical particles were observed.

Even though the work done in this thesis is only research based, there is a high scope for it to be used commercially. It is possible to upscale the production of particles using a microfluidics device by running the reaction continuously and/or having multiple output channels. increasing the size of the channel and/or running the reaction continuously.

7.2. Future Work

The synthesised particles (iron oxide, gold, palladium and silver particles and its core@shell) can be used in variety of applications. In the future, it would be interesting to use these particles in certain organic reactions, such as the Suzuki coupling reaction for the synthesis of biphenyl/biaryls compounds; used in pharmaceutical or agrochemical products. It would also be interesting to expand the work to form platinum particles and its core@shell particles.

The emulsion droplets formed in the microfluidic chip was dropped in a pot containing metal ions to form core@shell particles as opposed to running metal ions in the microfluidics chip. This was because it coats the inner walls of the chip, eventually causing the channel to become blocked. Hence in the future it would be interesting to use water-in-oil emulsions or double emulsions, as there would be less contact between the metal ions and the channel. This could result in a fully covered core@shell particles.

It would also be really interesting to use different types of chips such as 5µm etch depth, to form really small gold, palladium and silver particles. As these small nanoparticles could be bind with DNA or protein for further analysis.
**Attended conferences**

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<td>2016</td>
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Publications


2. S. Sachdev, R. Maugi, C. Kirk, Z. Zhou, S.D.R. Christie and M. Platt. “Synthesis and Assembly of Gold and Iron Oxide Particles within an Emulsion Droplet; Facile Production of Core@Shell Particles”, *Colloid and Interface Science Communications*, 2017, 16, 14-18