Exploration of the Interaction of Electromagnetic Fields with Nanoscale Materials

A thesis submitted to the University of London for partial fulfilment of the requirements for the degree of Doctor of Philosophy

By
Xiaoming Liu

Supervisors: Prof. Xiaodong Chen and Prof. Clive G. Parini

School of Electronic Engineering and Computer Science
Queen Mary University of London
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To My Family
Abstract

Nanoscale materials usually present strikingly different properties in comparison with their bulk counterparts, such as quantum size effects, surface plasmon resonance (SPR). To explore new properties as well as for novel applications, nanomaterials are being extensively investigated.

This project investigates the interactions of electromagnetic fields with nanoscale materials, particularly gold nanoparticles (GNPs), over a wide range of frequency bands, including static field, 261 kHz, 13.56 MHz, 2.45 GHz, millimetre wave, THz, and the visible light. Especially, the efforts have been devoted to the study of heating effect of GNPs in association with potential biomedical applications. To explain the electromagnetic heating of GNPs, dielectric properties of GNP dispersions has been studied from 100 MHz to 20 GHz, as well as in the millimetre wave and THz ranges. The static field induced effects on the size distribution of GNPs has also been examined using ultra-violet spectroscopy and correlated to SPR.

It has been revealed that purified GNPs cannot increase the specific absorption rate substantially at whichever frequency points of 261 kHz, 13.56 MHz, or 2.45 GHz. However, a greater temperature rise has been observed in the impurified GNP dispersions compared to deionised-water, after 10 min RF treatment at 13.56 MHz. The measurements on dielectric properties show that impurified samples have much higher effective conductivity than that of deionised-water, while the conductivity change of purified ones is very small and not detectable within the measurement accuracy. This observation supports that the heating effect of GNP dispersions is mostly contributed by the impurities and disproves that GNPs can increase the specific absorption rate significantly. The magnetic field heating at 261 kHz suggests that GNPs have very weak magnetic properties. It has been found that a static field can change the size distribution of GNPs. Up to 2 THz, it is measured that the dielectric properties of GNP dispersions have no convincing change compared to deionised-water, implying that the electromagnetic heating of GNP below 2 THz may be insignificant. In addition, it is confirmed that GNPs have strong absorption in the visible light range due to SPR.
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Abbreviations and Glossary

AC Alternating current
AFM Atomic force microscopy
CT Computed Tomography
DC Direct current
DI-water De-ionised water
DNA Deoxyribonucleic acid
EM waves Electromagnetic waves
EO Electro-Optic
FTIR Fourier Transform Infrared
GNPs Gold nanoparticles
GNRs Gold nanorods
HRTEM High-resolution transmission electron microscopy
IEEE Institute of Electrical and Electronics Engineers
IR Infrared
ISM Industrial, Scientific and Medical
MRI Magnetic resonance imaging
MUA 11-mercaptoundecanoic acid
NHS N-hydroxysuccinimide
PEG Polyethylene glycol
PT Thiol-derived polyethylene glycol
PTT Photothermal therapy
QO Quasi-optical
RF Radio frequency
SAR Specific absorption rate
SPR Surface plasmon resonance
SEM Scanning electron microscopy
STM Scanning tunnelling microscopy
SWCNs Single-walled carbon nanotubes
TEM Transmission electron microscopy
THz-TDS THz time domain spectroscopy
TNF Tumour necrosis factor
UV Ultra-violet
VNA Vector Network Analyser
# Symbols and Units

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<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
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<tr>
<td>$M$</td>
<td>Magnetisation</td>
<td>A/m</td>
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<tr>
<td>$H$</td>
<td>Magnetic field strength</td>
<td>A/m</td>
</tr>
<tr>
<td>$B$</td>
<td>Magnetic flux density</td>
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<tr>
<td>$\sigma(\omega)$</td>
<td>Frequency dependent effective conductivity</td>
<td>S/m</td>
</tr>
<tr>
<td>$\sigma_0$</td>
<td>DC conductivity (Ionic conductivity)</td>
<td>S/m</td>
</tr>
<tr>
<td>$C_w$</td>
<td>Specific heat capacity of water</td>
<td>J/K/kg</td>
</tr>
<tr>
<td>$T$</td>
<td>Temperature</td>
<td>°C</td>
</tr>
<tr>
<td>$t$</td>
<td>Time</td>
<td>s</td>
</tr>
<tr>
<td>$Z$</td>
<td>Impedance</td>
<td>Ω</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Mass density</td>
<td>kg/m$^3$</td>
</tr>
<tr>
<td>$\lambda$</td>
<td>Wavelength</td>
<td>m</td>
</tr>
<tr>
<td>$f$</td>
<td>Frequency</td>
<td>Hz</td>
</tr>
<tr>
<td>$SAR$</td>
<td>Specific absorption rate</td>
<td>W/kg</td>
</tr>
<tr>
<td>$E_g$</td>
<td>Energy band gap</td>
<td>eV</td>
</tr>
</tbody>
</table>
Chapter 1  Introduction

1.1 Overview

Nanoscience is generally defined as the study of materials on the scale of 1-100 nm. It has become a hot topic in a wide range of disciplines, such as physics, chemistry, biology, engineering, medicine and materials science. It is very much due to the fact that nanoscale objects often possess unique and distinct properties, which have the potential for novel and practical applications [1]. Since nano-objects have a size intermediating between atoms (or molecules) and bulk matter, the resulting physical properties are neither those of bulk ones nor those of molecular compounds, but strongly depend on the size, shape of the objects, and so forth [2]. Physically, they are on the edge of the quantum mechanism regime, while biologically, their size is comparable to many cellular components.

Nanotechnology, on the other hand, is more focused on producing novel functionalised materials and manipulating objects on the nanoscale. Nanomaterials can be made through two main approaches, i.e., ‘bottom-up’ and ‘top-down’ methods, as illustrated in Figure 1-1. For instance, the top-down method starts with a larger piece of material and breaks it into nanoparticles through etching or milling. In the bottom-up method, nanoparticles are produced through chemical synthesis or other means, followed by self-assembly into ordered structures by physical or chemical interactions. This approach is like building up a pyramid by piling up stones one by one. The concept of bottom-up was discussed in 1959 by Feynman in a lecture entitled There’s Plenty of Room at the Bottom [3]. Being so small, nanosized objects are usually characterised using techniques such as high-resolution transmission electron microscopy (HRTEM), scanning tunnelling microscopy (STM), atomic force microscopy (AFM), and X-ray scattering, which enable one to investigate nano-materials.
In the following sections, some unique properties of nanomaterials will be introduced. Their potential applications will be briefly reviewed, with an emphasis on the applications of gold nanoparticles (GNPs) in biomedical areas. Considering that this project is to explore the possibility of using GNPs as a RF heating agent for cancer treatment, a separate section is devoted to a more detailed review on this topic.

1.2 Physical properties

1.2.1 Surface-to-volume ratio and size dependent properties

Bulk materials only expose a small proportion of their atoms on the surface. When the object size goes down to nanometre, the number of atoms on the surface increases considerably. This phenomenon can be quantitatively described by using surface-to-volume ratio, which is a measure of how much the nanomaterials differ from the bulk ones. Taking nanoparticles as an example, a simplest model for describing nanoparticles is liquid drop. In the liquid drop model, a particle is simply represented as a sphere of radius $R$ containing $N$ atoms, and the number of
atoms is related to Wigner-Seitz radius $r_s$. The Wigner-Seitz radius comes from solid state physics [5] and is defined as the radius of a sphere whose volume, $v$, is equal to the volume occupied by one atom in the bulk material. Then, setting the volume of the particle to $Nv$, it immediately follows that

$$R = N^{1/3}r_s.$$  \hspace{1cm} 1-1

An estimation of surface-to-volume ratio can be achieved from a face-centred cubic lattice via counting the number of surface atoms for particles of different size, as summarised in Table 1-1.

<table>
<thead>
<tr>
<th>$N$</th>
<th>2R (nm)</th>
<th>Fraction of atoms on surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10$</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>$10^2$</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td>$10^3$</td>
<td>2.8</td>
<td>3.2</td>
</tr>
<tr>
<td>$10^4$</td>
<td>6.1</td>
<td>6.8</td>
</tr>
<tr>
<td>$10^5$</td>
<td>13.1</td>
<td>14.7</td>
</tr>
<tr>
<td>$10^6$</td>
<td>28.2</td>
<td>31.8</td>
</tr>
<tr>
<td>$10^7$</td>
<td>60.9</td>
<td>68.5</td>
</tr>
<tr>
<td>$10^8$</td>
<td>131.1</td>
<td>147.5</td>
</tr>
</tbody>
</table>

Figure 1-2 A 561-atom cuboctahedral cluster cut from a bulk face-centred cubic crystal [1]. Gray ones are only used to highlight the edge.
It can be calculated that at \( N = 300 \), half of the atoms are on the surface, and that the fraction does not fall below 10% until \( N \approx 80000 \). In Figure 1-2, a 561-atom cluster has more than 200 atoms on the surface. Having high surface to volume ratio, nanoparticles have high surface reactivity due to that the large proportion of atoms on the surface can increase the probability of atomic collision, which is preferred in chemical reactions [6]. For this reason, nanoparticles have been exploited for catalyst design since the 1960s [7]. The size dependent properties of a particle having \( N \) atoms might be characterised using a simple model on a per atom basis [1]

\[
x(N) = a + bN^{-1/3}.
\]

The first term is a bulk contribution, and the second term, a ‘surface’ contribution, depends on the size of a particle and represents the deviation from bulk behaviour. \( x(N) \) can be a measurable quantity. For instance, it is found that the melting temperature of cadmium sulfide (CdS) nanoparticles drops from 1600 °C to 400 °C in a nonlinear manner when the size decreases from bulk to several nanometres [8].

1.2.2 Quantum size effect

When a 3D bulk material shrinks in one dimension to nanometre size, it reduces to a quantum plate, known as nanoplate in nanoscience area. If it shrinks in two dimensions, it would be a nanorod, while it shrinks in three dimensions, it is a nanoparticle (nanocluster, nanocrystal in some literature).

![Figure 1-3 Density of states in one band of a semiconductor as a function of dimension [9]. Energy levels of a quantum dot are discrete.](image)
The quantum size effect is involved when the de Broglie wavelength of the valence electrons is of the same order as the size of the particle itself [10]. As illustrated in Figure 1-3, the energy of electron is discrete for 0D particles. It is therefore defined as quantum dot with a physical indication of that electrons are confined in all dimensions. Extensive investigations have been conducted associated with the quantum size effect, ranging from energy level to many macroscopic properties [8-11]. For instance, Viswanatha [12] and Delerue [13] have studied the phenomena of band gap increasing in semiconductor nanocrystals, and shown that band gap between conduction band and valence band is increasing with decreasing size, as shown in Figure 1-4. The size dependent feature of band gap can be observed by optical absorption spectroscopy. Semiconductor nanocrystals have been studied for applications in fabricating light-emitting diode [14-15].

\[
\Delta E_g \text{ is the difference between the band gap of particles and the one of bulk material.}
\]

Methods used:

- Dashed lines - effective mass approximation;
- Dashed-dotted lines – semiempirical pseudopotential method;
- Dotted lines with fitting (in black) – tight binding model;
- Experiment results from different groups are represented in circles, triangles.

Figure 1-4 Variation of band gap of the different semiconductor nanoclusters. Band gap increases with decreasing size of particles. Reprinted from [12].
Semiconductors already have a band gap in the macroscopic bulk state. Metallic particles, on the other hand, distinguish themselves by the fact that they have many more conductance electrons than semiconductor particles of the same size and yet not a band gap. It is for this reason that, so far, the influence of size quantisation with metal particles seems to be much smaller than with mesoscopic semiconductor particles and possible undetectable since the metal particle would be of molecular object size, as illustrated in Figure 1-5.

The quantum size effect is a key issue that has to be considered in the nanoelectronics [16]. In addition, it might be made use of in novel devices, such as single-electron devices, which manipulate single electron to fulfil their functionalities.

1.2.3 Superparamagnetism

The magnetisation of a ferromagnetic is usually described using the hysteresis curve [17]. When gradually increasing the external applied magnetic field, the magnetisation increases to a saturation value $M_s$. Decreasing the external applied magnetic field to zero does not eliminate the magnetisation, which remains at a value of $M_r$, the remnant magnetisation. An external magnetic field in the opposite direction of a certain value $H_c$, will bring the magnetisation to zero. And this value $H_c$ is referred to as the coercive force. A typical hysteresis curve is plotted in Figure 1-6. In contrast, the case of paramagnetism is much simpler, where the magnetisation is an instant and single-value response to the external applied magnetic field.
Figure 1-6 Typical ferromagnetic hysteresis curve. $M_s$ is the saturation magnetization, $H_s$ is the saturation field, $M_r$ is the remnant magnetization, and $H_c$ is the coercive force.

Figure 1-7 Blue curves for ferromagnetism, green curve for paramagnetism, and red curves for superparamagnetism [18].

Nanomagnetism usually considers nanoparticles with typical values ranging from 15-150 nm [18-19]. It is interesting to find that decreasing the size of a particle made of ferromagnetism materials causes the coercive force to change accordingly. When the particle size reaches a certain value, the coercive force decreases to zero, making the characteristic curve of the magnetisation resembling that of a conventional paramagnet. Owing to the much higher magnetic susceptibility of a ferromagnetic than that of conventional paramagnets, the resulting magnetisation is much stronger and this phenomenon is termed as superparamagnetism, as shown in Figure 1-7.

Although the physical mechanism governing superparamagnetism has not been fully understood yet, magnetic nanoparticles can be used as contrast enhancement agents in the magnetic resonance imaging (MRI) modality, or used in drug delivery and cancer therapy [20-22].
1.2.4 Surface plasmon resonance

A very interesting and important feature associated with metallic nanoparticles is the so-called surface plasmon resonance (SPR) [23]. SPR is an optical phenomenon and its frequency is dependent on the type, size, shape of metallic nanostructures, and dielectric constant of the surrounding medium. Bulk metals are good conductors since their electrons are not bound to individual atoms, but instead form a ‘cloud’ around the atomic cores. Due to the presence of this cloud, single photons of light cannot be absorbed by the atomic cores. It is, however, possible that phonons with a certain wavelength can be absorbed or scattered by the electron cloud. The process usually occurs at the surface of a material and is therefore called Surface Plasmon Resonance, which refers to the collective oscillations of the electron cloud. Since these oscillations occur on the boundary of the metallic nanoparticles, they are very sensitive to any change of the boundary and have been investigated extensively for biosensing applications [24-26].

1.3 Applications of gold nanoparticles

A wide range of applications of nanomaterials based on their unique properties have been proposed and are considered promising. For instance, the use of nanoparticles in catalysts in chemical area is due to the property of large surface-to-volume ratio [10], single-electron device is proposed from the quantum size effect [16], superparamagnetism affords the applications of bioimaging [20-22] and is an issue has to be considered in novel storage device [16]. A milestone is the invention of scanning tunnelling microscopy (STM) [27], which uses a metallic tip as a probe approaching the surface of the sample to produce tunnelling current taking place at a distance between the tip and the sample on an order of 1 nm, as illustrated in Figure 1-8. The tunnelling current is an exponential function of the distance and is utilised as the measurement signal. This technique, based on nanoscale, in return has greatly propelled the progress in nanoscience and nanotechnology. Nanostructures and nanomaterials can therefore be examined on the nanoscale.
Chapter 1 Introduction

Figure 1-8 Schematic representing of a scanning tunnelling microscopy: the tunnelling current is used as measurement signal, adapted from [16].

Table 1-2 Typical size of various objects [4].

<table>
<thead>
<tr>
<th>Objects</th>
<th>Size (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon atom</td>
<td>0.1</td>
</tr>
<tr>
<td>DNA double helix (diameter)</td>
<td>3</td>
</tr>
<tr>
<td>Ribosome</td>
<td>10</td>
</tr>
<tr>
<td>Virus</td>
<td>100</td>
</tr>
<tr>
<td>Bacterium</td>
<td>1,000</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>5,000</td>
</tr>
<tr>
<td>Human hair (diameter)</td>
<td>50,000</td>
</tr>
<tr>
<td>Resolution of unaided human eyes</td>
<td>100,000</td>
</tr>
</tbody>
</table>

A large number of nanomaterials have been investigated for various applications [18, 28-32], such as metallic nanoparticles, palladium (Pd), gold (Au), silver (Ag), magnetic nanoparticles, Fe₃O₅, Mn₃O₇, FePt, and semiconductors, cadmium selenide (CdSe), zinc selenide (ZnSe). The focus of this project is on the applications of gold nanoparticles (GNPs) in biological and biomedical areas.

Comparing nanomaterials with biological objects in terms of size, shown in Table 1-2, it is easy to understand the reason why nanomaterials have been studied intensively in biological and biomedical areas. It appears that nature has extensively used materials on a nanometre scale in making the biological systems.
Figure 1-9 Schematic diagram of functionalisation. Gold nanoparticle is coated with biomolecules so that gold nanoparticles can attach to cells. The functional group can be antibodies that can recognise specific cells. Reprinted from [33] and [34].

Other than the size, GNPs have good biocompatibility and facile conjugation to a group of chemical ligands (thiol ligands e.g.) and biomolecules (antibody, polyethylene glycol, e.g.). The process of treating each individual GNPs is referred to as functionalisation, which is to help nanomaterials either to stay longer in the cells or to target a specific molecule. This is normally implemented by coating the surface of GNPs with functional groups having biological significance. If the surface of GNPs is properly coated with peptides or antibody, they can easily attach to cancer cells or minimise immunological reactions [33, 34]. By introducing external intervention, for example, visible light illumination, laser irradiation, GNPs can act as agent in the biosensing, bioimaging, drug delivery, cancer diagnosis, and cancer treatment. Figure 1-9 illustrates how GNPs are functionalised to target cells.

1.3.1 Biosensing and bioimaging

The applications of GNPs in biosensing and bioimaging are very much based on two facts. One is that GNPs are biocompatible and can be coated with bio-probes, which are essentially functionalised biomolecules, to detect specific molecules or cells [33-37]. The other is that the presence of GNPs can increase the magnitude of scattering or absorption substantially so that the sensitivity of the conventional imaging modality can be enhanced [26, 32, 38]. For the second reason, GNPs are sometimes referred to as imaging enhancement agents. Moreover, unlike dye
labelling method, GNPs do not suffer from photo bleaching effect and can be used for long-term imaging [32].

In addition, the applications of GNPs in biosensing and bioimaging areas are frequently associated with the SPR. The wavelength of the SPR is sensitive to the change of the surrounding medium of GNPs, so that different biomolecules or tissues result in different wavelength of SPR [26, 36]. For instance, cancerous tissue has more water than benign tissues [33], which can be reflected by the response of SPR.

Furthermore, a number of novel imaging modalities have been explored based on the SPR of GNPs. For example, Choi [39] reported the development of plasmon resonance energy transfer based biomolecular imaging in living cells. This modality works on the phenomena that the resonant plasmonic energy transfers from a GNP probe to its conjugated target molecule, which has fingerprint spectral lines within the scattering spectrum of the probe. The principle is illustrated in Figure 1-10. If the fingerprint spectral line of a molecule falls in the scattering spectrum of the GNP, and the molecule is coated on the surface of the GNP, the so called quantised quenching dips will be created. Compared to the conventional SPR sensing modality, this method is more precise and offers higher specificity. It is particular useful for those molecules having their fingerprint spectral lines overlap with the scattering spectrum of the GNP probe.

Figure 1-10 Plasmonic resonance energy transfer based molecular imaging of living systems. When the fingerprint lines of a molecule overlap with the scattering spectrum of a GNP, selective energy transfer can generate distinguishable quench dips. Reprinted from [39].
1.3.2 Drug delivery and cancer treatment

GNPs are suitable for drug delivery for their easy preparation, functionalisation and good biocompatibility. The functionalised GNPs can easily carry anti-cancer drugs to their destination. Having large surface-to-volume ratio, GNPs can carry a large number of drug molecules, which should subsequently increase the specificity and efficacy of drug administration [40-44].

Paciotti, et al [43] developed a colloidal gold nanoparticle (cAu) vector for the delivery of tumour necrosis factor (TNF) to a solid tumour growing in mice. The optimal vector, designated as PT-cAu-TNF, consists of molecules of Thiol-derived Polyethylene glycol (PT) and recombinant human TNF that are directly bound onto the surface of GNPs. It is found that following an intravenous administration, PT-cAu-TNF accumulated rapidly in colon carcinoma tumours but not in the livers, spleens or other healthy organs of the animals.

1.4 Review of the interaction of electromagnetic waves with gold nanoparticles

Using GNPs in cancer diagnosis and treatment is not limited to drug delivery. The GNP mediated non-invasive hyperthermia therapy has received considerable interest. The conventional RF hyperthermia ablation utilises an antenna to deliver microwave or RF power into the tissue [45]. While destroying tumours, such a treatment also brings irreversible damage to surrounding benign cells. Therefore, targeted hyperthermia or ablation is preferred, the process of which is shown in Figure 1-11.

Having the peptides coated on GNPs, they can target and attach to cancer cells. Then the focused RF field is applied to generate heat causing localised temperature rise that causes damage to cancer cells. The scheme is therefore referred to as targeted hyperthermia therapy.
A number of methods can be employed to heat nanoparticles, including laser light in the ultraviolet–visible spectrum and electromagnetic field in the microwaves and RF spectrum. For instance, laser-based photothermal therapy (PTT) has been utilized to heat tissues injected with GNPs to produce a localised hyperthermia effect, which is due to the surface plasmon resonance phenomenon that has an absorption peak in the IR or UV-visible spectrum [10, 46-47]. Its applicability for thermal destruction of tumour cells has been demonstrated both in vitro and in vivo [46]. The tumour death rate has been observed to increase drastically in comparison with the control group. Due to the strong scattering and attenuation by body tissues, however, the penetration depth of laser is only a few centimetres. This limits its application to superficial cancer treatment.

In contrast, electromagnetic wave in RF spectrum can penetrate much more deeply, so can reach tens of centimetres into the tissues/bodies. Comparing to typical magnetic nanoparticles, it has been shown recently that a much higher specific absorption rate (SAR) can be achieved by using GNPs under RF spectrum, by using the Kanzius heating system [48-50]. The Kanzius heating system consists of a RF power generator working at 13.56 MHz, a matching module, and two parallel plates [51], as shown in Figure 1-12. The matching module is used to match the capacitive parallel plates to the power generator.
Figure 1-12 The diagram of the Kanzius heating system [50].

Figure 1-13 Temperature increase with time using 600 W RF field. Reprinted from [48].

Curley’s group in Texas University [48] reported that GNP dispersions at very low concentration, 1.1 µmol/L (~0.22 mg/L), for example, produced substantial increase in heating effect than DI-water by applying external RF field at 13.56 MHz. As shown in Figure 1-13, the heating of GNP dispersions at different concentrations shows a clear nonlinear behaviour with heating time. In a period of 5 min, the lowest concentration, 1.1 µmol/L, has more than 30 °C temperature increase, while the highest concentration, 67 µmol/L, can reach the boiling point in 2 min. It was reported that the field strength across the parallel plates was 16 kV/m at 600 W.
In addition, human cancer cell lines, pancreatic and hepatocellular cancer cells (Panc-1, Hep-3B), were treated with 67 $\mu$mol/L GNPs and then exposed to the external RF field. Markedly higher rates of cell death than the control samples not treated with GNPs were observed, as shown in Table 1-3. It is noticed that RF alone can produce cell death up to 75% over 5-minute exposure. It was also mentioned that GNPs alone at all concentrations produced no evidence of necrosis in either Hep-3B or Panc-1 cells. It is a bit surprising to observe that a 16 kV/m electric field can produce such significant heating effect on GNPs dispersions, even at very low concentration, and cause such a high rate of cell death.

Table 1-3 External RF field treatment of Hep-3B and Panc-1 human cancer cell cultures. GNPs = gold nanoparticles 67 $\mu$mol/L. Reprinted from [48].

<table>
<thead>
<tr>
<th>Cell type and treatment</th>
<th>RF exposure</th>
<th>Hep-3B control</th>
<th>Hep-3B GNPs</th>
<th>Panc-1 control</th>
<th>Panc-1 GNPs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 minutes</td>
<td>75.0±12.2</td>
<td>99.8±3.1</td>
<td>39.8±34.0</td>
<td>96.5±8.4</td>
</tr>
<tr>
<td></td>
<td>2 minutes</td>
<td>21±14.1</td>
<td>98.5±0.5</td>
<td>26.4±15.8</td>
<td>98.7±3.7</td>
</tr>
<tr>
<td></td>
<td>1 minute</td>
<td>17.6±8.4</td>
<td>99.0±0.2</td>
<td>15.3±9.8</td>
<td>98.5±2.1</td>
</tr>
</tbody>
</table>

Figure 1-14 (a) Gold nanoparticle dispersions (square), and water (diamonds) were exposed to 50 W RF field. Temperature increase with time; (b) Temperature increase under increasing power levels, 10 W, 50 W, and 100 W for 3 min. White – water, black – gold nanoparticle dispersion. Reprinted from [49].
Using the same heating system, Cardinal et al [49] applied 10, 50, 100 W RF fields to GNP dispersions for 5 min. DI-water had 4-5 Celsius degree increase in temperature when exposed to 100 W RF field for 5 min, while the temperature rise of GNP dispersion was much more substantial, more than 50 °C, as shown in Figure 1-14. Since at 600 W, the field strength is 16 kV/m, the field strength should be around 6.6 kV/m at 100 W, considering that the same Kanzius system has been utilised.

Their \textit{in vitro} study involved Hep-G2 cells cultured in the presence of GNPs. It was observed that the Hep-G2 cell cultures achieved sufficient heating to cause cell death upon exposure to the RF field for 7 min. The temperature rise, however, was less than 20 °C.

Their \textit{in vivo} study was conducted by injecting subcutaneously GNPs to male buffalo rats in the shoulders and then exposed to 35 W RF field. It was found that these animals experienced significant increases in temperature at the soft tissue injection site compared to control animals (water-injected). Tissue assessment indicated that subcutaneous injections of GNPs resulted in tissue destruction upon exposure to the RF field.

The results demonstrated by Cardinal et al [49] are quite promising. Currently, RF ablation devices in clinical use are approved for up to 200 W. The demonstrations in [49] are well within the regulations.

![Graphs showing heating rates of gold nanoparticles](image)

\textbf{Figure 1-15} (a) Heating rates of gold nanoparticles of different concentrations under 600 W RF field; (b) size dependent heating rates. Reprinted from [50].
Further study by Curley’s group [50] focused on size-dependent heating effect, Figure 1-15. Again, the heating of GNP dispersions is very substantial. Even the lowest concentration exhibits more than 30 °C increase in temperature after 2 min 600 W RF treatment. DI-water, however, exhibits 5 °C temperature rise after 2 min RF heating. Also, it was reported that small-sized GNPs could be heated quicker than larger ones given the same volume fraction.

To account for this heating phenomenon, the authors proposed a theoretical model, the Joule-heating model, which treats GNPs as conductors of constant cross section

\[ I^2R = \sigma(\omega) \cdot \left[ a \cdot d \cdot |E|^2 \right], \tag{1-3} \]

where \( \sigma(\omega) \) is the Drude model conductivity, \( a \) is the cross-sectional area of the GNP, \( d \) is the diameter, and \( |E| \) is the field strength in nanoparticles. The heating rate, in consequence can be written as

\[ \frac{dT}{dt} = N \cdot \frac{\sigma(\omega) \cdot a \cdot d \cdot |E|^2}{v \cdot C_w}, \tag{1-4} \]

where \( N \) is the number of GNPs, \( v \) is the volume of the dispersion, and \( C_w \) is the specific heat capacity of water. The authors used this model to calculate the heating rate of the dispersion of 100 nm diameter GNPs to be 1.9 °C/s, which was in fair agreement with the measurement 2.8 °C/s. However, it has to be pointed out that the electric field should be the one in GNPs rather that in water. The authors obviously calculated the heating rate using the field strength in the host water, \( |E| = 200 \text{ V/m} \). The field strength in a metallic particle, however, is several orders of magnitude smaller than that in the host water. Furthermore, the factor \( N a d/v \) in Eq.1-4 is 1.5 times the volume fraction. Since the volume fractions are the same for all GNP dispersions, the heating rate should not be size dependent according to this model. However, the experiment suggested otherwise. Therefore, this model cannot explain the results successfully.

Moreover, the temperature rise of DI-water is 5 °C, which is several orders of magnitude higher than the theoretical prediction.
where, $\rho$ is the density of water, and $t$ is the heating time. The theoretical value of the conductivity of water at 13.56 MHz is of the order of $10^{-4}$ S/m [52], resulting in a temperature rise in 2 min on the order of $10^{-4}$ °C. The field strength therefore has to be verified.

Nevertheless, a few in vitro studies [53-55] conducted in Curley’s group demonstrated that the combination of RF and GNPs is promising for cancer treatment.

Independently, Kruse et al [56] built a resonant circuit (as shown in Figure 1-16) and the field strength was measured to be 518 kV/m (8800 V across a 17 mm air gap). The heating study indicated that GNP dispersions could be heated very quickly following 30 s exposure to transmitted power of 125 W. It is worth mentioning that the field strength is more than 32 times higher than that of the Kanzius system.

In vitro study was conducted on two cancer cell lines, Met-1 and PC-3. For each cell line, the treatment included 60 and 30 s RF exposure at 100 W. Cells were incubated with 3 µmol/L 10 nm GNPs. It is seen that RF alone already produced massive cell death, up to 60%. The combination of GNPs and RF exposure increased the cell death by up to 20%, Figure 1-17.

![Figure 1-16 The resonant circuit used in [56]: (a) the circuit diagram, (b) a photograph.](image)
While the heating effect of GNP dispersions is encouraging, several issues still need to be considered critically:

- What is the field strength required to produce such a substantial temperature rise? 16 kV/m or much higher? This is due to that DI-water obviously gives abnormal temperature increase, 4-5 °C, as reported in [49], [50].

- Whether the heating effect is indeed produced by GNPs? And what is the physical mechanism underpinning this phenomenon?

Very recently, Hanson et al [57] theoretically investigated the interaction of electromagnetic waves with GNPs to verify if the abnormal specific absorption rate of GNPs is possible. The classic Mie’s theory [58], and quantum mechanisms were utilised in the analysis, to find that neither theory supports the claims of RF heating of GNPs. Li et al [59] reported that the heating effect was caused by the increase in effective conductivity. However, in the measurement of the complex permittivity of DI-water, Li et al [59] reported the real part to be 100, which is much larger than its room temperature value, 78. Therefore, the accuracy of their measurement is questionable, and more accurate measurement is required.
Ghahremani et al [60] studied the efficacy of microwave hyperthermia and chemotherapy in the presence of GNPs. In this study, Saos-2 human cells were incubated with GNPs of either 20 or 40 nm in diameter. The concentrations of GNPs were 13.2 and 26.4 $\mu$g/ml, equivalently 67 and 134 $\mu$mol/L. Microwave energy was delivered to these GNPs incubated cell lines for 50 s. The temperature rise of GNP incubated samples was observed to be a couple of centigrade higher than that in the absence of GNPs. Although the concentration of GNPs was much higher than that in some prior studies [48, 50], where the concentration was on the order of $10^{-6}$ mol/L, the temperature rise was much slower in contrast to these prior studies [48, 50]. However, it is noticed that the power level or the field strength has not been mentioned in this work. Therefore, it is impossible to judge the heating effect of GNPs from the given information in [60].

In this regard, the heating effect has not been verified independently and is controversial in the heating mechanism.

There are fewer heating studies of GNPs at other frequencies. However, there are a few studies on other nanomaterials. Xu [61] used 350 kHz, 5000 W magnetic field to heat cobalt nanoparticles with graphitic shells (in liquid dispersion), but did not find any statistical increase in heating rates. Mashal [62] prepared breast mimicking gel mixed with carbon-nanotubes and heated them with 3 GHz microwave at 1 W, showing a few degrees temperature rise compared with the sample without carbon-nanotubes. After carbon nanotubes were mixed with tissues, it was measured that the effective conductivity was increased. Therefore the heating rate was increased. Cook et al [63] reported microwave hyperthermia using iron-oxide nanoparticles monitored by ultrasound thermography. A 25 °C temperature rise in the iron-oxide injected tissue has been observed after 50 s microwave exposure, whereas the surrounding tissue reached an averaged increase of 8 °C. The authors attributed the temperature rise to the increase of electrical conductivity and additional heating due to magnetic loss.

Regarding the dielectric measurement, Park [64] studied the electrical properties of GNP assemblies linked by DNA, which is essentially the electron transportation between two adjacent GNPs linked by DNA. French [65] studied the conductivity of GNPs formed on glass substrate. Ganguly [66] experimentally measured the effective conductivity of alumina nanofluids. In the THz band, Schmuttenmaer [67] investigated the photoconductivity and charge transport
properties of semiconductor nanoparticles; Beard [68] investigated the size-dependent transient photoconductivity in CdSe (cadmium selenide) nanoparticles using THz-TDS. Han et al studied the optical and dielectric properties of ZnS (zinc sulfide) nanoparticles [69] and ZnO (zinc oxide) [70] using THz-TDS. However, the study on the dielectric property of GNP dispersions has not been conducted yet.

Also in the THz band, Oh et al [71] illuminated gold nanorods (GNRs) treated cancer tissue with THz wave and found that the intensity of the reflected THz waves did not show any striking difference to that reflected off the tissue without treatment with gold nanorods. However, when an extra IR laser was directed to the samples, the reflection signal from the gold nanorods treated tissues was increased by 12%-20% after the IR laser illumination for a few minutes, shown in Figure 1-18. The authors [71] attribute this to that the GNRs absorb IR energy and therefore modify the complex permittivity of the sample, then in turn increase the reflection signal. However, they did not measure the permittivity of the sample in the THz range or give a quantitative explanation. It is therefore desirable to conduct measurement on the permittivity of GNP dispersions in the THz range.

![Figure 1-18 Peak reflection changes of the THz signals from live cancer cells with and without gold nanorods at IR intensities of 10 and 20 W/cm² [71].](image)

Figure 1-18 Peak reflection changes of the THz signals from live cancer cells with and without gold nanorods at IR intensities of 10 and 20 W/cm² [71].
In the IR and optical ranges, GNP s have been extensively studied for various applications. In addition to the use for thermal destruction of tumours [46-47], the optical properties of GNP s have been investigated intensively [72-76], ranging from the absorption and scattering properties to quantum effects.

It is also interesting to look into the effect of static electromagnetic field on GNP s in water. Using a static electric field, Chandrasekharan [77] assembled GNP s as nanostructured films using an electrophoretic approach. Kumar [78] applied static field on a silicon surface to control the nanostructure fabrication.

Whilst the interaction of electromagnetic waves with nanomaterials has been extensively studied, it is far from complete. A lot of knowledge gaps still need to be bridged.

1.5 Research motivation

GNP size is far too small compared with RF wavelength. A big puzzle is what the heating mechanism is. This project intends to answer this question. More specifically, the interaction of electromagnetic field with GNP s will be investigated comprehensively from several aspects, such as dielectric properties, heating effect, and so forth.

It can be concluded from the forgoing reviews that most of the studies focus on a specific frequency range, either based on pure theoretical consideration or for some specific applications. In contrast, this thesis has the following two features:

- It studies GNP s interacting with EM fields over a wide frequency range, from DC to the visible light;
- It investigates a wide spectrum of physical properties of GNP s that will be correlated with real applications, such as cancer treatment.

The main tasks are schematically illustrated in Figure 1-19. The focus will be on the heating effect and dielectric properties of GNP s.
The heating effect study is to verify if GNPs do absorb substantial energy from electromagnetic field and hence increase the temperature of GNP dispersions significantly. Also it is to explore the possibility of using GNPs as agents in hyperthermia cancer treatment. Several frequency bands will be investigated:

- Heating effect at 13.56 MHz. To investigate the heating effect of GNPs using purified samples based on 16 kV/m RF fields;

- Heating effect at 261 kHz. To study the effect of using magnetic field to heat GNPs comparing with electric field heating;

- Heating effect at 2.45 GHz. To explore if there is any heating effect using higher frequency, shorter wavelength electromagnetic wave;

- Heating effect using 655 nm red-light laser.

The heating effect studies also aim at looking for an optimal frequency band that is most suitable for hyperthermia cancer treatment.

The dielectric properties of GNPs will be measured in the RF/microwave range (100 MHz – 20 GHz), millimetre wave range (75-170 GHz), and THz range. The dielectric measurement in the RF/microwave range is to correlate the heating effect of GNPs with the effective conductivity.
The measurement at millimetre wave/THz bands also serves as an indicator if the GNP dispersions can interact with EM fields.

All the previous studies are done with alternating EM fields. It is also interesting to see if there is any special phenomenon can be observed if static electric field is applied to GNP dispersions. The study by applying static electric field (DC voltage) to GNP dispersions in this project is to investigate the effects of static electric field on the optical properties of GNPs.

1.6 Summary and thesis outlines

This thesis presents a comprehensive study on the interaction of electromagnetic fields with GNP dispersions. The focus is the heating effect study and dielectric measurement over a few frequency bands.

An introduction to the background of nanoscience and nanotechnology is presented in Chapter 1, where some of the special physical properties are briefly discussed. A detailed review is given to the heating effect study of GNPs in recent years.

Chapter 2 covers the fundamental theories to be used in the following chapters, including the fundamentals of dielectric properties, the methods of dielectric measurement, and the Mie’s theory for calculating the scattering of electromagnetic waves by particles. In addition, the recipe of GNP preparation is briefly described.

In Chapter 3, a comprehensive study on the heating effect at several frequencies is given. The mechanisms by which GNP dispersions are heated are discussed in detail. The measured results of dielectric properties of GNP dispersions are included in this chapter. Also, the details of the exposure system are presented including the electric field characterisation. Then, the heating effects at 13.56 MHz, 261 kHz, and 2.45 GHz are investigated.

Chapter 4 is devoted to the dielectric measurement in the millimetre wave and THz ranges. The dielectric measurement in the millimetre wave range is carried out using a quasi-optical system, while the THz-Time domain spectroscopy is utilised for the measurement in the THz range. Numerical methods are employed to extract the dielectric properties.
Chapter 5 discusses the effects of static electric field on GNPs and the heating effect by using a 655 nm red-light laser. It presents the change in size distribution after static electric field is applied. Also, it includes the UV-visible spectroscopy measurement and quantitative colour measurement using the CIE chromaticity diagram. The heating effect is discussed in some detail. Further effort need to be made to understand the mechanism of how static electric field causes GNP aggregation.

Finally, a conclusion of the research and the future work are both presented in Chapter 6.

References


Chapter 1 Introduction


Chapter 2  Gold Nanoparticles: Synthesis, Dielectric and Optical Properties

2.1 Overview

Preparation of nanoparticles is an important step in the process of analysing their properties. There are four generic methods for nanoparticle synthesis [1]. (1) Preparation of pre-formed nanoparticles in the gas phase; (2) Deposition and self-assembly on surfaces; (3) Wet chemical methods by reduction of gold (III) derivatives; (4) Nanoparticles being cut from a larger metal. The samples in this project were produced by wet chemical methods.

The fundamentals of dielectric properties and optical properties of GNP dispersions (in water) will be discussed in this chapter. The calculation of electromagnetic wave propagation requires knowledge of the dielectric properties of the materials involved. However, this macroscopic property of nanoparticle ensembles has not been well studied, and further work would be beneficial to the better understanding of nanomaterials. Optical properties are considered of importance for several reasons. One of them is that the surface plasmon resonance frequencies of nanoparticles lie in the visible light range, which is useful in the applications of size characterisation, and biosensing.
2.2 Preparation of gold nanoparticles

The most commonly used wet chemical method for GNP synthesis is the citrate reduction of HAuCl₄ in water, which was introduced by Turkevitch in 1951 [2]. The chemical reaction formulae are described as

\[ \text{NaC}_6\text{H}_7\text{O}_7 + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_8\text{O}_7 + \text{Na}^+ + \text{OH}^- , \]

\[ 2 \text{HAuCl}_4 + 3 \text{C}_6\text{H}_8\text{O}_7 \rightarrow 2 \text{Au} + 3 \text{C}_3\text{H}_6\text{O}_5 + 8 \text{HCl} + 3 \text{CO}_2 . \]

The procedures using the citrate reduction method to produce GNPs between 10 nm and 20 nm in diameters are as follows¹

1. 50 μmol of HAuCl₄ in 190 ml of de-ionised water (DI-water) was heated until boiling;
2. Keep heating and stirring by a magnetic stirrer, at the same time 10 ml of 0.5% sodium citrate was added into the solution;
3. The solution was kept stirred for the next 30 minutes;
4. During the first 5 minutes, the colour of the solution changed in the order of light yellow, clear, grey, purple, dark purple, wine-red colour. The resultant fluid is referred to as impurified sample;
5. GNPs were purified using the membrane dialysis method for 4-6 days and then diluted to specific concentrations for measurement. The diameter of the membrane pores is 2-3 nm. The fluids diluted after going through the purification procedures are referred to as purified samples;
6. Citrate reduction GNPs were identified for their size and shape by transmission electron microscopy (TEM). The particle size distribution in liquid was measured by a dynamic light scattering device (Malvern nanosizer).

The gold colloid with the particle size in the range of 10 nm to 20 nm in diameter is dark pink colour as shown in Figure 2-1(a). The nanoparticles under TEM imaging are displayed in Figure 2-1(b), while the size distribution is plotted in Figure 2-2, showing a good single-peak

¹ This work is done by Miss Hui-Jiuan Chen from the School of Engineering and Materials Science, QMUL.
distribution. The size of the GNPs is identified as in the range of 10 – 20 nm. A more detailed description is referred to [3]. Unless otherwise specified, all the GNP samples used in this project are prepared based on the above citrate reduction method.

(a)  
(b)

Figure 2-1 (a) Gold nanoparticles in original concentration (250 μmol/L by calculation); (b) TEM characterisation of gold nanoparticles.

![Figure 2-1](image)

Figure 2-2 The size distribution of GNPs as measured by Malvern nanosizer.
2.3 Fundamentals of dielectric properties

2.3.1 Fundamentals

Mathematically, the dielectric properties are quantitatively described using permittivity $\varepsilon$ or relative permittivity $\varepsilon_r$ [4]. When an electric field is applied to a dielectric, several types of polarisation might be observed, electronic polarisation, ionic polarisation, and orientation polarisation. Whichever the polarisation is (as shown in Figure 2-3), the polarisation can be described using a vector $\vec{P}$

$$\vec{P} = \frac{1}{N} \sum_{j=1}^{N} \vec{P}_j = N \vec{p},$$  \hspace{1cm} (2-1)

where $\vec{p}$ is the averaged dipole moment per molecule, $N$ is the average number of dipoles per unit volume. The polarisation vector $\vec{P}$ is related to the local electric field $\vec{E}$ in the dielectric in a simple manner

$$\vec{P} = \varepsilon_0 \chi_e \vec{E},$$  \hspace{1cm} (2-2)

where $\chi_e$ is the electric susceptibility, which is a measure of the ability of the material to become polarised. In order to eliminate the explicit determination of $\vec{P}$, a new vector $\vec{D}$, the electric flux density, is defined as

$$\vec{D} = \varepsilon_0 \vec{E} + \vec{P},$$  \hspace{1cm} (2-3)

and can be further simplified

$$\vec{D} = \varepsilon_0 \vec{E} + \vec{P} = \varepsilon_0 \vec{E} + \varepsilon_0 \chi_e \vec{E} = \varepsilon_0 (1 + \chi_e) \vec{E} = \varepsilon_0 \varepsilon_r \vec{E} = \varepsilon \vec{E}.$$  \hspace{1cm} (2-4)

Since the polarisation is frequency dependent, the permittivity $\varepsilon$ and the relative permittivity $\varepsilon_r$ are also frequency dependent, and are denoted as $\varepsilon(\omega)$ and $\varepsilon_r(\omega)$, respectively.
Figure 2-3 (a) Electronic polarisation; (b) permanent dipole moment of a molecule of water. Both can be represented using a dipole.

Normally, the permittivity consists of a real part and an imaginary part. This is due to that the molecular dipoles try to follow the alternating electric field, whereas the intermolecular friction causes energy loss. In this regard, the permittivity is a frequency dependent complex function

\[
\varepsilon(\omega) = \varepsilon_0 [\varepsilon'_r(\omega) - j \varepsilon''_r(\omega)],
\]

wherein, the real part accounts for the polarisation produced by the electric field, while the imaginary part is called the ‘loss factor’ and is related to the effective conductivity \(\sigma\) of the material. In a relative format, the complex permittivity is usually adapted to

\[
\varepsilon_r(\omega) = \frac{\varepsilon(\omega)}{\varepsilon_0} = \left[ \varepsilon'_r(\omega) - j \frac{\sigma}{\varepsilon_0 \omega} \right]
\]

The response of a material to a field variation involves physical displacement of charge, and the kinetics of this displacement establishes the frequency response of the bulk properties, resulting in either relaxation or resonance forms. The relaxation responses of most materials can be described by the physical processes that are in terms of the relaxation time \(\tau\). The Debye relaxation theory is frequently used to characterise the dielectric properties of materials in terms of the relaxation time \(\tau\) [5, 6]

\[
\varepsilon_r(\omega) = \varepsilon_{\infty} + \frac{\varepsilon_{ss} - \varepsilon_{\infty}}{1 + j \omega \tau},
\]

where \(\varepsilon_{\infty}\) is the permittivity at frequencies where \(\omega \tau \gg 1\) (optical permittivity), \(\varepsilon_{ss}\) is the permittivity at low frequency where \(\omega \tau \ll 1\) (static region). This is the first-order Debye model.
For those materials having more than one relaxation, a higher order model can be employed with a general form of

\[
\varepsilon_r(\omega) = \varepsilon_{\infty} + \frac{\varepsilon_{r1} - \varepsilon_{\infty}}{1 + j\omega\tau_1} + \frac{\varepsilon_{r2} - \varepsilon_{r1}}{1 + j\omega\tau_2} + \cdots + \frac{\varepsilon_{rn} - \varepsilon_{r(n-1)}}{1 + j\omega\tau_n}.
\]

2-8

In addition to frequency dependency, the dielectric properties are also temperature dependent [64]. Figure 2-4 illustrates the temperature dependence of dielectric properties of DI-water in the temperature range of 0-30 °C. Both \(\varepsilon_r\) and \(\varepsilon_{\infty}\) decrease with temperature in a linear manner, and \(\lg(\tau)\) is a linear function of \(T^{-1}\). It has to be mentioned that the Debye model does not have a full physical interpretation. In most cases, parameters are optimised from measured data. Therefore, different literature often gives slightly different parameters to describe the dielectric properties of pure water. Some literature may even use a different model [6], for instance, the Cole-Cole model, which has a form of

\[
\varepsilon_r(\omega) = \varepsilon_{\infty} + \frac{\varepsilon_{r1} - \varepsilon_{\infty}}{1 + (j\omega\tau)^{1-\alpha}}.
\]

2-9

As an example, the dielectric properties of 25 °C DI-water using the first order Debye model are plotted in Figure 2-5, with \(\varepsilon_{r1} = 78.44\), \(\varepsilon_{\infty} = 5.08\), \(\tau = 8.2\) ps.

![Figure 2-4 Temperature dependence of dielectric properties of DI-water. (a) \(\varepsilon_{r1} = 87.8450 - 0.3766T\), (b) \(\varepsilon_{\infty} = 5.77 - 0.0274T\), (c) \(\lg(\tau) = 1097.5T^{-1} - 2.8\), \(\tau\) in ps. Data are retrieved from MCL dielectric property measurement software [7].](image)
2.3.2 Drude model for dielectric properties of metals

The Drude model [8] assumes that the abundant free electrons in bulk metals are not bound to a particular nucleus, and this assumption accounts for the high conductivity of metals. The frequency dependent nature of the conductivity of bulk metals is written as

\[ \sigma(\omega) = \frac{\sigma_0}{1 + j\omega\tau}, \]

where, \( \sigma_0 \) is the DC conductivity, and \( \tau \) is the relaxation time. The complex permittivity therefore can be written as

\[ \varepsilon_r(\omega) = 1 - \frac{j\sigma_0}{\omega\varepsilon_0(1 + j\omega\tau)}. \]

A perfect conductor, due to its infinite DC conductivity, has an infinite permittivity. Even imperfect metal has very high conductivity, leading to a considerably high value of permittivity. If a metallic particle is placed in a uniform electric field, as shown in Figure 2-6, the field strength inside the metallic particle can be calculated using [9]

Figure 2-5 Dielectric properties of DI-water at 25 °C based on the first order Debye model. Data from [7].
Figure 2-6 A metallic particle placed in a uniform electric field. The field strength in the particle is many orders of magnitude smaller than $E_0$.

\[
\vec{E}(r) = \begin{cases} 
  \hat{r}E_0 \left( 1 - \frac{\varepsilon - \varepsilon_1}{\varepsilon + 2\varepsilon_1} \frac{2R^3}{r^3} \right) \cos \theta + \hat{\theta}E_0 \left( 1 - \frac{\varepsilon - \varepsilon_1}{\varepsilon + 2\varepsilon_1} \frac{2R^3}{r^3} \right) \sin \theta & r > R \\
  -\hat{r}E_0 \frac{3\varepsilon_1}{\varepsilon + 2\varepsilon_1} & 0 \leq r < R 
\end{cases}
\]  

2-12

Considering the extremely high conductivity of a metal, the field strength will be dramatically reduced by many orders of magnitude.

2.3.3 Dielectric model for mixed medium

From a macroscopic point of view, the permittivity of a mixed medium can be modelled effectively using the Maxwell-Garnett model [10] for spherical metal particles embedded in a dielectric medium

\[
\frac{\varepsilon_{eff} - \varepsilon_1}{\varepsilon_{eff} + 2\varepsilon_1} = q \frac{\varepsilon_m - \varepsilon_1}{\varepsilon_m + 2\varepsilon_1},
\]  

2-13

where $\varepsilon_m$, $\varepsilon_1$ are dielectric constants for the spherical metal particles and surrounding medium, respectively, $q$ is the volume fraction of the metal, $\varepsilon_{eff}$ the effective dielectric constant. The Maxwell-Garnett model, as a rule of thumb, should apply whenever the wavelength of the electromagnetic wave is much longer compared with the size of the particles and their separation distances. It is worth mentioning that this is a small-$q$ theory, where $q$ is the volume fraction of the metal in the mixed medium.
2.4 Dielectric measurement methods

A range of methods for dielectric measurement have been developed [11-12], such as parallel plate method, transmission line, open-ended coaxial probe, resonant cavity techniques, and free space method. The parallel plate method is mostly suitable for low-frequency measurements. Transmission line method is an accurate measurement technique, and is particularly useful for solid sample measurement. Open-ended coaxial method is a simple and fast method requiring a reference material for calibration. In the millimetre-wave range, however, the radiation effect of the probe becomes pronounced that the open-ended coaxial method is not accurate. Resonant cavity method gives the most accurate measurement. However, its narrow-band feature limits its application in a wide-band measurement. The free space measurement is often used in solid sample measurement. But it is also suitable for liquid sample measurement if a proper sample holder is fabricated. In this section, we will only discuss the open-ended coaxial method and free space technique.

2.4.1 Open-ended coaxial method

The dielectric measurement in the microwave range was carried out using the open-ended coaxial method in this work. Open-ended coaxial probes have been extensively used in dielectric spectroscopy of biological tissues due to their simplicity, broad-band response, and capacity for non-invasive measurements [13-16]. The probe is typically used in conjunction with a vector network analyser (VNA) to record the frequency-dependent complex reflection coefficient. The VNA-probe system is first calibrated so that the reflection coefficient measurements are referenced to the probe aperture plane. The dielectric parameters are then retrieved from the calibrated reflection coefficients.

In a real situation, the probe can be equivalently modelled as Figure 2-7. In the equivalent circuit, $Z$ or $C_f$ represents the part of impedance which is independent from the dielectric sample, or accounts for the fringing field; $Z(\varepsilon_r)$ represents the part of impedance terminating the line; $C(\varepsilon_r) = C_0\varepsilon_r$ is a lossy capacitance and $C_0$ is the capacitance when the line is placed in air. An open coaxial line, placed in contact with a test sample, is therefore used as a sensor. The
sample must be homogeneous within a volume sufficiently large to simulate a slab which is electrically infinite in size.

This equivalent circuit is valid at frequencies where the dimensions of the line are small compared with the wavelength so that the open end of the line is not radiating and all the energy is concentrated in the fringe or reactive near field of the line. It also requires that the sample is large enough so that the fringing capacitor is not modified, which is usually a concern in the low frequency range. At higher frequencies, the value of the capacitance \( C_0 \) increases with frequency, due to the increase in the evanescent TM modes being excited at the junction discontinuity. The operating frequency range is subsequently subjected to the above conditions.

If the frequencies of interest are in the range where the equivalent circuit is applicable, the input reflection coefficient at the plane of the discontinuity can be calculated from

\[
\hat{\Gamma} = S_{11}e^{i\phi} = \frac{1 - j\omega Z_0 \left[C(\varepsilon_r) + C_f\right]}{1 + j\omega Z_0 \left[C(\varepsilon_r) + C_f\right]}
\]

Solving for the permittivity, one has

\[
\varepsilon_r = \frac{1 - \hat{\Gamma}}{j\omega Z_0 C_0 \left[1 + \hat{\Gamma}\right]} \cdot \frac{C_f}{C_0}
\]

Figure 2-7 Open-ended coaxial line sensor. Geometry and equivalent circuit [14].
The relative dielectric constant and the loss factor are therefore calculated as

\[
\left\{
\begin{align*}
\varepsilon' &= \frac{2S_{11} \sin(-\phi)}{\omega z_0 C_0 \left[1 + 2S_{11} \cos\phi + S_{11}^2\right]} C_f \\
\varepsilon'' &= \frac{1 - S_{11}^2}{\omega z_0 C_0 \left[1 + 2S_{11} \cos\phi + S_{11}^2\right]}
\end{align*}
\right.
\]

2-16

2.4.2 Free-space method

The dielectric measurement in the millimetre wave range was performed by using the free space method in this work. For free space method, a sheet of solid sample is placed between a transmitting horn and a receiving horn, forming an air-sample-air multilayer structure. The dimensions of the solid sample have to be twice the beam size where it is placed, which has been described by Yang et al [17]. However, for liquid sample measurements, a more complicated structure has to be considered since measuring liquid sample requires the use of a sample holder, building a more complicated multi-layer structure. Window materials are commonly chosen as low loss in the frequency range to be measured.

As described in [17], multilayer structures can be analysed using the transfer matrix \( T \) or \( ABCD \) matrix. For instance, if a slab of planar sample having a thickness of \( L \) is placed in the free space, as shown in Figure 2-8 (a), the transfer matrix \( T \) can be derived as

\[
T = \begin{bmatrix}
A & B \\
C & D
\end{bmatrix} = \begin{bmatrix}
\frac{e^{j\beta L} + e^{-j\beta L}}{2} & \frac{e^{j\beta L} - e^{-j\beta L}}{2Z} \\
\frac{e^{j\beta L} - e^{-j\beta L}}{2} & \frac{e^{j\beta L} + e^{-j\beta L}}{2}
\end{bmatrix},
\]

2-17

where, \( \beta \) is the wave number of the sample, and \( Z \) the wave impedance of the corresponding layer.
Chapter 2 Gold Nanoparticles: Synthesis, Dielectric and Optical Properties

From the transfer matrix, the reflection and transmission coefficients are derived as

\[
\begin{align*}
  r &= \frac{(AZ_0 + B) - (CZ_0^2 + DZ_0)}{(AZ_0 + B) + (CZ_0^2 + DZ_0)}, \\
  t &= \frac{(AZ_0 + B) + (CZ_0^2 + DZ_0)}{2Z_0}.
\end{align*}
\]

with \(Z_0\) the free space wave impedance. Since the complex permittivity is the only one unknown, the retrieve process can be done mathematically or using iterative process [11-12].

For more complicated structures, Figure 2-8 (b), the resultant transfer matrix is the multiplication of the one of each layer, that is \( T = T_1 \cdot T_2 \cdot T_3 \). Unlike a single slab of sample, the transfer matrix is much more complicated and the derivation of the mathematical converse formulae is so involved that it may not be possible. Besides, it is realised that the mathematical converse formulae of a single slab of sample cause phase ambiguity [11-12]. In contrast, an iterative method is quite competent, defining a function in terms of either the reflection or transmission coefficient or of both [11-12]. Starting with a first guess, the iteration stops when a sensible value leads to the defined function become convergent.
2.5 Optical properties

The scattering and absorption of light by small particles can be quantified by the Mie’s theory [18-20], in terms of their extinction, scattering, and absorption efficiencies, $Q_{\text{ext}}$, $Q_{\text{sca}}$, and $Q_{\text{abs}}$. For homogeneous spheres, they are expressed as

$$Q_{\text{ext}} = \frac{2}{x^2} \sum_{n=1}^{\infty} (2n+1) \text{Re}(a_n + b_n), \quad 2-19$$

$$Q_{\text{sca}} = \frac{2}{x^2} \sum_{n=1}^{\infty} (2n+1) \left| a_n^2 + b_n^2 \right|, \quad 2-20$$

$$Q_{\text{abs}} = Q_{\text{ext}} - Q_{\text{sca}}, \quad 2-21$$

$$a_n = \frac{m \psi'_n(mx) \psi'_n(x) - \psi_n(x) \psi''_n(mx)}{m \psi'_n(mx) \xi'_n(x) - \xi_n(x) \psi''_n(mx)}, \quad 2-22$$

$$b_n = \frac{\psi'_n(mx) \psi'_n(x) - m \psi_n(x) \psi''_n(mx)}{\psi'_n(mx) \xi'_n(x) - m \xi_n(x) \psi''_n(mx)}, \quad 2-23$$

where, $m$ is the ratio of refractive index of the sphere $n_s$ to that of the surrounding medium $n_m$, $x$ is the size parameter given as $2m n_s R / \lambda$, $\psi_n$ and $\xi_n$, are the Riccati-Bessel functions. The Mie’s theory is in essence a solution to the Maxwell’s equations. The surface plasmon resonance, denoted by a wavelength $\lambda_{\text{max}}$, describes where the extinction efficiency peaks. The calculation based on the Mie’s theory was done using a program provided by Pennsylvania State Centre for Nanoscale Science [21]. The refractive index of water was set to 1.33, which is a good approximation in the wavelength range of 300-800 nm. The refractive index of gold was taken from [22].
Figure 2-9 (a) The measured extinction efficiency and, (b) transmission of gold colloids. Transmission is defined as the ratio of the transmitted to the incident power density.

Experimentally, the absorption and scattering by small particles can be measured using ultraviolet visible (UV-visible) spectroscopy (Hitachi-U3000 was utilised in this work). The measured results for GNPs in the range of 5-10 nm in radius (10-20 nm in diameter) are plotted in Figure 2-9. From the results, it can be seen that the resonant wavelength is $\lambda_{\text{max}} = 518$ nm. The comparison between the calculated data and the measured results are summarised in Figure 2-10. The extinction efficiency of the GNP dispersion lies between that of GNPs of 7.5 and 10 nm in radius, showing that the synthesised GNPs are in the range of 15-20 nm in diameter, in agreement with the size measurement, Figure 2-2.

It is worth mentioning that the extinction efficiency consists of the absorption and scattering components. In a UV-visible spectroscopy, only the transmittance is measured, and the extinction efficiency can be derived from

$$Q_{\text{ext}} = -\log(T)$$  \hspace{1cm} (2-24)  

For small particles, the scattering effects are less dominant, while large particles produce more scattering.
Figure 2-10 The extinction efficiency of gold nanoparticles. Size of gold nanoparticles is in radius, an input parameter to the software provided by Pennsylvania State Centre for Nanoscale Science [21]. Refractive index of gold taken from [22].

![Figure 2-10 The extinction efficiency of gold nanoparticles.](image)

Figure 2-11 (a) The extinction efficiency of various sized-GNPs; (b) The wavelength where the extinction efficiency peaks against the radius measurement for [23-25].

![Figure 2-11](image)

The extinction efficiencies of GNPs of 5, 7.5, 10, 15, 20, 25, 40, 50 nm in radius are plotted in Figure 2-11(a), with the corresponding maximum wavelengths $\lambda_{\text{max}}$ located at 523, 523, 523, 525, 528, 530, 548, 569 nm, respectively, shown in Figure 2-11(b). It is seen that the measured $\lambda_{\text{max}}$ [23-25] agree well with the calculation. When the radius is smaller than 25 nm, $\lambda_{\text{max}}$ does not shift too much, while the shift is much more apparent when the radius is increased from 25
nm to 50 nm. Yin [26] attributes this to that when the size of a GNP is much smaller than the wavelength, the particle is polarised and the maximal wavelength is only determined by \( \varepsilon_{Au}(\lambda) + 2\varepsilon_{Medium} = 0 \). The permittivity of gold at 524 nm is around \(-2.5421+0.1400j\) [22], water has a permittivity of 1.33, which should predict that \( \lambda_{max} \) is around 524 nm. While for bigger particles, scattering and electron damping are involved and red shifts the spectral peak.

2.6 Summary

The preparation of GNP dispersions using the citrate reduction method has been described. Individual GNPs were characterised using TEM, while the size distribution was measured by dynamic light scattering using a Malvern nanosizer. A brief introduction to the fundamentals of dielectric properties has also been presented, including the Drude model of the dielectric property of metallic materials, and the dielectric model for mixed media. The optical resonant properties of GNPs, which are mostly described using the Mie’s theory, are now termed as surface plasmon resonance to describe the extinction peak of GNPs in the visible light range.

References


Chapter 3  Study of GNPs’ Heating effect for Cancer Treatment

3.1 Overview

GNPs are being intensively explored for medical applications because of their favourable physical and chemical properties [1-3]. Their surface properties allow for facile functionalisation and targeting to specific biological structures. In addition, GNPs have good biocompatibility.

One of these potential applications is the so called non-invasive radio frequency (RF) hyperthermia cancer therapy, in which high intensity RF energy is delivered to the tumour to destroy cancer and surrounding malignant tissues with heat. Recently, GNPs have been proposed as potential agents for non-invasive RF hyperthermia application [4-7]. It is reported that, with the aid of GNPs, tissues can absorb far more energy from RF fields and have much more substantial temperature increase than those without GNPs treatment. Though a couple of groups have reported encouraging results, the heating mechanism has not been provided. Very recently, Hanson [8] pointed out in theory that the absorption of RF radiation by GNPs is negligible. There exists considerable controversy amongst the published results, and a need for some experimental aspects to be verified.

In order to shed further light on the GNPs mediated absorption of RF radiation, or the heating effect of GNPs, we have conducted the following studies:

- To investigate whether GNPs significantly enhance the specific absorption rate of RF radiation, and in consequence increase the temperature substantially;
- To theoretically investigate the possibility of GNPs mediated RF heating. This will mainly focus on the dielectric property measurement on GNP dispersions compared with DI-water;

- To explore the heating effect of GNPs at several frequencies, 13.56 MHz, 261 kHz, and 2.45 GHz. This is not only a revealing study, but is also to search for an optimal operating frequency for GNPs mediated RF heating;

- To check some experiment ambiguities, such as the impurity effect, and field strength.

3.2 Dielectric measurement

3.2.1 Experimental setup

Measurements have been performed using two systems. One is Microwave Consultant Ltd. (MCL) dielectric measurement system [9], which was subsequently found to produce unreliable results. The second measurement system is based on Agilent dielectric property measurement system 85070E [10], working from 100 MHz to 20 GHz, shown in Figure 3-1. A flange is fabricated on the tip of the probe to facilitate the calibration involving open-air, short circuit, and reference material. The minimum sample volume required is such that the lateral dimension must be larger than the size of the flange and have sufficient depth to submerge the flange to minimise the fringing capacitance effect. The sample holders used in the measurement have a diameter of 50 mm and a depth of 50 mm, which is large enough for the measurement. The DC conductivity was measured using a DC conductivity meter, EC-1382B Analytical Instruments, Figure 3-1(c).

![Figure 3-1 Agilent system. (a) VNA N5230C; (b) Probe [10]; (c) DC conductivity meter.](image-url)
3.2.2 Measured results

At first, the measurements using Agilent software 85070E were carried out on formamide and methanol first for the purpose of calibration. The purity of both samples was better than 99.9%. The comparison between the measurement and theory is plotted in Figure 3-2 and Figure 3-3, for formamide and methanol respectively. The temperature was monitored using an optical fibre temperature sensor, *Omega FOB100*, having an accuracy of ±0.1 °C. It is clearly seen that the agreement in the lower frequency range, 100 MHz – 2GHz, is within a relative error of 5% for both formamide and methanol. For instance, at 100 MHz, the theoretical value of permittivity of formamide is 109.9, while the measurement gives 110.1. The maximal discrepancy of the loss factor of formamide is around 3 GHz, ~10%. It is worth mentioning that, the maximal discrepancy always occurs where the loss factor peaks. The reason might be that the parameters of the first order Debye model are normally derived from measurement, which might not be faithful in describing the transition region, where the loss factor has its maximal value.

![Figure 3-2 Dielectric properties of formamide at 24.5 °C, theoretical [11].](image-url)
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Then, two groups of GNP dispersions were measured, one group were impurified samples, and the other group were purified ones. From the preparation recipe, it can be seen a few kind of impurities exist in the resultant product, such as Na\(^+\), Cl\(^-\), and other residual species that have not been fully involved in the chemical reactions. GNP dispersions have been purified by using membrane dialysis method. Impurified and purified samples are defined in Chapter 2, Section 2.2.

There are several reasons for measuring both impurified and purified samples. One is to investigate how much difference in the loss factor is induced by the presence of residual ions and impurities. The other is to investigate whether the presence of those impurities makes any contribution to the heating process of GNP dispersions. This also serves to clarify if the heating effect in recent published literature [4-7] is caused by impurities, or to determine the impact of those impurities on the heating effect. The GNP dispersions have been prepared in several concentrations, 1.1, 11.1, 37.5, 75, and 150 μmol/L, with the first three concentrations as those in [4], and the last two concentrations prepared for better assessment of the heating effect.
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(a) Relative Permittivity

(b) Loss Factor - relative
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Figure 3-4 The dielectric property of impurified GNP dispersions. (a) Relative permittivity; (b) Loss factor; (c) Conductivity. Temperatures: 24.3±0.2°C.

The measured results of impurified GNP dispersions are plotted in comparison with that of DI-water in Figure 3-4. It is shown that the permittivities of GNP dispersions are very similar to that of DI-water. At 100 MHz, DI-water has a value of 79.69, while the values are 79.14 and 79.93 for the lowest and highest concentrations, respectively. Considering the temperature variation, ±0.2°C, and the measurement uncertainty, altogether should be larger than 2% [10], the variation in permittivity is still within the measurement error. However, when examining the loss factor, the difference is obvious, particularly in the range of 100 – 500 MHz, showing a concentration dependent feature. It tends to increase when the concentration increases, except for the lowest concentration, 1.1 μmol/L, which might be too low to cause any substantial change in the loss factor. For other concentrations, it is convincing to conclude that the loss factor increases with concentration.
Figure 3-5 Conductivities of impurified GNP dispersions. (a) From 100 to 500 MHz, (b) DC conductivity and conductivity at 100 MHz.
Conductivities are calculated from the loss factor and are plotted in Figure 3-4 (c), and Figure 3-5 (b). It is not surprising to see that the conductivities of GNP dispersions have striking difference from that of DI-water. The DC conductivities were measured using a DC conductivity meter with an accuracy of 1 $\mu$S/cm. The DC conductivity is a good indicator of the effective conductivity in the RF range. The comparison between the DC conductivities and the ones at 100 MHz of the samples are plotted in Figure 3-5 (b). Clearly, the DC conductivity also increases with the increase in concentration, albeit always smaller than the one at 100 MHz. This is owing to the fact that the effective conductivity consists of the DC conductivity and the loss contribution from molecular friction when the dipole of a molecule tries to follow the alternating electric field. This means that the conductivity at 13.56 MHz should be larger than the DC conductivity, but smaller than the conductivity at 100 MHz.

The results for the purified sample are plotted in Figure 3-6. However, no marked difference can be observed either for permittivity or loss factor.
Figure 3-6 The dielectric property of purified GNP dispersions. (a) Relative permittivity; (b) Loss factor; (c) Conductivity.
Figure 3-7 Conductivities of purified GNP dispersions. (a) From 100 to 500 MHz, (b) DC conductivity and conductivity at 100 MHz.
Again the DC conductivities were measured, shown in Figure 3-7. It is seen that the conductivity slightly increases with the concentration, which can be attributed to residual ions. Also, the effective conductivity of DI-water at 100 MHz is smaller than 25 \( \mu \text{S/cm} \), suggesting that it must be even smaller at 13.56 MHz.

Comparing the results of impurified and purified samples, Figure 3-5(b) and Figure 3-7(b) it is convincing to suggest that the increase in the conductivity is simply due to the impurities in the impurified samples, mostly contributed by the residual ions, \( \text{Na}^+ \), and \( \text{Cl}^- \) for instance, rather by GNPs. Also, it can be concluded that the presence of GNPs in DI-water does not change the permittivity or the loss factor markedly, if the concentrations are below 150 \( \mu \text{mol/L} \).

3.2.3 Discussion

The permittivity of a mixed medium can be modelled using the Maxwell-Garnett model [12] (also in Chapter 2, section 2.3.3), which is particularly applicable to the GNP dispersions. Due to the extremely low volume fraction of the gold, on an order of \( 10^{-6} \), there is no surprise that the effective dielectric properties undergo almost no change, smaller than \( 7.8 \times 10^{-5} \) by calculation, for the highest concentration of 150 \( \mu \text{mol/L} \).

From a microscopic point of view, the dielectric properties are due to the collective dynamics of molecules under the influence of the electromagnetic field. In the case of GNP dispersions, GNPs can be assumed uniformly dispersed in DI-water, and act as dipoles under the influence of the electric field, as shown in Figure 3-8. The amplitude of this dipole is derived as [13]

\[
p = 4\pi r_0^3 \varepsilon_0 E, \tag{3-1}
\]

where \( r_0 \) is the radius of the particle. According to Eq. 2-1, the polarisation consists of two parts, one contributed by water, and the other by polarised nanoparticles, and can be expressed as

\[
\vec{P} = \varepsilon_0 \left[ 1 - \frac{4\pi r_0^3}{3d^3} \chi_{\text{water}} \right] \vec{E} + \frac{4\pi r_0^3}{3d^3} \varepsilon_0 \vec{E} + \frac{4\pi r_0^3}{3d^3} \varepsilon_0 \vec{E} = \varepsilon_0 \vec{E} \left[ 1 - \frac{4\pi r_0^3}{3d^3} \chi_{\text{water}} + 2 \frac{4\pi r_0^3}{3d^3} \right]. \tag{3-2}
\]
where $d$ is the distance between two adjacent particles. Since $\frac{4\pi r_0^3}{d^3}$ can be considered as the volume fraction of GNPs, it is evident that the polarisation undergoes very small change, less than $7.8 \times 10^{-5}$, owing to the fact that the volume fraction is on an order of $10^{-6}$. The prediction is in agreement with the calculation using the Maxwell-Garnett model. Such a small change cannot be detected using the Agilent dielectric measurement system.

As regards conductivity, within metallic materials, there are abundant free electrons, making the conductivity of most metallic materials on an order of $10^7$ S/m. In an insulator, on the other hand, electrons are tightly bounded to their associated nucleus, giving far lower conductivity. The conductivity of electrolyte solution comes from the transportation of ions. In summary, conductivity requires transportation of either electrons or other charge carriers. In the situation of GNP dispersions, GNPs are suspended in DI-water. The mixed GNP dispersion might not show an increase in conductivity due to the lack of electron transportation. Indeed, the measured results suggested that the increase in conductivity is much smaller for purified samples compared to impurified samples. Par [14] discussed the possibility of hopping conductivity, which is dominated by jumping electrons from one particle to the neighbouring particles. This is in essence a tunnelling current, taking place when the gap between two metallic electrodes is on the
order of 1 nm. The distance in Figure 3-8, however, is more than 100 nm, ruling out the possibility of contribution to conductivity by this means.

It should be noted that, the previous discussions are applicable to static dielectric properties. However, in the range of 0-1 GHz, the dielectric properties do not vary significantly with frequency, which is also confirmed by measured results. This can be explained using the Debye model, which indicates that the static permittivity dominates in the lower frequency range, and implies that if no significant change occurs in static dielectric properties, the change in dielectric properties would not be very much in the lower frequency range.

3.3 RF heating study

3.3.1 Microstrip waveguide exposure system

The experiment requires a power generator operating at 13.56 MHz, and a module transforming the power to alternating field. The applicator used here is a novel microstrip line waveguide. The radio frequency exposure systems employed in [4-6, 15] were as shown in Figure 1-12, the Kanzius system [16]. And Figure 1-16, is a high-Q resonant circuit built by Kruse et al [7].

3.3.1.1 Theoretical design

The field strength across the parallel plates of the capacitively coupling system was reported to be ~16 kV/m at 600 W [6]. In order to demonstrate the concept, a microstrip waveguide was designed and fabricated in this study. One reason for choosing the microstrip waveguide is that it has uniform field distribution across the gap. Another is that it is easy and inexpensive to fabricate. Furthermore, it has broadband response that may be useful for multi-band study.

The characteristic impedance of a microstrip waveguide using air as substrate can be simplified to [17]
where $W$ is the width of the upper metallic strip, and $d$ is the thickness of the air gap, as illustrated in Figure 3-9 (a). A triangle taper plate at each end of the copper conductor is used for impedance matching to a 50 $\Omega$ coaxial line.

\[
Z_0 = 377 \left[ \frac{W}{d} + 1.98 \left( \frac{W}{d} \right)^{0.172} \right]^{-1}
\]

**Figure 3-9 Schematic of microstrip line waveguide.** (a) Profile of a microstrip line; (b) side view; (c) plan view.

**Figure 3-10 Dimensions of the microstrip waveguide.** Impedance = 38.60.
Figure 3-11 The schematic model of exposure system with a Petri dish on site.

Figure 3-12 (a) Photograph of the fabricated microstrip waveguide; (b) dBDCommunications & Management Consultancy Ltd, HTF-5500-3 N M-R termination.

The dimensions of the microstrip waveguide are given in Figure 3-10. The width of the upper copper conductor is 70 mm, and the air gap is 10 mm, which is designed to accommodate a Petri dish 10 mm in height whilst producing as high an electric field as possible. The characteristic impedance of this microstrip waveguide is $38.6 \, \Omega$. A CST model of the microstrip waveguide with a Petri dish in situ is plotted in Figure 3-11, while the fabricated version is shown in Figure 3-12.

3.3.1.2 Reflection and transmission performance

The simulated reflection coefficients and insertion loss with and without the Petri dish on site are plotted in Figure 3-13. The simulation frequency range was $0 \rightarrow 50 \, \text{MHz}$, over which $-10 \, \text{dB}$
return loss was achieved. At 13.56 MHz, S11 is less than -30 dB and S21 is almost 0 dB, indicating that power delivery is efficient enough. It can be seen that the Petri dish does increase the reflection coefficient below 50 MHz. At around 13.56 MHz, however, the reflection coefficient is still below -30 dB, and the transmission coefficient is almost 0 dB. This implies that the presence of the Petri dish has little influence on the reflection or transmission coefficients at 13.56 MHz.

Figure 3-13 Simulated S11 and S21 of the exposure system without and with sample in place.

Figure 3-14 Measured results of S11 and S21, 0-50 MHz.
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The measured results are shown in Figure 3-14. It can be seen that the measured reflection coefficients are below -20 dB for both cases of without and with sample in presence. At 13.56 MHz, the reflection is smaller than -25 dB, and the transmission coefficient is approximately 0 dB, which confirms that the standing wave effect is negligible.

3.3.1.3 Characterisation of the field distribution

The field strength across the air gap of the waveguide was simulated using 1 W feeding power. Several E-field probes were placed in the air gap along the vertical central line of the structure to monitor the electric field as a function of the vertical distance to the ground plate. Only the vertical component $E_y$ of the electric field in the air gap was recorded since other components are negligible compared to $E_y$.

The field strength is tabulated in Table 3-1, and plotted in Figure 3-15. It has been observed that the field strength along the vertical central line is uniform and has a value of 702.94(±0.01) V/m. The field strength immediately above the top plate was observed to be 0 V/m.

<table>
<thead>
<tr>
<th>Position (mm)</th>
<th>dBV/m</th>
<th>V/m</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>56.94</td>
<td>702.93</td>
</tr>
<tr>
<td>1.5</td>
<td>56.94</td>
<td>702.94</td>
</tr>
<tr>
<td>2.5</td>
<td>56.94</td>
<td>702.93</td>
</tr>
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<td>3.5</td>
<td>56.94</td>
<td>702.93</td>
</tr>
<tr>
<td>4.5</td>
<td>56.94</td>
<td>702.94</td>
</tr>
<tr>
<td>5.5</td>
<td>56.94</td>
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<td>6.5</td>
<td>56.94</td>
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<td>702.95</td>
</tr>
<tr>
<td>10.5</td>
<td>-200</td>
<td>0</td>
</tr>
</tbody>
</table>

*The sampling points are illustrated in Figure 3-15.*
Figure 3-15 Field distribution along the vertical central line. Waveguide is not shown to scale.

Figure 3-16 The field distribution over the cross section of the waveguide.
The field distribution over the cross section of the waveguide is shown in Figure 3-16. It is evident that the field above the top plate is negligible, while the field strength between the two plates is very strong, in the range of 523 – 900 V/m. This observation highlights the fact that most of the power is confined between the two plates.

When the input power is 600 W, the field strength can be calculated from the square law relationship between the power and the field strength of a TEM wave $P \propto |E|^2$, or $|E| \propto \sqrt{P}$, which immediately yields a value of 17.22 kV/m. This indicates that the goal of 16 kV/m field strength has been achieved when assessed by simulation.

It is understandable that the presence of a Petri dish in the air gap changes the regional field distribution near the Petri dish. Made of plastic with a dielectric constant of 2.2, the Petri dish has a diameter of 36 mm, and a height of 10 mm. During the CST simulation, the Petri dish was half full of pure water.

Table 3-2 The field strength at difference sampling points in the gap of the waveguide, when a Petri dish is placed inside. The input power in the simulation is 1 W.

<table>
<thead>
<tr>
<th>Position (mm)</th>
<th>dBV/m</th>
<th>V/m</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>57.17</td>
<td>722.07</td>
</tr>
<tr>
<td>1.5</td>
<td>25.62</td>
<td>19.10</td>
</tr>
<tr>
<td>2.5</td>
<td>25.12</td>
<td>18.03</td>
</tr>
<tr>
<td>3.5</td>
<td>25.58</td>
<td>16.94</td>
</tr>
<tr>
<td>4.5</td>
<td>24.00</td>
<td>15.84</td>
</tr>
<tr>
<td>5.5</td>
<td>61.84</td>
<td>1236.41</td>
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<tr>
<td>6.5</td>
<td>61.84</td>
<td>1235.50</td>
</tr>
<tr>
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<tr>
<td>10.5</td>
<td>-200</td>
<td>0</td>
</tr>
</tbody>
</table>

*The sampling points are illustrated in Figure 3-17.
Figure 3-17 Field distribution along the vertical central line when a Petri dish is in place. Waveguide and Petri dish not in real scale. The Petri dish is made of plastic having a dielectric constant of 2.2. The diameter of the Petri dish is 36 mm, and the height is 10 mm. The Petri dish is not shown to scale, only for demonstration purpose.

Figure 3-18 The field distribution over the cross section of the waveguide when a Petri dish is in place.
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Figure 3-19 The field distribution over the cross section of the Petri dish then it is placed in the air gap of the waveguide.

The field along the vertical central line is shown in Table 3-2 and Figure 3-17. It is observed that the presence of the Petri dish has reshaped the field distribution considerably. For example, the field strength in the air gap is increased from 702.94 to 1236 V/m. The field strength in DI-water is in the range of 15.8 – 19.1 V/m, which conforms to the boundary condition for the perpendicular component of E-field $E_{\perp}\varepsilon_1 = E_{\perp}\varepsilon_2$. If 600 W power has been delivered to the waveguide, the field strength in the water will be in the range of 387.02 – 467.85 V/m.

The field strength distribution over the cross section of the air gap when a Petri dish is in presence is shown in Figure 3-18. It can be seen that the field distribution in DI-water is symmetric about the vertical central line of the waveguide. The minimal value is located at the central part of the sample, shown as a yellow strip. The field distribution over the cross section of the Petri dish is rendered in colour in Figure 3-19. The colour bar is in the range of 20 – 40 V/m (the minus sign indicates the negative direction of y-axis). Obviously, over most of the sample, the field strength is larger than 20 V/m.
3.3.1.4 The exposure system

The 13.56 MHz power generator is RFX 600A, Advanced Energy Industries, Inc. as shown in Figure 3-20. On the front panel, the standby switch is used for temporary switching off the RF output signal, and RF on indicator signals that the generator is supplying RF signal. The overtemperature indicator reminds that the generator is working beyond its temperature limit. On the rear panel, a 25-pin female subminiature-D type interface facilitates remote control. RF output is via an N-type, female coaxial connector.

Figure 3-20 13.56 MHz high power generator. Advanced Energy Industries, Inc. Module RFX 600A. (a) Front panel; (b) Rear panel.

Figure 3-21 Schematic diagram of the complete exposure system.
Control of the generator is by means of a circuit consisting of switches, a DC power supply acting as activation signal, and output ports for measuring power including generated, delivered, and reflected ones. The circuit operates below 24 V, which is at a safe voltage level.

The schematic diagram of the exposure system is shown in Figure 3-21. The DC power supply, together with the control circuit, is to activate the RF power generator (See Appendix-II for the wiring information of the control circuit). The multimeter is used to measure the generated, delivered or reflected power, linearly scaled to the measured voltage signal that 0-10 V corresponds to 0-600 W. The microstrip waveguide acts as a 50 Ω load to the generator.

### 3.3.2 Power calibration and field strength measurement

#### 3.3.2.1 Power calibration

The calibration method employed here uses a coupler to measure the output power in the range of 0-60 W, and a dipole antenna to measure the output power from 60-600 W, as shown in Figure 3-22, and Figure 3-23, respectively. This method allows use of lower cost RF components.

The bi-directional coupler has a maximal input power of 60 W. One port of the coupler was connected to a power meter (the spectral analyzer can also be used in power measurement). Another one was connected to the power generator, and the remaining two were connected with matching loads. The response of the coupler was first measured using a VNA. The efficiency of the coupler is plotted in Figure 3-24. It can be seen that at 13.56 MHz, the efficiency of the coupler is -38.71 dB. The power meter was connected with an extension head that is capable of picking up 13.56 MHz RF signal. The insertion loss of the power meter at 13.56 MHz is -0.5 dB. Therefore the measured output power can be expressed as

\[
P_o(dBm) = P_{pm}(dBm) - k_c(dB) - k_{pm}(dB),
\]

where \( P_o \) is the calibrated output power, \( P_{pm} \) is the power indicated by the power meter, \( k_c \) is the coupler efficiency, and \( k_{pm} \) is the loss factor of the power meter.
Figure 3-22 Diagram of calibration of the output power. A coupler is employed with two ports connected with matching load.

Figure 3-23 Block diagram of output power calibration. A probe is placed inside the gap and aligned with the electric field. A spectral analyser is used to record the signal level picked up by the probe.

Figure 3-24 Efficiency of the coupler varying with frequency, -38.71 dB at 13.56 MHz.
Table 3-3 The calibration data from the power meter and spectral analyser. Nominal output power is voltage controlled between 0-10 V corresponding to 0-600 W. $V_c$, the controlling voltage, $P_n$, the nominal power, $P_{pm}$, power measured by the power meter, $P_{sa}$, power measured by the spectral analyser.

<table>
<thead>
<tr>
<th>$V_c$ (V)</th>
<th>$P_n$ (W)</th>
<th>$P_{pm}$ (dBm)</th>
<th>$P_{sa}$ (dBm)*</th>
</tr>
</thead>
<tbody>
<tr>
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<td>-26.00</td>
<td>-53.18</td>
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<tr>
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<td>-40.86</td>
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</tr>
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</tr>
<tr>
<td>1.00</td>
<td>60</td>
<td>8.01</td>
<td>-31.20</td>
</tr>
</tbody>
</table>

*Measured with a dipole antenna, explained later on.

The raw calibration data are tabulated in Table 3-3, and plotted in Figure 3-25. The linear fitting line has an expression of $P_o = 0.9P_n - 0.4$. This indicates that for the low-power range (0-60 W), the real output power has very good linearity with the nominal output power or the controlling voltage. In Table 3-3, it is noticed that when the controlling voltage is 0, there is still some residual power picked up by the power meter. It is an indication of power leakage when the power generator is turned on. The power leakage is -26 dBm measured by the power meter, which is 23.56 dB lower than -2.44 dBm (corresponding to 6 W nominal input power). When measured using a dipole, the power difference is 12.32 dB between the leakage and that of 6 W nominal input power in Table 3-3. Therefore, the effect of this power leakage is negligible. The slope of the linear fitting line, which is 0.9, shows that the real output power is 10% less than the nominal output power. Except for the zero point, the linear fitting has a good agreement with the measurement within a relative error of less than 3.0%.

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Although the output power has good linearity in the low-power range (0-60 W), it is not secured when the controlling voltage increases. The dipole antenna is therefore utilised to confirm the linearity of the output power with regard to the nominal output power. In the low-power range, the sampling interval was set to be 6 W, the same as that in the measurement by using a coupler (results shown in Table 3-3), while in the high-power range (60-600 W), the sampling interval was set as 60 W (results shown in Table 3-4).

The measured results using the dipole probe are plotted in Figure 3-26, where the inset zooms in the low-power range, data tabulated in Table 3-3 and Table 3-4. It is shown that the power level picked up by the probe (read from a spectral analyser) is related to the nominal output power in a highly linear manner, expressed as $P_o = (13P_n - 2.1) \times 10^{-9}$. In addition, it is seen that in the low-power range, the fitting line still sticks to the measured data closely. The overall difference between the fitting line and measurement is less than 2.5%. It confirms that the output power has good linearity, and that the prediction on the output power over the entire range can be obtained by using the calibration curve in the low-power range, i.e. $P_o = 0.9P_n - 0.4$. In the high-power range, 60-600 W, it is reasonable to neglect the second term. Therefore, the real output power can be readily calculated by multiplying the nominal output power by 0.9.

Figure 3-25 The measured results and fitting results. Fitting line $P_o = 0.9P_n - 0.4$. 
Table 3-4 Calibration data for high-power calculation. Notations as in Table 3-3.

<table>
<thead>
<tr>
<th>$V_c$ (V)</th>
<th>$P_n$ (W)</th>
<th>$P_{sa}$ (dBm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>60</td>
<td>-31.20</td>
</tr>
<tr>
<td>1.50</td>
<td>90</td>
<td>-29.46</td>
</tr>
<tr>
<td>2.00</td>
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<td>180</td>
<td>-26.45</td>
</tr>
<tr>
<td>4.00</td>
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<tr>
<td>5.00</td>
<td>300</td>
<td>-24.23</td>
</tr>
<tr>
<td>6.00</td>
<td>360</td>
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<td>-21.63</td>
</tr>
<tr>
<td>10.00</td>
<td>600</td>
<td>-21.20</td>
</tr>
</tbody>
</table>

Figure 3-26 Power read from the spectral analyser varying with nominal output power.
3.2.2.2 Field strength measurement

Based on this dipole probe technique, the E-field strength can also be measured if calibration of the field strength is conducted. Theoretically, \( P = k_{dipole}E^2 \), which implies that the power picked up by the dipole probe at given field strength can be used as benchmark data for field strength measurement. The calibration diagram is the same as Figure 3-23, with the power generator replaced by a function generator (HP 3325A). The voltage generated by the function generator, as well as the voltage across the top and ground plates of the waveguide, is measured by an oscilloscope. Voltage generated from the function generator is expressed in peak-to-peak voltage. The measured power varying with the output voltage is tabulated in Table 3-5, and plotted in Figure 3-27. The fitting curve has an expression of \( P = (4.1E^2 + 1.2E - 1) \times 10^{-11} \). The dominant term, \( P = 4.1E^2 \times 10^{-11} \), is also plotted to indicate its significance. It can be seen that the leading term alone gives very good agreement with the measured results, within a relative error of 2.7%, confirming that \( P = kE^2 \) holds.

Table 3-5 Calibration data for E field measurement. \( V_0 \) is the nominal output voltage (peak-to-peak) generated by the function generator, \( V_g \) is the voltage across the parallel plates, \( P_{sa} \) is the power picked up by the probe, measured by a spectral analyser.

<table>
<thead>
<tr>
<th>( V_0 ) (V)</th>
<th>( V_g ) (V)</th>
<th>( P_{sa} ) (dBm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>0.90</td>
<td>-73.30</td>
</tr>
<tr>
<td>1.50</td>
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<td>3.00</td>
<td>2.70</td>
<td>-64.09</td>
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<td>4.00</td>
<td>3.60</td>
<td>-61.67</td>
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<tr>
<td>5.00</td>
<td>4.50</td>
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</tr>
<tr>
<td>6.00</td>
<td>5.40</td>
<td>-58.10</td>
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<td>7.00</td>
<td>6.30</td>
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<td>8.00</td>
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<td>9.00</td>
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<tr>
<td>10.00</td>
<td>9.00</td>
<td>-53.80</td>
</tr>
</tbody>
</table>
The field strength $E$ for other power can therefore be calculated, based on these benchmark data, using the following formula

$$E = \frac{V_g}{2d} \sqrt{\frac{P_o}{P_{sa}}}$$  \hspace{1cm} (3-5)

where $V_g$ is the peak-to-peak voltage across the top and bottom plates, $P_{sa}$ is the power read from the spectral analyser corresponding to $V_g$, and $d$ is the thickness of the air gap of the waveguide.

It has to be mentioned that the measured voltage across the top and bottom plates is proportional to the nominal peak to peak voltage multiplied by a factor of 0.9, accuracy within 0.5%. Therefore, in the computation of $E$ field strength, $V_g$ should be replaced by $0.9V_0$. The fitting curves take the form of

$$E = a\sqrt{P_o} + b.$$  \hspace{1cm} (3-6)

![Figure 3-27 Power level picked up by the spectral analyser varying with nominal voltage by the function generator. Quadratic fitting $P = \left(4.1E^2 + 1.2E - 1\right) \times 10^{-11}$, $P = kE^2$ indicates the leading term $P = 4.1E^2 \times 10^{-11}$.](image-url)
For each $V_g - P_{sa}$ pair, there is a corresponding $a-b$ pair. The resultant $a-b$ pair was calculated by averaging over the set of $a-b$ pairs, which takes the form of $E = 734.59\sqrt{P_o} + 80.60$. It should be mentioned that, in the calculation of $a$ and $b$, the power level $P_o$ should be the real output power and can be calculated from Table 3-3 and Table 3-4 by simply multiplying the nominal output power by 0.9.

The field strength can also be calculated from antenna theory. The impedance of an infinitesimal linear dipole can be written as

$$Z = 20\left(\frac{2\pi}{\lambda}\right)^2 - j120\frac{\ln\left(\frac{l}{2a}\right)}{\tan\frac{\pi l}{\lambda}} - 1,$$

where $l$ is the length of the dipole, $a$ is the diameter of the metallic arm, $\lambda$ is the wavelength in free space [19]. The mechanism of a receiving antenna can be modelled using an equivalent circuit model, which is illustrated in Figure 3-28. The electric field induces a flow of current on the arms of the dipole. The current flows through the arms to receiving circuits or loads. It is therefore clear that a dipole antenna acts as a driving source with self-impedance $Z$. According to antenna theory, the voltage induced by the electric field can be derived as $E/2$ [20-21], where $E$ is the field strength. Normally, the load impedance is 50 $\Omega$. The dipole used in the measurement has an inner pin of 0.505 mm in diameter, and a length of 7.00 mm.

Based on the circuit model, it can be derived that the power received by the load is

$$P = \text{Re}\left(\frac{1}{2}VV^*\right) = \frac{1}{2}\left(\frac{E}{2}\right)^2 \frac{Z_{\text{load}}}{|Z + Z_{\text{load}}|^2}.$$  \hspace{1cm} 3-8

Subsequently, the field strength can be readily calculated as

$$E = \frac{2\sqrt{2P} \cdot |Z + Z_{\text{load}}|}{l\sqrt{Z_{\text{load}}}}.$$  \hspace{1cm} 3-9
The E field strength is plotted against the output power in Figure 3-29, which includes the CST simulation results and calculation results from dipole antenna theory. The CST simulation assumes 1 W input power. The field strength can be scaled up according to $E = k\sqrt{P}$, and it is evident that at 540 W, the real full output power, the field strength is greater than 16 kV/m.

**Figure 3-28** A circuit model of the receiving probe. $Z_{\text{load}}$ here is 50 Ω.

**Figure 3-29** Fitted field strength varying with power level (from measured data), solid line, square mark; CST simulation, dashed line, and dipole theory prediction solid line.
The measurement error can be analysed from Eq. 3-5

\[
\Delta E = \frac{\partial E}{\partial V_0} \Delta V_0 + \frac{\partial E}{\partial d} \Delta d + \frac{\partial E}{\partial P_0} \Delta P_0 + \frac{\partial E}{\partial P} \Delta P. \tag{3-10}
\]

The relative error can be readily calculated from

\[
\left| \frac{\Delta E}{E} \right| = \sqrt{\left( \frac{\Delta V_0}{V_0} \right)^2 + \left( \frac{\Delta d}{d} \right)^2 + \left( \frac{\Delta P_0}{2P_0} \right)^2 + \left( \frac{\Delta P}{2P} \right)^2}. \tag{3-11}
\]

The accuracy of the voltage and air gap thickness measurement is within 0.5%. For power measurement, the measurement error is below 0.2 dBm, which results in an estimated error of 2.3% at 600 W. It can therefore be estimated that the overall measurement error should be within 5.0%. Using simulation and dipole probe circuit mode as contrast, it can be seen that the measurement is well within the 5.0% error level.

### 3.3.3 Heating effect study

#### 3.3.3.1 Influence by the Ohmic loss of the metallic plates

In order to eliminate the thermal effect of the matching load, only the microstrip waveguide was placed in the chamber, as shown in Figure 3-30. Also, another two measures were taken to minimise the thermal effects. The first is that all of the samples were put into the chamber before any measurement was performed to ensure thermal equilibrium with the chamber. The other measure is that, after each measurement, the next sample was placed in the air gap, and the RF source was turned off until the temperature of the new sample was stable. This stabilisation process takes more than 20 min.

Even though those improvements have been made, one more factor still needs careful consideration is the Ohmic loss produced by the metallic plates of the waveguide.

It is obvious that high power going through the waveguide induces a large current to flow through the metallic plates, which inevitably produces Ohmic loss and temperature fluctuation.
Chapter 3 Study of GNPs’ Heating effect for Cancer Treatment

The Petri dish is so close to the two metallic plates that heat generated by Ohmic loss can easily diffuse to the sample, resulting in artefacts. The following measures can remove or measure the background temperature rise effectively:

- Measure the temperature rise in the air gap in the absence of the sample;
- Measure the temperature gradient from the air gap to some distance away from it.

**Figure 3-30** Schematic diagram of the experiment setup.

**Figure 3-31** The temperature rise caused by the metallic plates due to Ohmic loss.
Three measurements have been done for the first measure on three different days. The RF devices were kept running for either 10 or 20 min. As shown in Figure 3-31, the temperature in the air gap keeps increasing with the heating time. The temperature rise is $0.3 \pm 0.1^\circ C$ after 10 min, or $0.7 \pm 0.1^\circ C$ at the end of 20 min RF treatment.

The second measurement samples the temperature at several points, 5, 10, 15, and 20 cm away from the air gap after running the RF devices for 20 min, as indicated in Figure 3-32. The temperature gradient provide strong evident that the temperature rise only occurs around the air gap since the ambient temperature was measured to be $20.3 \pm 0.1^\circ C$. This implies that the temperature rise is not caused by ambient temperature rise, but instead is due to the Ohmic loss of the metallic plates of the microstrip waveguide.

It is therefore concluded that the Ohmic loss from the metallic plates can cause $0.3 \pm 0.1^\circ C$ temperature rise in the air gap after running the RF device for 10 min. This magnitude of temperature rise will be used as the background for all of the samples.
3.3.3.2 Measurement on gold nanoparticles

Two groups of measurement have been done, one group are impurified samples, and the other group are purified samples. The order of the sequence of each group is shown in Figure 3-33. For the impurified samples, the sequence of GNP dispersions is so arranged to ensure that the temperature rise of higher concentration is not due to the thermal effects of long-time operation of RF device, while purified ones are randomly arranged. To be more precise, the following steps are strictly executed:

- All samples are stored in the chamber for at least half an hour to remove the temperature difference between the sample and the ambient environment. It has been observed that half an hour is long enough to achieve thermal equilibrium;

- After each measurement, the next sample to be heated was placed in the air-gap for 20 min to remove the temperature difference between the sample and the air gap. It has been observed that 20 min is sufficient to stabilise the temperature in this measurement. Each sample has a volume of 4 ml.

![Experiment flowchart for impurified samples and purified samples.](image-url)
Figure 3-34 Transient temperature, fitting data for impurified samples. 600 W, 10 min.

<table>
<thead>
<tr>
<th>μmol/L</th>
<th>0</th>
<th>1.1</th>
<th>11.1</th>
<th>37.5</th>
<th>75</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw data (°C)</td>
<td>0.3</td>
<td>0.2</td>
<td>0.5</td>
<td>0.6</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Fitting (°C)</td>
<td>0.498</td>
<td>0.059</td>
<td>0.522</td>
<td>0.588</td>
<td>0.84</td>
<td>0.9</td>
</tr>
</tbody>
</table>

The transient temperature rise of impurified samples is plotted in Figure 3-34. The magnitude of the temperature rise is tabulated in Table 3-6. The final temperature rises of impurified samples are also plotted in Figure 3-35.

It is clearly shown in Figure 3-34 that, the temperature rise exhibits a concentration dependent feature. Furthermore, except for the 1.1 μmol/L GNP dispersion, the remaining impurified GNPs dispersion can all be heated up quicker than that of DI-water. The reason for the exception of 1.1 μmol/L might be that its concentration is too low to cause an enhancement in temperature rise that can be detected in the accuracy of the temperature sensor. It has been measured that, the thermal effect from the metallic plates due to Ohmic loss can cause temperature rise by 0.3±0.1 °C, Figure 3-31. One can expect the temperature rise to be 0.6±0.1 °C for the highest concentration of GNP dispersion, 150 μmol/L.
Figure 3-35 Final temperature rise, plotted as the sequence of measurement for impurified samples. 600 W, 10 min, plotted from raw data. The red line sets a background measurement, which represents the thermal effect of the metallic plates.

Since DI-water is the last sample and shows only 0.3 °C increment, it is convincing to claim that, by taking the aforementioned two measures into consideration, the thermal effects due to long-time operation of RF device and other factors are negligible.

It has been mentioned that a few impurities exist in the impurified samples. How much effect the GNPs have still needs to be investigated. DI-water was the first measured sample, while GNP dispersions were randomly measured. If GNP dispersions do not perform better than DI-water, then it can be concluded that GNPs do not increase the heating effect compared to DI-water. If the heating effect of impurified samples is purely from GNPs, then purified samples will also show similar temperature rises as impurified ones.

The transient temperatures of purified GNP dispersions are plotted in Figure 3-36. The final temperature rise after 10 min, 600 W RF heating is listed in Table 3-7. From the graphic plots, it is clear that the temperature rise is below 0.4 °C. Taking into account the thermal effect of the metallic plates, the temperature rise of the samples is almost negligible, or less than 0.1 °C.
Figure 3-36 Transient temperature, fitting data for purified samples. 600 W, 10 min.

Table 3-7 The temperature rise of purified samples.

<table>
<thead>
<tr>
<th>μmol/L</th>
<th>0</th>
<th>1.1</th>
<th>11.1</th>
<th>37.5</th>
<th>75</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw data (°C)</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Fitting (°C)</td>
<td>0.192</td>
<td>0.222</td>
<td>0.288</td>
<td>0.126</td>
<td>0.27</td>
<td>0.252</td>
</tr>
</tbody>
</table>

As seen from Figure 3-37, the final temperature rise of purified samples does not show evidence that GNPs can absorb RF energy effectively or in consequence results in high temperature rise. The temperature rise looks more likely due to the heat diffusion produced by Ohmic loss of the metallic plates.

Considering the substantial temperature rise in [4-7], there is one possibility that the E-field strength therein might be incorrectly reported. This problem will be treated later on. However, it can be concluded that GNPs alone do not dissipate RF energy significantly. The temperature rise is caused by the impurities in GNP dispersions.
3.3.4 \textit{In vitro} study

It was reported that GNPs incubated cancer cells are susceptible to RF radiation [5]. The cell death increases dramatically compared to that without GNPs treatment after exposed to RF field, up to 80% cancer cells died. Also, it has been shown that \textit{in vivo} subcutaneous injection of GNPs results in tissue destruction upon exposure to the RF field. The \textit{in vitro} study here is to investigate if GNPs incubated cancer cells are susceptible to 16 kV/m RF field. Or in other words, if 16 kV/m RF field is higher enough to cause damage to GNPs incubated cancer cells.

Functionalised GNPs are purchased from \textit{Sigma-Aldrich}, (11-Mercaptoundecyl) tetra (ethylene glycol) functionalised GNPs, having core diameters in the range of 3.5-5.5 nm, as shown in Figure 3-38. It has been reported that ethylene glycol or its derivatives can be used in cellular targeting through adherence to the cell membrane [23]. HeLa cancer cell lines were incubated in the presence of GNPs for 3-4 days, and then exposed to RF field for either 5 or 10 min. After the RF treatment, all the HeLa cancer cell lines were put back to an incubator. The RF treated cancer cells were examined after 24 or 48 hours for their growth situation.
The optical imaging of cancer cells are shown in Figure 3-39. It is seen that after 24 hours, cancer cells are still growing no matter how long they have been treated with RF field. No massive cancer cells death has been observed. After 48 hours, the number of cancer cells is increasing with incubation time after RF treatment. Clearly shown in Figure 3-39 (d), the cancer cells have fully filled the imaging area. It has also been observed that, cancer cells without GNP treatment but treated with RF field (not shown) did not show substantial cell death.

Therefore, it is evident that 16 kV/m RF field does not cause fatal damage to GNPs incubated HeLa cancer cells when the RF treatment is up to 10 min. This is in contrast to Gannon’s finding [4], where even 16 kV/m RF field alone caused up to 75% cell death. This might be suggesting that the field strength in the Kanzius system is incorrectly estimated.

Figure 3-38 Chemical formula and TEM characterisation 3.5-5.5 nm [24].

Figure 3-39 Optical imaging of RF treated cancer cells incubated with GNPs after 24 or 48 hours. (a) 5 min RF, 24 hours, (b) 5 min RF, 48 hours, (c) 10 min RF, 24 hours, (d) 10 min RF, 48 hours.
3.4 Heating effect using Kanzius exposure system

The difference between the results in published literature [4-7] and the ones produced by using the microstrip waveguide is so marked that it is necessary to investigate the reason for this difference. A set of GNP dispersions were sent to the MD Anderson Cancer Centre in Houston, Texas for measurement, including the concentrations of 1.1, 11.1, 33.3, 66.6 $\mu$mol/L. The samples were prepared using the recipe detailed in Chapter 2. This helped to clarify the difference in the electric field strength between the microstrip waveguide and the Kanzius system, since the GNP dispersions were the same. Also, it serves to double check the effects of impurities on the heating effect.

Both purified and impurified samples were included. Furthermore, two impurified samples, 33.3, 66.6 $\mu$mol/L, were centrifuged in MD Anderson Cancer Centre to remove GNPs in order to investigate the heating effect of the base fluid. The process of removing GNPs and retrieve the base fluid is schematically illustrated in Figure 3-40, where the supernatant is the base fluid.

Figure 3-40 Illustration of the process of removing GNPs from the base fluid. The impurities include sodium ions, chloride ions, et al.

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2 The measurement was conducted by Dr. Stuart J. Corr in the MD Anderson Cancer Centre in Houston, Texas, USA. Samples were prepared using citrate reduction method in QMUL and then posted to the USA through FedEx.
All samples were exposed to 600 W RF field in the Kanzius system for 20 to 120 s. The temperature was monitored using an IR-camera, the accuracy of which is specified to be ±1 °C. The temperature rise against time of purified samples is plotted in Figure 3-41. Evidently, the temperature rise is not as much as previously reported in [4-7]. For the highest concentration, 66.6 μmol/L, the temperature rise is 4.5 °C after 120 s. Other concentrations did not perform better than DI-water within the accuracy of measurement, all gave ~2 °C temperature rise. It has been measured that even for purified samples, there are still a small fraction of impurities causing the conductivity several times higher that that of DI-water, as shown in Figure 3-7. This could be the reason why 66.6 μmol/L gave twice the temperature rise of DI-water.

The impurified samples, in contrast, gave substantial temperature rise as shown in Figure 3-42. For the highest concentration, the temperature could be increased by more than 50 °C from the ambient temperature within 20 s. Even for the lowest concentration, the temperature rise could be as high as 5 °C after 120 s RF field treatment. The results clearly show the concentration dependent feature of the heating effect.
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Figure 3-42 The transient temperature of impurified GNP dispersions under 600 W RF field using the Kanzius RF system. The peak points indicate the time point when the RF device was turned off.

Figure 3-43 The comparison between purified and impurified GNP dispersions. The peak points indicate when the RF device was turned off.
To highlight the difference between purified and impurified samples, the temperature rises of both are plotted in Figure 3-43. Obviously, the impurified samples, even at the lowest concentration, can be heated faster than the purified ones at the highest concentration. It is convincing that GNPs alone do not enhance the dissipation of RF energy, while the impurified samples do absorb RF energy and significantly increase the specific absorption rate. In order to confirm that the heating effect is mostly due to the impurities, GNP dispersions of 33.3 and 66.6 μmol/L were centrifuged to remove GNPs. The supernatant layer, or the base fluid, was heated for several tens of seconds. As shown in Figure 3-44, the heating up speed of the GNP dispersions are almost the same as that of their base fluids. The small difference of the heating speed between impurified samples and their corresponding base fluids might be attributed to, for example, temperature monitoring accuracy, and power fluctuation of the RF instrument.

Therefore, it is convincing to conclude that GNPs alone do not absorb significant RF power. Rather, the heating effect is mostly attributed to the impurities, particularly residual ions, that increase the conductivity. Very recently, Li et al [15] reported similar results as shown here. These authors also attributed the heating effect to the impurities.

Figure 3-44 The comparison between impurified GNP dispersions and their base fluids. The peak points indicate when the RF device was turned off.
Examining the difference between the results produced by the Kanzius system and the microstrip waveguide, it is noted that DI-water was heated up to 1.5 °C in two minutes by the Kanzius system. However, using the microstrip waveguide did not give detectable temperature rise if taking account of the thermal effect of the Ohmic loss of the metallic plates. Quoting Eq. 1-5, the field strength in the sample will need to be considerably high, may be more than 6 kV/m, in order to see 1.5 °C increase in two minutes. Equivalently, the field strength in the air gap might be more than 500 kV/m, rather than 16 kV/m. In the estimation, the effective conductivity of DI-water at 13.56 MHz is assumed to be smaller than 14 μS/cm, as shown in Figure 3-7. Based on this estimation, the equivalent temperature rise of impurified GNP dispersion of 150 μmol/L should be more than 35 °C in two minutes, when 500 kV/m electric field is applied in the microstrip waveguide system. Recently, Kruse [7] measured the electric field and found that the field strength was more than 518 kV/m with the input power being 125 W. According to a private communication, it is realised that the field strength was estimated rather than measured. Therefore, it is plausible to suggest that the field strength in Kanzius system might be much higher than 16 kV/m.

3.5 Discussions on the RF heating study

Based on these experiments presented in sections 3.2-3.4, a few conclusions can be drawn:

1) The presence of the impurities increases the conductivity substantially;

2) Impurified samples can be heated up quicker than purified samples. Purified samples produce undetectable temperature increase, under 16 kV/m, 13.56 MHz RF field;

3) 16 kV/m RF field does not cause lethal damage to cancer cells;

4) The heating effect is mostly contributed by the base fluid. Field strength in the Kanzius system might be much higher than 16 kV/m corresponding to 600 W input power.

Regarding the first two conclusions, the heating effect due to the increase in conductivity has been studied by using diluted NaCl solutions. The heating effect is correlated to the value of conductivity and has shown that acceptable agreement has been achieved between measurement
and theoretical calculation, see Appendix I. This also supports the assumption that the residual ions can increase heating effect. For the last two conclusions, one point still needs to be checked is the electric field strength crossing the parallel plates in the Kanzius system. There has been an obvious gap between the theoretical calculation and measurement when examining the result for DI-water. Other authors [7] reported a much higher value of the electric field, 518 kV/m.

Also, it is still worth theoretically investigation of how much energy can GNP absorb from RF field. Hanson et al [23] theoretically studied the mechanism of heating effect using both classical Mie’s theory and quantum mechanism. It was concluded that by Mie’s theory, the absorption of energy from electromagnetic waves by GNP is negligible below low THz regime. In addition, it is mentioned that at 1.7 THz the phonon contribution becomes smaller than that of electron-hole pair surface contribution, not mentioning even lower frequencies as in this study. Consequently, the quantum mechanism does not support the conclusion that GNP increase EM absorption significantly either. The absorption is predominantly caused by the impurities in the GNP samples.

People might argue that the Ohmic loss in individual GNP can contribute to the heating effect. However, according to the calculation from Eq. 2-12, the field strength is extremely low (smaller than 10^{-10} V/m), which cannot increase the bulk temperature substantially.

### 3.6 Magnetic heating effect

This work is to explore the possible effects on GNP produced by low frequency magnetic fields. All of the measurements were carried out at Cheltenham Induction Heating, Ltd. The experiment setup is shown in Figure 3-45. This system consists of three parts, a power generator, a magnetic field generator, and a thermocouple temperature sensor. The power generator provides 0-6 kW tuneable power, with the operating frequency varying with the size of the coil. The magnetic field generator contains a cooling tank filled with running water to prevent overheating. The temperature sensor has an accuracy of ±1°C. This system, working around several hundreds kHz, is designed for heating materials having high conductivity and magnetic properties. A demonstration showed that an iron rod could be heated to 1000 °C in a couple of minutes.
Several samples were measured, including DI-water, NaCl solutions, iron(II, III) oxide (Fe₃O₄), Ni, and purified GNP dispersions. DI-water was used as the control group; NaCl solutions have been measured to have a conductivity of 5-8 S/m; bulk Fe₃O₄ and Ni have magnetic properties. GNP dispersions, however, need to be investigated.

The operating frequency was 261 kHz, and the power was 5000 W. A volume of 2 ml sample was dropped in a glass cuvette, the bottom section of which was placed in the middle of the coils, and then each sample was heated for 90 s. The temperatures of all samples were measured using the thermocouple before and after the heating process.

The temperature increase of each sample is summarised in Table 3-8. The temperature of DI-water increased from 14 °C to 16/17 °C. NaCl solutions showed relative faster temperature increase, roughly 9 °C and 13 °C for the concentrations of 3.5 wt% and 7.0 wt%, respectively. For magnetic nanoparticles, Ni particles gradually precipitated to the bottom of the cuvette, while the temperature increased 3-4 °C. The concentration of Fe₃O₄ was unknown at the time of measurement. The temperature, however, did increase 5-6 °C. Again, Fe₃O₄ nanoparticles gradually precipitated to the bottom of the cuvette under the reaction of magnetic field. For GNPs, the temperature increase was almost the same as that of DI-water.

![Figure 3-45 Magnetic field heating system. EasyHeat, Cheltenham Induction Heating, Ltd. Power used 5000 W, frequency 261 kHz.](image)
### Table 3-8 Heating effect of various samples under magnetic field.

<table>
<thead>
<tr>
<th>Species</th>
<th>concentration</th>
<th>Volume (mL)</th>
<th>T begin (ºC)</th>
<th>T end (ºC)</th>
</tr>
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<tr>
<td>DI-water</td>
<td>-</td>
<td>2</td>
<td>14</td>
<td>16/17</td>
</tr>
<tr>
<td>NaCl</td>
<td>3.5 wt%</td>
<td>2</td>
<td>15</td>
<td>24/25</td>
</tr>
<tr>
<td>NaCl</td>
<td>7.0 wt%</td>
<td>2</td>
<td>16</td>
<td>29/30</td>
</tr>
<tr>
<td>GNPs</td>
<td>150 μmol/L</td>
<td>2</td>
<td>15</td>
<td>17/18</td>
</tr>
<tr>
<td>Fe₃O₄</td>
<td>unknown</td>
<td>2</td>
<td>18</td>
<td>23/24</td>
</tr>
<tr>
<td>Ni</td>
<td>450 μmol/L</td>
<td>2</td>
<td>16</td>
<td>19/20</td>
</tr>
</tbody>
</table>

Power: 5000 kW; Frequency: 261 kHz; Heating period: 90 s.

It should be mentioned that the Ohmic loss produced by a large current flowing through the coil also has an impact on the temperature rise, which is estimated to be a couple of degrees centigrade. For DI-water, the conductivity is small and its magnetic property is very weak. It is to be expected that the temperature did not increase too much after removing the impact from Ohmic loss. In contrast, NaCl solutions have much better conductivity and can dissipate energy due to the eddy current loss under magnetic field. Magnetic particles precipitated to the bottom due to the magnetic interactions. For GNPs, during the course of the experiment, the colour did not undergo observable change, indicating that magnetic field did not cause very strong effects on GNPs. In addition, the temperature did not change as much as other nanoparticle dispersions. This observation implies that GNP dispersions probably have no noticeable increase in conductivity. In connection with the dielectric measurement, this could be further evidence for the low conductivity of GNP dispersions. Furthermore, GNPs did not precipitate to the bottom of the cuvette, suggesting that GNP has weak magnetic property. These two reasons explain why the temperature increase was only comparable to that of DI-water.

### 3.7 Microwave heating effect

#### 3.7.1 Experiment setup

This work is to investigate the possible heating effect of microwave on GNP dispersions by using a microwave oven with a peak power of 800 W, as shown in Figure 3-46. Inside the
microwave oven, a plastic bowel was fixed using sticky tapes to keep the sample holder at the same height with the microwave source. A hole of 2.7 cm in diameter was drilled on the top ceiling of the microwave oven chamber. An IR temperature sensor was placed above the hole to record the temperature variation against heating time. Five power levels, from 160 W to 800 W at a step of 160 W, are available. The microwave oven generates pulsed microwave every 30 seconds, the width of the pulse is 5 seconds for the lowest power level and 25 seconds for the highest power level.

![Setup of microwave heating system. (a) Diagram and critical dimensions; (b) Photograph of the real system.](image)

**Figure 3-46** Setup of microwave heating system. (a) Diagram and critical dimensions; (b) Photograph of the real system.

![A schematic illustration of the relation between the spot size and distance. Red solid lines stand for laser, used for aiming purpose, while dashed lines are the lateral profile of the IR beam, used for temperature detection; (b) photograph of the IR temperature sensor.](image)

**Figure 3-47** (a) A schematic illustration of the relation between the spot size and distance. Red solid lines stand for laser, used for aiming purpose, while dashed lines are the lateral profile of the IR beam, used for temperature detection; (b) photograph of the IR temperature sensor.
Chapter 3 Study of GNP’s Heating effect for Cancer Treatment

The IR temperature sensor is shown in Figure 3-47. The temperature sensor measures the surface temperature of an object with an accuracy of ±1 °C. Accurate measurement requires that the surface area of the sample to exceed the spot size of the IR beam. The spot size S is dependent on the distance D from the sample to the unit’s optical lens. As illustrated in Figure 3-47 (a), the distance to spot size ratio is 12:1, or equivalently the spot size is 12.5 mm at 150 mm away from the optical lens. In addition, it should be noted that steam can prevent accurate measurement by obstructing the unit’s optical lens.

As shown in Figure 3-46 (a), the size of the hole on the top ceiling of the microwave oven chamber is 27 mm in diameter, and the distance between the hole and the unit’s lens is 100 mm, where the spot size should be 8.4 mm, indicating that the hole is large enough not to obstruct the unit’s optical lens. The surface of the sample is 250 mm away from the unit’s optical lens, while the diameter of the sample holder is 55 mm, larger than the spot size (~21 mm).

It has to be mentioned that the IR temperature sensor cannot be placed too close to the hole, as doing so produces abnormal reading, which can be attributed to the electromagnetic interference to the sensor. The sample holders are 100 ml glass beakers, as shown in Figure 3-48. Each sample has a volume of 50 ml.

![Figure 3-48 GNP dispersions of varying concentrations. Volume of each sample: 50 ml.](image-url)
3.7.2 Experiment results

Experiments were conducted on DI-water, NaCl solutions and GNP dispersions. Both DI-water and NaCl solution were used as control samples. NaCl solution has a concentration of 3.5 wt%, approximately the concentration of seawater. GNPs were diluted to 1.1, 11.1, and 33.3 \( \mu \text{mol/L} \), to correlate with Gannon’s work [4].

Figure 3-49 The schematic diagram of the calibration setup of temperature sensor.

Figure 3-50 Calibration data and fitting line 22 – 96 °C.
As is mentioned, the accuracy of the temperature sensor can be degraded by the obstruction of steam. It is therefore necessary to calibrate the temperature sensor to verify the trustworthy temperature range of the sensor. The calibration was done in the following way. A thermometer was inserted into a kettle, while the unit’s lens was adjusted to 25 cm away from the water surface of the kettle. Both readings of the thermometer and temperature sensor were recorded, as shown in Figure 3-49. The raw data is plotted in Figure 3-50, where the linear fitting curve is \( y = 0.96x + 1.8 \). The fitting line implies that the sensor does not agree very well with the thermometer, particularly in the temperature range of 90-100 °C. This is largely caused by the steam from the kettle. It was found that when temperature increased to 84 °C, the increase of the reading of the IR temperature sensor tended to slow down. The fitting below 84 °C is shown in Figure 3-51, where the linear fitting line is \( y = x + 0.13 \), showing a good agreement between the two set of readings. The results confirmed that the steam from the sample does affect the accuracy of the IR temperature sensor, but only when the steam is strong enough. In this situation, the trustworthy detection range should be in the range of 22 – 84 °C.

![Figure 3-51 Calibration data and fitting line 22 – 84 °C.](image)
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Three groups of measurements have been conducted. The first group of measurement consisted of three samples, DI-water, 3.5 wt% NaCl solution, and GNP dispersion of 150 $\mu$mol/L. The NaCl solution was produced to mimic seawater [25]. The power was set to 800 W.

The temperature variation with heating time is plotted in Figure 3-52 (a), and (b), for raw data and fitting plots, respectively. It is clearly seen that the heating of NaCl solution is faster than that of both DI-water and GNP dispersion. The temperature of NaCl solution increased from 22 °C to 72 °C in 20 s, and to roughly 84 °C in 30 s. In the same heating period, the temperature of DI-water increased to 58 °C, and 70 °C, respectively, while for GNP suspension, the temperature increased to 60 °C, and 72 °C. The corresponding heating rates in the first 20 s for NaCl, DI-water, and GNP suspension are 2.5 °C/s, 1.8 °C/s, 1.9 °C/s, respectively.

It is confirmed that 3.5 wt% NaCl solution does increase the heating rates in comparison with DI-water. However, it can be seen from the plots, the curve for GNP suspension almost overlaps with that of DI-water. Therefore, it is not convincing to suggest that GNP suspension increases the heating rate.

![Figure 3-52 Plots of temperature increase with heating time. (a) Raw data; (b) Fitting curves. Power: 800 W.](image-url)
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Figure 3-53 Plots of temperature increase with heating time of varying concentrations. Fitting curves. Power: 800 W.

The second group of measurement involved DI-water, 1.1, 11.1, and 33.3 μmol/L GNP dispersions. Power was still set to 800 W. The transient temperatures of these samples are plotted in Figure 3-53. From the fitting curves, it can be seen that the difference of heating speed between GNP dispersions and DI-water is rather small and may still within the measurement uncertainty. Furthermore, it is not seen that the heating rate increases with the concentration of GNP suspension. For instance, the highest concentration 33.3 μmol/L has the lowest heating up speed, which is contrary to the intuitive reasoning that if GNPs do absorb microwave energy, higher concentration should lead to quicker temperature rise.

The third group of experiment was performed on DI-water, 1.1, 11.1, and 33.3 μmol/L GNP dispersions. The power was set to 480 W to prolong the heating time. The results are shown in Figure 3-54. Again, no convincing evidence can be found to support that GNP suspension increases the heating rate.

It can be concluded that the increase in heating rates of GNP dispersions might be very small and undetectable using the current system.

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3.8 Summary

Heating effects have been studied at several fixed frequencies: 13.56 MHz, 261 kHz, and 2.45 GHz. Dielectric measurements were performed to explain the possible heating effect of GNP.

It is found in the measurement that the residual impurities due to chemical reactions can increase the conductivity considerably. It is the impurities that absorb RF energy and cause temperature rise. The presence of the impurities, however, does not change the real part of the complex permittivity too much.

Also, it has been observed that 16 kV/m electric field is not high enough to cause substantial temperature rise in a few minutes. Comparing the heating results by using the Kanzius system and the microwave guide, it might be possible that the field strength might be incorrectly estimated in some published literature.
Chapter 3 Study of GNPs’ Heating effect for Cancer Treatment

The magnetic field heating study at 261 kHz suggests that GNPs do not have sufficient strong magnetic properties to cause convincing heating effect as possessed by magnetic nanoparticles, such as Ni, and Fe₃O₄. The results may also indicate that GNP dispersions do not have larger conductivity than DI-water.

It is manifested in the microwave study that GNPs might not have strong absorption of microwave energy. By contrast, water is sufficient absorptive in the microwave range that it can be heated up quickly, reaching its boiling point in a couple a minutes when 800 W microwave power at 2.45 GHz is applied. Such a strong heating effect can mask the weak effect created by GNP dispersion.

A few theoretical models also conclude that GNPs cannot absorb energy from EM fields or waves from the low frequency to microwave range.

In summary, the heating effect of GNPs below the microwave range is not significant compared to that of DI-water. So in this frequency range, it might not be suitable for use in the modality of hyperthermia cancer treatment.

References


Chapter 3 Study of GNPs’ Heating effect for Cancer Treatment


Chapter 4  Study of GNP’s Interaction with Millimetre and THz Waves

4.1 Overview

The millimetre wave and THz bands lie between the microwave and visible light on the electromagnetic spectrum. Both bands are relatively unexplored for material characterisation. According to IEEE definition, the millimetre wave band covers the frequency range of 30-300 GHz. For the conventional microwave technologies, it is expensive to fabricate small-sized coaxial or waveguide transmission lines and other components. Also, the increasing attenuation makes precise measurements very challenging in the millimetre wave band. In comparison, free space transmission technology permits one to measure transmission or reflection characteristics of materials in a coherent format, and provides one with details of such as permittivity of materials. Quasi-optical (QO) technology has been well developed in last century. It is particularly useful in the millimetre wave applications due to its low-loss transmission, and multi-polarisation capability. Although not strictly defined, the term terahertz is nowadays used to describe the spectrum from 0.1 to 30 THz. Due to the technical difficulties involved in making effective compact sources and detectors, the THz band is referred as ‘THz gap’. The situation has been improved in the last two decades. The first effective photonic source using photoconductive films dated back to 1984 [1]. The photoconductive source has found many applications in THz technology.

In this chapter, the dielectric properties of GNP’s dispersions will be studied in millimetre-wave, THz bands using Quasi-optical, and THz-TDS systems.
4.2 Operating principles and experiment instrumentations

4.2.1 Quasi-optical techniques

A comprehensive description of QO techniques can be found in [2]. The QO techniques are based on Gaussian beam. Its amplitude profile over the cross section conforms to a Gaussian distribution. A Gaussian beam propagating along z-axis can be described mathematically as

\[ E(r, z) = \left( \frac{2}{\pi w^2} \right)^{0.5} \exp \left( -\frac{r^2}{w^2} - jkz - \frac{j\pi r^2}{\lambda R} + j\phi_0 \right) \]  

where \( R = z + \frac{1}{z} \left( \frac{\pi w_0^2}{\lambda} \right) \) is the wavefront radius, and \( w = w_0 \left[ 1 + \left( \frac{\lambda z}{\pi w_0^2} \right)^2 \right]^{0.5} \) is the beam radius, while \( \tan \phi_0 = \frac{\lambda z}{\pi w_0^2} \) stands for phase shift. The beam radius describes the spot size where the field strength drops to \( 1/e \) of that on the propagation axis. It should be noted that at \( z = 0 \), the beam radius has a minimal value and is called beam waist \( w_0 \), where Gaussian beam acts like a plane wave, as illustrated in Figure 4-1.

A Gaussian beam can be refocused using an ellipsoidal, paraboloidal, or spheroidal reflector, which provides a way of energy manipulation. A reflector acts similarly to a lens, as shown in Figure 4-2. The difference is that a lens collimates parallel rays to a focal point, while a reflector transforms a Gaussian beam into another beam with different size. This property not only allows one to manipulate energy efficiently, but also facilitates measurement since the beam waist can be relocated using either reflectors or lenses. As shown in Figure 4-3, a beam launched from a corrugated horn can be refocused to another beam with its beam waist located between two reflectors or lenses. One benefit of QO technique for measurement lies in its free space transmission, which gives low transmission loss. The measurement is often performed with the sample located at the beam waist position, which results in a better measurement accuracy due to the reduction of off-axis reflection and transmission.
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Figure 4-1 Longitudinal section of a propagating Gaussian beam. At the beam waist, the beam radius has a minimal value, and the wavefront resembles a plane wave front. While propagating, the beam starts spread out producing a growing beam radius.

Figure 4-2 Analogy between a reflector and a lens. A reflector transforms a Gaussian beam to another one with different beam size, while a lens collimates incoming rays to a focal point.

An example of QO measurement bench is shown in Figure 4-4, where two corrugated horns are utilised as transmitter and receiver. Two ellipsoidal mirrors are used to refocus the beam launched from the transmitter. A sample holder is placed at the middle of the two mirrors, where is the location of the beam waist. The attenuator is employed to control the power, while polariser is used to produce linear polarisation. The transmitting and receiving horns are connected to millimetre wave modules that extend the operating frequency of a VNA up to 325 GHz. This system was originally set up to measure the permittivity and permeability of magnetic materials [3].
Figure 4-3 By using a series of reflectors or lenses, the beam from a launching horn can be steered efficiently to couple into a receiving horn. Both the launching and receiving horns can be corrugated horn antennas. At the beam waist, a Gaussian beam has minimal lateral profile and plane wave phase distribution.

Figure 4-4 A Quasi-optical measurement bench. The sample holder is located at the beam waist between two mirrors. The attenuator is used to decrease the power, polarizer is used to produce linearly polarisation.

4.2.2 THz time domain spectroscopy

The TeraView TDS system is shown in Figure 4-5 (a), and a schematic illustration of the optical path arrangement of a THz-TDS is shown in Figure 4-5 (b). A typical TDS system consists of three parts, the THz generation part, the measurement part, and the detection part. Moreover, it also requires a laser for THz generation and detection, a beam splitter and a time delay unit.
Figure 4-5 (a) TeraView TDS system [4]; (b) Schematic of a typical setup for generation and detection of THz pulses using femtosecond optical pulses [5]. BS: beam splitter.

As shown in Figure 4-5 (b), the beam splitter divides the laser into a pump beam and a probe beam. The pump beam is directed to excite THz radiation, while the probe beam is diverted for THz detection. THz waves are collimated by a series of reflectors and focused on the sample. After going through the sample, the THz waves are again collimated by reflectors and directed to the detector. The time delay unit varies the relative arriving time $\Delta t$ of the probe laser to the THz waves, and in this way mapping out the time-domain THz pulse.

THz waves can be generated by using photoconductive antenna, as shown in Figure 4-6. A laser beam is directed to a semiconductor substrate, on which two metal electrodes are mounted and connected to a DC bias voltage. Electron-hole pairs in the substrates are excited by laser
illumination and accelerated by the bias voltage, resulting in transient current. The transient current in turn generates THz radiation.

When the THz wave going through the material, it usually undergoes a series of reflection and transmission, the resultant signal is the summation of multi-transmission, as depicted in Figure 4-7(a). For liquid samples, the transmission is more complicated due to that a window has to be employed to confine the liquid. A sample holder for Fourier Transform Infrared (FTIR) compatible to the TeraView TDS system is employed in this work, as shown in Figure 4-7(b).

![Figure 4-7](attachment:image.png)  
(a) Transmission of THz wave through a single flat layer [5]; (b) A sample holder for liquid sample measurement, d=100 μm [6].

![Figure 4-8](attachment:image.png)  
(a) Schematic diagram of THz pulse detection with a PC antenna; (b) mapping out the THz pulse by varying the delay time Δt [5].
Chapter 4 Study of GNP’s Interaction with Millimetre and THz Waves

Figure 4-9 (a) THz time domain pulse, (b) Spectral information [5].

The detection of THz waves is almost identical to the THz generation. The time-resolved detection of THz waves using a photoconductive antenna is illustrated in Figure 4-8. When the probe laser beam illuminates the substrate, the electron-hole pairs are accelerated by the THz pulse, and hence a transient current is induced. Therefore, the THz waves perform the role of a DC voltage. The amplitude of the current is proportional to the field amplitude of the THz radiation focused on the photoconductive antenna. By varying the time delay $\Delta t$ between the THz pulse and the optical probe, the THz pulse shape can be mapped out, as shown in Figure 4-8(b). An example of the THz pulse is given in Figure 4-9 (a). To obtain the spectral information, the Fourier transform can be employed, as shown in Figure 4-9 (b).

4.3 Experiment results

4.3.1 Dielectric properties in the millimetre wave range

4.3.1.1 Sample holder

Two sample holders are built to form a glass-air-glass multi-layer structure, as shown in Figure 4-10 (a) and (b), respectively. The first sample holder shown in Figure 4-10 (a) is sealed with
two small syringe holes for sample injection. The two holes are so small that it is difficult to inject GNP dispersion without producing air bubbles. It is also a difficulty to clear the sample holder since GNPs tend to aggregate around the hole. During the measurement, liquid samples sometimes stream out from the syringe hole resulting in instable measurement. The second sample holder is designed to overcome these drawbacks with three sides sealed leaving only the top side open for sample injection, Figure 4-10 (b).

![Sample holders](image)

Figure 4-10 Sample holders, (a) old version. Four sides are sealed leaving two holes for sample injection; (b) new version. Three sides are sealed leaving top side open for sample injection.

![Dimensions of sample holder](image)

Figure 4-11 The dimensions of the sample holder. The yellow strips are spacers of 0.720 mm thick, Silica-boron glass windows are 100×100 mm², and 1.1 mm in thickness. The dashed circle indicates the beam size at the location of the sample holder. (a) Side view; (b) front view.
The window material is silica-boron glass, supplied by Instrument Glasses Ltd. The silica-boron glass has an area of 100×100 mm², and is 1.1 mm in thickness. Two sheets of glass are separated by a plastic spacer, 0.720 mm in thickness, as depicted in Figure 4-11. The dimension of the sample holder is so chosen that it is twice of the beam width at the location of the sample holder to ensure 99.99% power interception. In this QO system, the beam width at the location of the sample holder is 50 mm.

### 4.3.1.2 Transmission measurement

The measurement was performed on DI-water and GNP dispersions of different concentrations over two separate frequency ranges, W-band (75 – 110 GHz), and D-band (110-170 GHz). A QO bench has a much wider bandwidth than a horn antenna. Therefore, only the replacement of horns is required when switching the measurement from W band to D-band. The transmission coefficients S21, of empty sample holders, DI-water, and GNP dispersions of 37.5, 50, 75, 100, 150 μmol/L are plotted in Figure 4-12. For the empty sample holder, the results are shown in Figure 4-12, there is a standing wave with peak around 75 GHz, and valley around 100 GHz, caused by the multi-reflection in the multilayer structure. Apparently, DI-water produces high damping in the electromagnetic signal, down to -24 dB, due to its high-loss property in the millimetre wave range. Comparing GNP dispersions to DI-water, the results show that there is no distinguishable difference in either amplitude or phase of transmission coefficients.

Each sample has been measured three times with a temperature monitoring before and after the measurement of S21. For the W-band measurement, the temperature was measured to be 25±0.3°C, using an optical fibre temperature sensor having an accuracy of ±0.1°C. The measured accuracy of ±0.3°C is attributed to room temperature fluctuation.

The thickness of the sample holder filled with liquid sample was measured to be 0.725±0.001 mm, using a vernier calliper. The change may be caused by surface tension on the interface of liquid sample and glasses.
Chapter 4 Study of GNP’s Interaction with Millimetre and THz Waves

Figure 4-12 The transmission properties of the empty sampler hold, DI-water, and GNP dispersions of different concentrations. (a) $S_{21}$ amplitude, (b) $S_{21}$ phase.

(a)

(b)

Figure 4-12 The transmission properties of the empty sampler hold, DI-water, and GNP dispersions of different concentrations. (a) $S_{21}$ amplitude, (b) $S_{21}$ phase.
For the D-band, the measured temperature was $26 \pm 0.3^\circ C$ for all samples. It is evident from Figure 4-13 that the loss is more prominent than that in the W-band. Again, no significant difference was observed between GNP dispersions and DI-water.

![Figure 4-13 S21 of the sample holder and GNP dispersions. (a) Amplitude; (b) Phase.](image-url)
4.3.1.3 *Retrieving complex permittivity*

Retrieving the complex permittivities of DI-water and GNP dispersions is an inverse process of calculating S21. The complex permittivity of the glass has to be known as *a priori* and validated by the measurement of S21 of a single-layer glass and the empty sample holder. The dielectric constant of the glass at 25 °C, 1 MHz is 4.6–0.017j as given in [7]. However, the permittivity of the glass should be slightly different in the millimetre wave range, and is measured to be 4.4–0.066j. The theoretical transmission coefficients calculated using Eq. 2-18 are plotted in Figure 4-14 in comparison with measured results. It is evident that the measurement is in good agreement with the theoretical calculation. The maximal amplitude difference is 0.1 dB, while the maximal phase discrepancy is 2 degree.

The permittivity of the glass is further verified by comparing the theoretical calculation of the multi-layer sample holder and the measured results, shown in Figure 4-15. The agreement again is very promising, the maximal amplitude difference 0.15 dB, and 2 degree of phase deviation. It is therefore confirmed that 4.4-0.066j can be used as *a priori* in the calculation of the complex permittivities of DI-water and GNP dispersions.

![Graph showing S21 Amplitude-dB vs. Frequency-GHz](a)
Figure 4-14 The transmission coefficients of a single layer borosilicate glass. (a) Amplitude; (b) phase.
As described in Chapter 2, formulation of a mathematical expression that gives the complex dielectric permittivity based on the measured data of a multi-layer structure is very difficult. The mathematical formulae even give vague phase information that complicates the procedure of retrieving the complex permittivity. A commonly used alternative is the iterative method that defines an error function and minimises the error function by iterative procedure. The error function defined here is

\[
f(\varepsilon', \varepsilon^*) = T(\varepsilon', \varepsilon^*) - S21
\]

where \( T(\varepsilon', \varepsilon^*) \) is the calculated transmission coefficient using Eq. 2-18, and \( S21 \) is the measured transmission coefficient. To start the iterative process, the initial value for the complex permittivity is calculated from the first order Debye model of DI-water. Although it is not accurate enough to describe the complex permittivity of DI-water in the millimetre wave range, it is a good starting point for iteration. To minimise the error function, a global convergent method for nonlinear systems was employed to obtain a global solution [8]. The relative error is set to be \( 10^{-6} \), when it is met the iteration stops.
Figure 4-16 Complex permittivity in the W-band. (a) The real part; (b) The imaginary part. Temperature $25\pm 0.3^\circ C$. Circle-blue, cross-green, and square-red marks are data for DI-water from the literature [9], [10], [11], respectively at $25^\circ C$. 

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The real part and imaginary part of the permittivities of DI-water and GNP dispersions of 37.5, 50, 75, 100, and 150 μmol/L in the W-band are plotted in Figure 4-16 (a), and (b), respectively. Some published results of DI-water from the literature are plotted as a contrast. The real part of the DI-water is close to the previous published results, with a maximal difference of 1 at 79 GHz. It should be noted that the results from the literature are slightly different from each other. For instance, at 79 GHz, the difference between the result measured by Czumaj [9], and that measured by Mattar [10] can be more than 1.5. Therefore, the difference between the measured results in this work and some published results is acceptable. For the imaginary part, the results in this work are slightly smaller that the published ones. However, the difference is within 1, except the one at 79 GHz.

Comparing the complex permittivities of GNP dispersions to that of DI-water, no clear difference is noted, indicating that GNPs do not have strong interaction with millimetre waves. This can be explained using the Maxwell-Garnett model according to which the wavelength of millimetre wave is comparatively too long.
The W-band measurements were performed at 25 °C while the D-band measurements were carried out at 26 °C. No measured data at 26 °C is found in open literature. Considering the temperatures of 25 °C and 26 °C are close to each other, the published data can give a rough idea of how accurate the measurement is, as shown in Figure 4-17.

Again, it is clearly shown by the measurement in D-band that GNP dispersions have no significant difference compared to DI-water in either real or imaginary permittivity. The small difference might be attributed to measurement uncertainty. Since the transmission coefficients do not show any significant difference between GNP dispersions and DI-water in amplitude or phase, it is not surprising that the complex permittivity has no big difference.
4.3.2 Dielectric properties in the THz range

The sample holder used in the *TeraView* TDS system is a conventional liquid sample holder for Fourier Transform Infrared (FTIR) measurement. The window material is polyethylene, 3.05 mm thick. The spacer is 100 μm in thickness. Due to the prominent absorption of water in the THz range, the spacer cannot be thicker.

The compartment enclosing the optical module, where the measurement is performed, is nitrogen purged to a degree when the spectral signal below 2.5 THz is stable. Beyond 2.5 THz, the signal suffers strong noise and is not considered in this measurement. DI-water, and GNP dispersions of 37.5, 50, 75, 100, 150 μmol/L are measured. The measured transmittance is plotted in Figure 4-18. The transmittance is defined as the ratio of the transmitted power and the incident power in a spectroscopy system. It is seen that the transmission across the sample holder is used as the reference, and is set to unity. Only the transmittance below 2 THz is presented here due to that the signal beyond 2 THz does not show stable results.

![Figure 4-18](image)

**Figure 4-18** The transmission coefficients measured by *TeraView* TDS system. (a) Transmittance; (b) phase.
The transmittance, albeit varies with the concentration, does not show a concentration dependent feature. It neither increases nor decreases monotonically with the concentration. The maximum difference in transmittance between different samples occurs at 0.5 THz, where the 37.5 $\mu$mol/L GNP dispersion gives a transmittance of 0.165, while the 75 $\mu$mol/L sample has a value of 0.190, giving a difference of 0.025. For other concentrations, the difference of their transmittance to that of DI-water is within 0.01. Such a small variation cannot guarantee that it is caused by GNPs.

A retrieving program coded by London Nanocentre Imperial College is then used to calculate the complex permittivity. Similar to the one used in the millimetre wave range, the program tries to minimise an error function using iterative method, as detailed in [13]. The calculated complex permittivities of all the samples are summarised in Figure 4-19. As shown in Figure 4-19, it is clear that the complex permittivities of different concentrations are very similar to each other. Again, it is indicated that the GNPs cause little variation to the complex permittivity. The wavelength of the THz wave being in the region of tens of $\mu$m is too long comparing to the 20 nm GNPs. As shown in Figure 2-10, the surface plasmon resonance takes place at the wavelength of several hundreds of nm. The absorption of EM waves by GNP dispersions drops quickly at THz wavelength. It is reasonable to suggest that GNPs do not absorb large amount of energy from THz waves.

![Figure 4-19 Complex permittivity. (a) The real part; (b) The imaginary part. 20.0±0.1 °C.](image-url)
Chapter 4 Study of GNP’s Interaction with Millimetre and THz Waves

Results of this study is related to the observations in the experiments done by Oh et al [14], where the THz wave reflection from gold nanorods treated tissues does not show any meaningful difference to that from the tissues without gold nanorods treatment. It might be due to the fact that the presence of gold nanorods does not modify the complex permittivity. After illuminated by IR laser, gold nanorods are heated up and cause temperature rise, which subsequently changes the complex permittivity and increases the reflection coefficient. It is because of that the complex permittivity is also dependent on temperature, as illustrated in Figure 2-4.

4.4 Summary

The transmission coefficients of GNP dispersions at different concentrations have been measured in the millimetre wave (W-band and D-band) and THz ranges, using a QO bench and the TeraView THz-TDS, respectively. The complex permittivities have been calculated from the transmission coefficients by iterative methods.

The transmission coefficients of DI-water and GNPs dispersions have shown no significant difference in either the millimetre wave range or the THz range. Therefore, the complex permittivity of GNP dispersions do not show any marked difference to that of DI-water. Therefore, it can be concluded that the electromagnetic waves in the millimetre wave and THz ranges do not interact with GNPs.

References


Chapter 5  Study of Static Electric Field Induced Size-dependent Optical Properties of GNP

5.1 Overview

Optical property of GNP has been extensively investigated for various applications ever since Faraday’s experiment back to 1857 [1]. For instance, the surface plasmon resonance (SPR) of GNP has been employed in the applications of biosensing and bioimaging [2, 3]. The SPR manifesting itself with a peak on the UV-visible spectrum is highly dependent on the size of GNP. This chapter focuses on how static field affects the optical properties of GNP, such as the UV-visible spectrum, the colour. It also covers a preliminary study of the effects of static electric field on the size distribution, the heating effect of GNP using a 655 nm laser, and the heating effect using 13.56 MHz RF field.

5.2 Static field induced change in size distribution

5.2.1 Experiment setup and procedures

The experiment setup for applying static electric fields to GNP dispersions is schematically depicted in Figure 5-1 (a). Two metallic electrodes are connected to a DC voltage source. An insulator stick is bound to the bottom tips of the two electrodes to maintain the electric field constant when a given DC voltage is applied. The distance between the two electrodes is 10 mm.
The study includes several parts, the size distribution, the UV-visible spectroscopy, the colour quantification, the size-dependent laser heating, RF heating, and examination of morphology as shown in the diagram of Figure 5-1 (b). The experimental procedure is as follows:

- DC voltage is applied to GNP dispersions of 150 μmol/L. Two groups of measurements are carried out at (1) 5 V for 0, 1, 3, 7, 9 min; and (2) 3, 7, 9, 11 V for 3 min;
- GNP dispersions after static field is applied are examined for size distribution and UV-visible spectrum. The UV-visible spectroscopic data is used to identify the colour quantitatively;
- The heating effects are characterised using a 655 nm red laser and 13.56 MHz RF field.

### 5.2.2 Size distribution measurement

The size distributions of the GNP dispersions applied with static electric fields were measured using a dynamic light scattering device (Malvern nanosizer). The measured results for the first group, with 5 V DC voltage and varying time are presented in Figure 5-2 and Figure 5-3.
Figure 5-2 The size distribution of the GNP dispersions after DC voltage is applied. (a) 5 V – 1 min; (b) 5 V – 3 min; (c) 5V – 7 min; (d) 5 V – 9 min.
Figure 5-3 Size distribution of GNP dispersions after 5 V DC voltage is applied for varying time. The original sample (0 min) is plotted for contrast.

The size distribution is expressed as scattering intensity in percentage contributed from GNPs of different size. Although percentage in volume or number of particles can also be utilised for the description of size distribution, the scattering intensity is a direct quantity measured by the device, and does not introduce conversion error.

It is seen from Figure 5-2 that the size tends to increase with the time when the voltage is fixed. This might suggest that GNPs prone to aggregation and increase of their size under static field. It is interesting to observe that when the static field is applied for 1 min, a two-peak distribution appears. When the static field is applied for 3 min, the two peaks gradually merge with each other. After 7 or 9 min, bigger GNPs become more populated and span a much wider range on the size axis. It has also been observed that there is a small fraction of GNPs larger than 1000 nm in diameter.

The results for the second group, varying the voltage in the meanwhile fixing the time to 3 min, are plotted in Figure 5-4 and Figure 5-5. It is shown that the size tends to increase with the increase of voltage. In most of the cases, the GNPs mostly concentrate around 100 nm in diameter. A two-peak distribution has also been observed in Figure 5-4 (a). Increasing the voltage also tends to merge the two peaks, Figure 5-4 (b).
Figure 5-4 The size distribution of the GNP dispersions after DC voltage is applied. (a) 3 V – 3 min; (b) 7 V – 3 min; (c) 9 V – 3 min; (d) 11 V – 3 min.
Figure 5-5 Size distribution of GNP dispersions after applied 1, 3, 7, 9, 11 V DC voltage for 3 min. The original sample (0 min) is plotted for contrast.

The physical process of how GNPs aggregate under the interaction with static electric field is not yet clear. One hypothesis is that the static field polarises the GNPs and subsequently leads to the formation of bigger-sized GNPs under the dipole interaction.

### 5.2.3 Examination of morphology

Apparently, the size distribution of GNPs has been modified under the influence of static electric field. Therefore, it will be interesting to examine the morphology change of GNPs. The SEM back-scattering imaging of GNPs is shown in Figure 5-6. It is seen that GNPs aggregate to form sponge-like clusters after static electric field has been applied. The morphology clearly shows that the aggregated clusters are not solid particle anymore. Nevertheless, the sponge-like clusters are likely to scatter more light than monodispersed GNPs, so that the instrument detects larger particles existing in the sample. Since the morphology or shape has been changed, the corresponding optical properties, such as colour, UV-visible spectra, and so forth may be also different from those of monodispersed GNP dispersions. This is the focus of the next section.
Figure 5-6 SEM imaging of GNP after DC voltage of 11 V is applied for 3 min. It is observed that GNPs are aggregated to form sponge like cluster, which shows GNPs are not tightly bonded.

5.3 Quantitative description of colour

5.3.1 Fundamental of the CIE chromaticity diagram

The CIE1931 (International Commission on Illumination) measure is a basic industry standard for colour specification. The CIE1931-XYZ colour space, created by the CIE, is one of the first mathematically defined colour spaces [4]. It describes a colour quantitatively by using two coordinates, x and y on a two dimensional plane, see Figure 5-7. Each point on the boundary of the colour space is a monochromatic light, while the middle part is polychromatic light, which can be reconstructed by properly mixing the three primary colours, red, green and blue.
Figure 5-7 The CIE chromaticity diagram [5]. The curved edge is monochromatic light. The figures are the corresponding wavelength. Inside the curved triangle, the colour is a combination of the three primary colours of red green and blue.

The retina of a person contains millions of colour-detecting nerves, categorised as rods and cones. Rods serve as sensors detecting luminance or brightness, while cones are responsible for colour measurement, or chromaticity. Hence, it implies that the colour perceived may have the same chromaticity but different brightness, or vice versa. For instance, white and grey are of the same colour in terms of the chromaticity, but differs from each other in brightness. In other words, the grey colour has the same spectral components as the white colour does, while it is less bright than the white colour. Analogous to a train of electromagnetic wave, the chromaticity is the frequency, while the brightness is the amplitude.

Three types of cones, together with the rods, form a tristimulus measuring system, which is described by the tristimulus values, X, Y, and Z. The sensitivities of the three types of cones are modelled using three spectral response functions to mimic the perceiving of colour by human eyes, as shown in Figure 5-8.
The tristimulus values for a colour with a spectral power density distribution $I(\lambda)$ are given in terms of the standard observer by

$$\begin{align*}
X &= \int_0^\infty I(\lambda)\bar{x}(\lambda)d\lambda \\
Y &= \int_0^\infty I(\lambda)\bar{y}(\lambda)d\lambda \\
Z &= \int_0^\infty I(\lambda)\bar{z}(\lambda)d\lambda 
\end{align*}$$

As already mentioned, the concept of colour can be divided into two parts, the brightness and the chromaticity. The CIE1931-XYZ colour space was deliberately designed so that the Y parameter was a measure of the brightness or luminance of a colour. The chromaticity of a colour was then specified by the two derived parameters x and y, given by normalised values. Therefore, the CIE-xyY colour space can be constructed from

$$\begin{align*}
x &= \frac{X}{X + Y + Z} \\
y &= \frac{Y}{X + Y + Z} \\
z &= \frac{Z}{X + Y + Z} = 1 - x - y 
\end{align*}$$

To extract the colour, the following procedures may be applied:

- Measurement on the spectrum of a light source;
- Convoluted the spectrum with the three spectral response functions to obtain X, Y, Z;
- Normalised X, Y, Z to obtain x, y, which can be located on the CIE chromaticity diagram to retrieve the colour.

The procedures are also graphically illustrated in Figure 5-9. There are maybe other standards, for example CIE-RGB space. All of them actually are based on the same methodology described herein. A Matlab GUI has been developed to specify the colour from transmission UV-visible spectroscopy, see Appendix-III.

**Figure 5-9** An overview of colour quantification. The transmission spectral is convoluted with the colour matching functions to obtain the normalised values x, y, and Y, which can be mapped to the CIE chromaticity diagram. The tristimulus values can also be transformed to other standards.
5.3.2 UV-visible spectroscopy

When a beam of white light illuminates on one side of a prism, one standing on the other side can perceive seven colours, red-orange-yellow-green-blue-indigo-violet in sequence. The prism therefore acts as a spatial filter. Likewise, when a beam of light going through GNP dispersions, some frequencies will be filtered out and the remaining components construct a different colour, shown in Figure 5-10. In a UV-visible spectroscopy, the transmittance is utilised to quantitatively describe the chromaticity of the colour [7].

![Figure 5-10 Measuring the chromaticity of colour from the transmission mode [7].](image)

Figure 5-11 (a) The UV-visible spectra of GNP dispersions with DC voltage applied for different time scales; (b) The peak absorption occurs at 519, 520, 521, 524, and 527 nm for the samples treated with 5 V DC voltage for 0, 1, 3, 7 and 9 min.
The response of GNP dispersions to UV-visible light is plotted in Figure 5-11 (a), for the first group of fixed voltage (5 V) and varying time. In the long-wavelength range, for example, 700-800 nm, the transmittance are larger than 0.6, while in the short-wavelength range, $\lambda<550$ nm, the transmittance is less than 0.2. It implies that GNP dispersions absorb more short-wavelength light than long-wavelength light. It is also seen that after static field is applied, the transmittance at long-wavelength light is lowered down with the increasing period of time.

It is interesting to observe that the peak absorption wavelength shifts towards longer wavelength, as plotted in Figure 5-11 (b). Due to that the dispersions contain GNPs of different size or GNP aggregations, the absorption become more complicated. This phenomenon will be discussed further later.

From the UV-visible spectra, the x, y coordinates and the Y parameter have been extracted and plotted in Figure 5-12. Clearly, both x and y decrease monotonically with the time for which the static field is applied. The Y component, representing the luminance, also decreases with the time applied.

![Graph of x, y, and Y vs time](image)

**Figure 5-12** The variation of x, y and Y with the time of applying DC voltage. The values of x and y account for the chromaticity, while Y represents the brightness of a colour.
Figure 5-13 Tracing the change of the chromaticity of the colour of the GNP dispersions. The solid arrow in the diagram indicates the direction of the change of colour. The dashed curves link the GNP dispersions to the colour point.

Mapping the x and y coordinates to the CIE chromaticity diagram, we can trace the colour change of GNP dispersions under the static field treatment. It is seen that the colour gradually moves from the red region towards the blue region, indicating that the percentage of short-wavelength component is increased, while the weight of long-wavelength component is reduced. The illumination is represented by the value of Y, which is decreasing continuously since the transmission is lowered down. And this is why the sample applied with static field is slightly darker than the original sample.

For the second group, where the time is fixed with varying voltage, the results as plotted in Figure 5-14, Figure 5-15, and Figure 5-16, for the transmission spectra, the values of x, y, and Y, and the colour on the CIE chromaticity diagram, respectively.

It is seen from Figure 5-14 (a) that the transmittance decreases when larger-sized GNPs become dominant. The peak absorption wavelength, as plotted in Figure 5-14 (b), increases with the magnitude of the voltage. This is in consistence with the measurement on size distribution, where
the size tends to increase with the voltage applied. The values of x, y, and Y are shown in Figure 5-15. Again, all of the three quantities decrease with the magnitude of the applied voltage.

Figure 5-14 (a) The UV-visible spectra of GNP dispersions with DC voltage applied for fixed time with varying voltage; (b) The peak absorption occurs at 519, 523, 525, 529, and 530 nm for the samples treated with 0, 1, 3, 7, 9, and 11 V DC voltage for 3 min.

Figure 5-15 The variation of x, y, and Y with the magnitude of the applied DC voltage.
Tracing the colour on the CIE chromaticity diagram, it is seen that the colour tends to move from the red region towards to the blue region. It gradually changes from light red to light violet, indicating that the weight of short-wavelength component increases.

5.4 Size-dependent laser and RF heating effect

5.4.1 Laser heating effect

The experiment setup for size-dependent heating effect study is shown in Figure 5-17. The samples were placed in the chamber of a microwave oven beneath a hole drilled on the top ceil of the oven. A 655 nm red light laser was aligned to the centre of the cuvette to heat up GNP dispersions. The temperature monitoring was done using an optical fibre sensor of an accuracy of ±0.1 °C with the optical fibre attached to the inner wall of the cuvette to avoid direct laser illumination. The laser produces a rectangular spot size of 1 cm in length and 0.5 cm in width,
either dimension of which is smaller than the size of the cuvette, 1.25 cm by 1.25 cm. The power of the laser is 0.5 W. Before the measurement, all samples were placed in the chamber of the microwave oven to achieve thermal equilibrium. The volume of each sample was 4±0.1 ml. The transient temperature against time is plotted in Figure 5-18 (a), and Figure 5-18 (b), for the first group and the second group of samples, respectively.

Figure 5-17 Experiment setup for heating effect study. A cuvette is placed in the chamber of a microwave oven; the 655 nm red laser is aligned to GNP dispersions.

Figure 5-18 The heating effect of DI-water, GNP dispersions without static field treatment and GNPs dispersions treated with DC voltage at (a) 5 V for 1, 3, 7, 9 min; (b) 3, 7, 9, 11 V for 3 min. The laser is working at 655 nm, full power 0.5 W.
It is clearly shown in Figure 5-18 (a), GNPs have higher heating rate than DI-water. After 10 min laser illumination, DI-water had a temperature rise of 7.6 °C, while the temperature rise for the original GNP dispersion without static field treatment was 12 °C. For the GNP dispersions treated with 5 V DC voltage for 1, 3, 7, and 9 min, the temperature rises were 12.4, 13.1, 15.6, and 18.0 °C, respectively.

For the second group, Figure 5-18 (b), the temperature rise of GNPs treated with different voltages for 3 min also showed higher heating rate than DI-water in a voltage dependent manner. This is a clear manifestation of that the size of GNPs does make difference to the heating rate if illuminated with a 655 nm red light laser.

Also, GNP dispersion has been treated with DC voltage for a longer time, 10 min under 10 V in order to further increase the size of GNPs, Figure 5-19. However, the size of GNPs may be too big that sedimentation can be clearly seen on the bottom of the cuvette. The laser heating effect measurement has been carried out, with the results being summarised in Figure 5-20. GNP dispersions exhibit a higher temperature rise after 10 min laser illumination. The GNP dispersion at 11.1 μmol/L was nearly the same with DI-water, which is due to the low concentration of GNPs.

Figure 5-19 GNPs dispersions after applying DC voltage of 10 V for 10 min. Sedimentation appeared.
5.4.2 RF heating

Another group of GNP dispersions were applied with static electric field and exposed to 13.56 MHz RF field in order to check if the size increased GNPs can enhance the RF heating. The results are summarised and plotted in Figure 5-21. It is observed that when treated with RF field, the heating effect is not enhanced at all. The temperature rise is around 0.3 centigrade for all of the samples, which suggests that GNPs do not enhance the heating effect after the size distribution has been changed. The small temperature rise, as mentioned in Section 3.3.3, is mostly attributed to the Ohmic loss of the metallic plates.
Figure 5-21 Heating of GNP dispersions after DC voltage is applied. (a) Fitting results for 5 V with varying time period; (b) Fitting results for varying voltage and fixed time period; (c) Final temperature rise for 5 V with varying time period; (d) Final temperature rise for varying voltage and fixed time period.

5.5 Discussion

It is apparent that static field causes GNPs to aggregate to form larger-sized ones, albeit the mechanism is not clear yet. The investigation into the mechanism causing the aggregation will be
a focus of the future work. One possibility is to use molecular dynamics simulation giving a microscopic insight into the process.

All the optical observations here look strongly related to the size-dependent properties. In theoretical consideration, it is often explained by using the Mie’s theory [8], used in the quantitative calculation of the interaction of EM waves with particles. All of the calculation formulae have been enclosed in Chapter 2, Eq. 2-19 to Eq. 2-23. However, it has to be mentioned that the Mie’s theory is based on homogenous spheres. It has been shown in Figure 2-1(a) that GNPs are solid ones in the range of 10-20 nm in diameter. After GNP dispersions are treated with static field, GNPs aggregate to form larger ones. SEM imaging shows that the morphology of aggregated GNPs is different from a sphere. As clearly shown in Figure 5-6, GNPs aggregate to form clusters that are not solid spheres at all. The size of these clusters is varying significantly. Subjected to the irregular morphology, wide range of size distribution, and sponge-like structure of GNPs, the Mie’s theory is not suitable to predict the UV-visible spectra accurately. One evidence is the shift of $\lambda_{\text{max}}$, see Figure 2-11(b) for the calculation, and Figure 5-11 (b) and Figure 5-14 (b) for the measured results. According to the calculation, $\lambda_{\text{max}}$ should be around 560 nm since the size is measured to be centred at 100 nm in diameter, as shown in Figure 5-2(c), (d) and Figure 5-4 (c), (d), while the measured results show that the $\lambda_{\text{max}}$ is below 530 nm, as shown in Figure 5-11 (b) and Figure 5-14 (b). The morphology of the GNPs after DC voltage is applied is shown in Figure 5-6. It is clear that the Mie’s theory does not agree with the measurement. The irregular profile and loose structure may produce much more complicated interaction with EM waves.

Regarding the laser heating effect, it has been demonstrated that aggregated GNPs produce higher heating rate, as shown in Figure 5-18, showing that the absorption has been enhanced. In theory, the Mie’s theory can also calculate the absorption rate, by using Eq. 2-21. However, the same issue has to be considered is that aggregated GNPs are not homogenous or solid particles. It is therefore worth doing more theoretical study regarding how aggregated GNPs interact with EM waves, which might be very different from the case of separated GNPs. One possibility is that the resonance frequency, as shown in Figure 5-11 (b) and Figure 5-14 (b), is more close to the operating frequency of the laser and subsequently the SAR is increased. Another possibility
is that the sponge-like structure forms an array and presents multi-scattering effects, which might increase the SAR. By multi-scattering effects, it is meant here the light can be scattered inside the sponge-like structure successively until it is completely absorbed.

The 13.56 MHz RF heating, however, does not show any enhanced heating effect compared to DI-water. The reason might be that the particles are still far too smaller than the working wavelength.

Referring to the size distribution, a good explanation is that aggregated GNPs enhance the scattering intensity, even though they are not solid particles. The enhanced scattering intensity fools the instrument to think that larger solid particles exist in the dispersion. From the measured results, as shown in Figure 5-2, and Figure 5-4, some particles are even larger than 1 μm. However, no clear sedimentation has been observed, see Figure 5-13, and Figure 5-16. One possible reason is that the buoyant force and Brownian motion for sponge-like structure is still sufficient high to suspend aggregated GNPs.

We conclude that all the experimental observations, such as varying UV-visible spectra, changing colour, and enhanced temperature rise, are all due to the aggregation of GNPs. But the mechanism of how static field modifies the size distribution, however, still needs further investigation. The interaction of EM wave with aggregated GNPs is also another interesting topic in the future investigation.

5.6 Summary

The static electric field has been applied to GNP dispersions with various magnitude and time duration. It is found that static electric field can cause GNPs to form larger clusters. It is observed that the UV-visible light spectra of GNPs has changed accordingly and in turn leads to the colour transition on the CIE chromaticity diagram. It has also been observed that the aggregated clusters have enhanced the absorption of 655 nm red light laser considerably, while the heating effect at 13.56 MHz has not been enhanced.
The mechanism of how static field causes the GNPs aggregate needs further study. The interaction of EM wave with aggregated GNPs will also be studied in the future work.

References

Chapter 6  Summary and Future Work

6.1 Conclusions

Throughout the work in this project, the interaction of electromagnetic fields with gold nanoparticles has been investigated across a wide range of frequency bands, including the static field, 261 kHz, 13.56 MHz, the microwave range from 100 MHz to 20 GHz, W-band (75-110 GHz), D-band (110-170 GHz), the THz band, and the visible light. Particularly, the research focus is on the dielectric measurement and the heating effect of GNPs by using electromagnetic fields of different frequencies.

The heating effect study at 13.56 MHz has shown that the temperature rise in impurified GNP dispersions can be in large attributed to the impurities. Purified samples have not shown convincing temperature rise compared to that of DI-water. Therefore, the contribution of GNPs to the RF heating at 13.56 MHz has not been manifested. By using the Kanzius system, it has also been demonstrated that the heating effect is mostly contributed by impurities. Moreover, the magnitude of temperature rise is much larger than using the microstrip waveguide system. From the results using the microwave waveguide system and the Kanzius system, it is concluded that the impurities contribute much more than GNPs to the heating effect of GNP dispersions. Also, it is very likely that the field strength to produce such high temperature rise over a few minutes might be substantially larger than 16 kV/m.

The heating effect studies at 261 kHz and 2.45 GHz also suggest that GNPs do not increase the specific absorption rate in contrast to DI-water. In addition, the study at 261 kHz suggests GNPs have very weak magnetic properties.
Correlating to the heating effect study, the dielectric measurements clearly show that the effective conductivity of purified GNP dispersions does not have obvious increase within the measurement accuracy compared to that of DI-water. However, the increase in conductivity of impurified GNP dispersions is significant and clearly shows a concentration dependent feature. The simulation using CST has confirmed that the increase in the effective conductivity is responsible for the heating effect.

The dielectric properties of GNP dispersion were also measured and did not show any observable difference compared to DI-water in the millimetre and THz bands. By the same argument, the specific absorption rate of GNPs should not change much compared with that of DI-water.

Differing from the aforementioned frequencies, GNPs show absorption peak in the visible light range due to surface plasmon resonance. This has been confirmed both by spectral measurement using UV-visible spectroscopy and theoretical calculation. The static field has been observed to have effects on the size distribution, which manifests itself by the change in colour. Along with the UV-visible spectroscopy, the size distribution measurement shows that indeed the size distribution has been reshaped. At the same time, the absorption rate has been enhanced. All these effects are related to the aggregation of GNPs.

6.2 Key contributions

The key contributions from this project include:

1) Dielectric measurements of GNP dispersions have been conducted in the range from 100 MHz to 20 GHz, in millimetre wave range, W-band (75-110 GHz), D-band (110-170 GHz), and in the THz range. In the microwave range, it has been demonstrated in the experiment that purified GNP dispersions do not show significant change in complex permittivity compared to their base fluid, DI-water. The increase in effective conductivity of impurified GNP dispersions is caused by the residual impurities, such as Na$^+$ and Cl$^-$. In the millimetre wave and THz ranges, it has also been shown that purified dispersions do not have an obvious difference in complex permittivity compared to that of DI-water;
2) Heating effect of GNP dispersions has been studied at 261 kHz, 13.56 MHz, and 2.45 GHz to understand how GNPs enhance absorption of electromagnetic waves. It is found that GNPs have very weak magnetic properties through the 261 kHz magnetic field heating study. A more thorough study at 13.56 MHz suggests that the temperature rise of impurified GNP samples are contributed mainly by the impurities rather than GNPs, which is in consistence with the dielectric property measurement. Also, it is noted that none of the three frequencies produces any difference in the heating rate of GNP dispersions and DI-water within the accuracy of measurement. These observations disprove the claim in some studies elsewhere that GNPs can enhance the specific absorption rate dramatically.

3) Static field induced aggregation has been studied and characterised by size distribution measurement. The UV-visible spectroscopy also confirms that the size distribution of GNPs has been modified. As a consequence, the colour of GNP dispersions has also been changed after applying static field for some period of time. The CIE1931 standard has been employed to quantitatively describe the colour of GNP dispersions from the transmission data of UV-Visible spectroscopy. The heating effect study using 655 nm red laser has shown a rapid temperature rise after static field is applied. However, the heating effect at 13.56 MHz has not been enhanced at all after static field has been applied to GNP dispersions.

4) In order to carry out the heating effect study at 13.56 MHz, a RF exposure system has been developed. The RF characterisations, such as S11, S21, and electric field have been measured and simulated using CST. Especially for the electric field measurement, a dipole antenna has been utilised to calibrate the power level and measure the field strength in the air gap of the microstrip waveguide in an inexpensive way.

5) For the dielectric measurement in the millimetre wave range, a sample holder has been built to facilitate liquid sample measurement by using the QO technique. An iterative method has been proved particularly useful for multilayer structure to extract the complex permittivity.
Chapter 6 Summary and Future Work

6.3 Future work

Though a significant deal of research work has been conducted in the fields of nanoscience and nanotechnology, there are still many issues to be addressed. The work in this project only focuses on the interaction of electromagnetic fields with GNPs. Even on this, many areas deserve further study. Future work may include the following areas:

- The dielectric measurement is only done up to 2 THz. In the infrared range, how GNPs affect the dielectric properties requires further investigation. This can be fulfilled using a conventional Fourier Transform Infrared (FTIR) to bridge the gap between the THz and visible light bands.

- Regarding the heating effect, the work has been done on GNPs. However, it is worthy of investigations to more materials. There exist a vast number of nanomaterials to be explored. For instance, materials having superparamagnetism might present different response to magnetic field compared to the bulk ones. Also, composite nanomaterials have never been investigated in this study.

- Although it has been demonstrated that static field can cause GNPs to aggregate. The physical mechanism has not been unveiled yet. The improvement to precisely control the change of size distribution still requires a large amount of effort to either improve the experiment processes or understand the physics behind this phenomenon. One possibility to investigate the mechanism might be using molecular dynamic simulation to gain an insight in a microscopic way.

- It has also been demonstrated that aggregated GNP clusters can absorb more 655 nm laser than separated GNPs. This is also an interesting phenomenon and requires further study. The interaction of EM wave with aggregated GNPs is more complicated and might need numerical modelling.
List of publications

Journal papers


Conference papers


Appendix I – Conductivity Dependent Field Strength and Temperature Rise

It is established that the relative permittivity can be written as:

\[ \varepsilon_r(\omega) = \varepsilon_r^0(\omega) - j\varepsilon_r^0(\omega) = \varepsilon_r^0(\omega) - j \frac{\sigma(\omega)}{\varepsilon_0\omega} \]  

where \( \sigma(\omega) = \sigma_d(\omega) + \sigma_0 \). The conductivity actually consists of the contribution of dipole relaxation, \( \sigma_d(\omega) \), and free ions transportation under the reaction of electric field, \( \sigma_0 \). In the heating effect study, a circular Petri dish is placed between two parallel plates, in which case the boundary condition for perpendicular components of electric field takes effect \( E_{1\perp} \varepsilon_1 = E_{2\perp} \varepsilon_2 [1] \).

![Graph showing electric field strength and temperature rise](image-url)
The NaCl sample used in the CST simulation has a DC conductivity of 3.53 S/m, which will reduce the field strength in the NaCl solution significantly. In order to verify this observation, the field distribution in the sample has been simulated and plotted in Figure A1. The field strength in the sample was substantially reduced from 1238 V/m to 0.28 V/m, which is in agreement with theoretical prediction by \( E_{1\perp} \varepsilon_1 = E_{2\perp} \varepsilon_2 \). The complex permittivity of the NaCl solution at 13.56 MHz is approximately 78 - 4685.8j. It has to be mentioned that the dielectric constant must be the complex permittivity when the boundary condition is enforced. A phase discontinuity has been observed on the air-NaCl solution interface. The magnitude of the phase difference also agrees with the boundary condition for the perpendicular component \( E_{1\perp} \varepsilon_1 = E_{2\perp} \varepsilon_2 \).

The field distribution inside the Petri dish is shown in Figure A2. From the colour representation, it is evident that the field strength in the sample is less than 0.3 V/m.
Figure A2 (a) Field strength distribution over the cross section of the waveguide, (b) strength distribution over the cross section of the Petri dish. The input power is 1 W.
Appendix I – Conductivity dependent field strength and temperature rise

Table A1 Electric field distribution (V/m) of NaCl solutions of different conductivities. Input power 1 W.

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Since the conductivity has great impact on the electric field, it must greatly impact the heating effect as well. To investigate the conductivity dependent feature, the field strength inside NaCl solutions of different DC conductivities was simulated in CST and tabulated in Table A1. The sampling points inside the samples are highlighted in Table A1 and plotted in Figure A3. It is seen that with the increase of the DC conductivity, the field strength inside the NaCl sample decreases dramatically. However, since the DC conductivity is increasing, the temperature rise must peaks at a certain value of DC conductivity, according to

$$\Delta T = \frac{\sigma(\omega) \cdot |E|^2 \cdot t}{2 \rho \cdot C_w}. \quad \text{A1-2}$$

The comparison between the CST simulation, and experiment measurement is plotted in Figure A4. It is seen that they agree with each other comfortably. The discrepancy between the CST simulation and the measurement may be attributed to measurement error and thermal diffusion effects in accompany with the heating process.
Figure A3 Field distribution at different sampling points v.s. DC conductivity. Figures in the legend denote the distance of the sampling points to the bottom of the Petri dish.

Figure A4 Comparison between the measurement with CST simulation and theoretical calculation of the temperature rise. Scaled to 600 W input power, 10 min RF treatment. The effect of thermal effect of the parallel is removed from the results.
Appendix I – Conductivity dependent field strength and temperature rise

It has to be noted that the dielectric properties are strongly dependent on the frequency, quoting the first order Debye model with ionic conductivity $\sigma_0$ (or DC conductivity)

$$
\varepsilon_r(\omega) = \varepsilon'_r - j\varepsilon''_r = \varepsilon_{r\inf} + \frac{\varepsilon_{r0} - \varepsilon_{r\inf}}{1 + j\omega \tau} - \frac{j\sigma_0}{\omega \varepsilon_0}, \quad \text{A1-3}
$$

where

$$
\begin{align*}
\varepsilon'_r &= \varepsilon_{r\inf} + \frac{\varepsilon_{r0} - \varepsilon_{r\inf}}{1 + (\omega \tau)^2} \\
\varepsilon''_r &= \frac{(\varepsilon_{r0} - \varepsilon_{r\inf})\omega \tau}{1 + (\omega \tau)^2} + \frac{\sigma_0}{\omega \varepsilon_0} \\
\sigma(\omega) &= \frac{(\varepsilon_{r0} - \varepsilon_{r\inf})\omega \tau \varepsilon_0}{1 + (\omega \tau)^2} + \sigma_0
\end{align*}
\quad \text{A1-4}
$$

According to [2], the static permittivity $\varepsilon_{r0}$, high-frequency permittivity $\varepsilon_{r\inf}$, relaxation time $\tau$, and ionic conductivity $\sigma_0$ all depend on the salinity $S$ (the concentration of NaCl solution, expressed in part of one thousand). In consequence, the complex permittivities are frequency, temperature, and salinity dependent

$$
\begin{align*}
\sigma_0 &= k(N, \Delta) \cdot \sigma_{NaCl}(25, N) \\
k(N, \Delta) &= 1 - 1.962 \times 10^{-2} \Delta + 8.08 \times 10^{-5} \Delta^2 \\
&\quad - N\Delta[3.02 \times 10^{-5} + 3.922 \times 10^{-5} \Delta + N(1.721 \times 10^{-5} - 6.584 \times 10^{-6} \Delta)] \\
\sigma_{NaCl}(25, N) &= N[0.394 - 2.3776N + 0.68258N^2 - 0.13538N^3 + 1.0086 \times 10^{-2} N^4] \\
N &= S[1.707 \times 10^{-2} + 1.025 \times 10^{-5} S + \times 10^{-5} S^2] \\
\Delta &= 25 - T
\end{align*}
\quad \text{A1-5}
$$

$$
\begin{align*}
\varepsilon_{r0} &= a(N) \cdot \varepsilon_{r0}(T, 0) \\
a(N) &= 1 - 0.2551N + 5.151 \times 10^{-2} N^2 - 6.889 \times 10^{-3} N^3 \\
\varepsilon_{r0}(T, 0) &= 87.74 - 0.4008T + 9.398 \times 10^{-4} T^2 + 1.41 \times 10^{-6} T^3 \\
\tau &= b(N, T) \cdot \tau(T, 0) \\
b(N, T) &= 1 - 4.896 \times 10^{-2} N - 2.967 \times 10^{-2} N^2 + 5.644 \times 10^{-3} N^3 + 0.1463 \times 10^{-2} NT \\
\tau(T, 0) &= 1.1109 \times 10^{-10} - 3.824 \times 10^{-12} T + 6.938 \times 10^{-14} T^2 - 5.096 \times 10^{-16} T^3
\end{align*}
\quad \text{A1-6, A1-7}
$$
Appendix I – Conductivity dependent field strength and temperature rise

The above equations are valid for $0 \leq S \leq 260$. Therefore, at a given frequency, the complex permittivity, especially the imaginary part, strongly depends on the salinity as shown in Figure A5 (a), and (b), for 13.56 MHz and 2.45 GHz, respectively. Particularly at 13.56 MHz, the loss factor increases dramatically from below 1 to more than 7000 when the salinity is increased to 40. While at 2.45 GHz, the influence of the salinity is much less, the loss factor is only increased from 10.6 to 50.5. The real part, however, is less affected by the salinity.

![Figure A5](image.png)

Figure A5 The concentration dependent complex permittivity of NaCl solutions. (a) 13.56 MHz; (b) 2.45 GHz. Temperature 20°C.
Appendix I – Conductivity dependent field strength and temperature rise

Figure A6 Frequency dependent complex permittivity of NaCl solution. Salinity 35, temperature 20°C. (a) From 1 MHz to 100 GHz; (b) 13.56 MHz; (c) 2.45 GHz.

At a given salinity, the frequency dependent feature is also obvious, shown in Figure A6 (a-c). Again, the content of NaCl has more influence in the low frequency range that it does in the high frequency range. In the low frequency range, the loss factor is so large that the field strength will be reduced to a small value that the dissipation of energy is negligible. This is verified experimentally, as shown in Figure A4. However, at 2.45 GHz, the magnitude of the complex permittivity does not change significantly, so the field strength in the NaCl solution should remain at the same level of that in DI-water. On the other hand, the loss factor is increased from 10.47 to 45.98, which leads to a much quicker temperature rise according to Eq. A1-1 and Eq. A1-2.

The reason why in the low frequency range, the loss factor are much larger than that in the high frequency range can be explained using Eq. A1-3. The loss factor consists of a term $\frac{\sigma_0}{\omega \varepsilon_0}$, contributed by the ionic conductivity, which is inversely proportional to the frequency. Considering that the value of $\varepsilon_0$ is so small $8.84 \times 10^{-12}$ that the contribution from the ionic conductivity to the loss factor dominates in the low frequency range. While with the increase of
the frequency, the value of the denominator increases accordingly and decreases the weight of the contribution from the ionic conductivity.

Furthermore, it is noticed from Figure A4 that the temperature rise of 13.56 MHz RF heating peaks at a certain value of ionic conductivity, or at a certain concentration, see Eq. A1-5 for the relation between the ionic conductivity and the concentration. The ionic conductivity, where the SAR peaks, should vary with the frequency, as plotted in Figure A7. It is seen that when the operating frequency increases, the SAR peaks at higher ionic conductivity. At 13.56 MHz, the peak SAR occurs at the point, where the ionic conductivity is 602.2 μS/cm, or 0.06022 S/m, which is in agreement with Kruse’s calculation using a circuit model [3].

In conclusion, the dissipation of EM energy by NaCl solutions depends on the concentration and the frequency. The simple rule of that the higher the conductivity, the higher the SAR is based on the assumption that the field strength is the same. However, in a real apparatus, the generated EM fields or EM waves has to conform to the boundary conditions, enforcing which has great impact on the field strength in the samples.

![Figure A7 (a), Ionic conductivity dependent temperature rise; (b) the ionic conductivity when the peak SAR can be observed at a given frequency.](image-url)
Appendix I – Conductivity dependent field strength and temperature rise

If an electromagnetic wave incidents on the surface, part of it will be reflected off with the remaining transmits through. The reflection and transmission coefficients of the parallel and perpendicular polarised component are derived as [4]

\[
\begin{align*}
\Gamma_\parallel &= \frac{\varepsilon_r^2 - \cos(\theta) - \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}}{\varepsilon_r^2 - \cos(\theta) + \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}} \\
T_\parallel &= \frac{2 \cdot \varepsilon_r^2 \cdot \cos(\theta)}{\varepsilon_r^2 - \cos(\theta) + \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}} \\
\Gamma_\perp &= \frac{\varepsilon_r^2 - \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}}{\varepsilon_r^2 - \cos(\theta) + \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}} \\
T_\perp &= \frac{2 \cos(\theta)}{\varepsilon_r^2 - \cos(\theta) + \sqrt{\varepsilon_r^2 - 2 \varepsilon_r^2 \sin^2(\theta)}}
\end{align*}
\]

And the specific absorption rate can be adapted to

\[
SAR = \frac{\sigma(\omega) \cdot |E|^2}{2 \rho} = \frac{\sigma(\omega) \cdot \left(\varepsilon_r^2 \cdot T_{\parallel}^2 + |E_\perp \cdot T_{\perp}|^2\right)}{2 \rho}.
\]

The transmission coefficient from air to NaCl solution of 3.5% by weight is plotted in Figure A8. It is seen at 13.56 MHz, the transmission coefficient of NaCl solution is much lower than that of DI-water, while it is almost the same of both samples at 2.45 GHz.

**Figure A8** The transmission coefficient of an EM incident on an air-dielectric interface. (a) 13.56 MHz; (b) 2.45 GHz.
Appendix I – Conductivity dependent field strength and temperature rise

Figure A9 (a) The dependence of SAR on the salinity and frequency, at normal incidence; (b) heating rate. Assuming the incident electric field is 1 V/m, sample 2.75 in thickness.

Again, the SAR is dependent on the frequency and the ionic conductivity, or the concentration of the NaCl solution. For simplicity, assuming that the incident angle is zero degree, and that the incident electric field is 1 V/m, the SAR is plotted in Figure A9. It is seen that below 3 GHz, the SAR is increasing with the frequency and also increasing with the concentration when S<100. It is also observed that in the low frequency range, when S>1, the SAR does not increase significantly with the increasing of the concentration, while in the microwave range, the increase of the SAR become accelerated after S>1.

At 2.45 GHz, since the transmission coefficient from air to the NaCl solution is almost the same, while the loss factor of the NaCl solution is several times higher than that of DI-water, as shown in Figure A6(c), NaCl solution should be heated quicker compared to DI-water, see Figure A9(b), which explains the results in Figure 3-52 (a).

To calculate the heating rate, assuming the thickness of the material is 2.75 cm, which is the radius of the beaker, as shown in Figure 3-46(a). The heating rate can be derived as

\[
\frac{dT}{dt} = \int_0^\infty \frac{\sigma(\omega) \cdot |\bar{E}|^2}{2 \rho \cdot C \cdot \nu} \, dv = \frac{\sigma(\omega)}{2 \rho \cdot C} \left( |E_{||} \cdot T_{||}|^2 + |E_{\perp} \cdot T_{\perp}|^2 \right) \cdot \frac{1 - e^{-2\alpha d}}{2\alpha d},
\]

A1-10
where, the influence of penetration has been included, with $C$ the specific heat capacity, $V$ the total volume, and $d$ the thickness. The density and heat capacity here is from reference [5]. It is seen from Figure A9(b) the heating rate of NaCl solution is 1.2 times that of DI-water.

References


Appendix II – Control Circuit

This is the schematic diagram of the controlling circuit of the power generator. Each wire is explained in the notes immediately after the diagram.

Figure A10 The schematic diagram of the controlling circuit.

Notes:
3: Logic low disables RF output
4: RF on, momentary contact +24 V
7: 0 1 0 1
8: 0 1 0 1
FP LP DC FP
11: Power setpoint
0-10 V corresponding to 0-600 W

13& 23: Interlock
24& 25: Interlock
14: RP-Reflected Power
15: LP-Load Power
16: FP-Forward Power
18: SC-Signal Common
19: PC-Power Common
Appendix III – CIE Colour Diagram

The following figure shows the graphic user interface of calculating the CIE colour coordinates. The operation of this calculation is quite straightforward and the meaning of each component is explained therein.

Figure A11 Graphic user interface of CIE coordinates calculation.