An Investigation of the Impedance Properties of Gold Nanoparticles

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Abstract. Over recent years there has been rapid growth in the research being carried out on nanoparticles. In the field of medical imaging, this interest has focussed primarily on the potential for drug delivery and using nanoparticles as a contrast agent, e.g. super-paramagnetic iron-oxide (SPIO) particles in MRI. More recently gold nanoparticles have been used in radiotherapy treatment of tumours to provide dose enhancement by increasing the efficacy of the radiation absorption. Nanoparticles coated with molecules such as glucose or cancer-specific antibodies can be directed towards specific cancer cells in vivo. Such targeting combined with the properties of nanoparticles shows great promise for localised therapy of tumours while leaving neighbouring healthy tissue unaffected. However, on the nanoparticle scale of sub-100nm the weighting of various factors and inter-atomic interactions which determine the bulk properties of a material changes. Many properties of the bulk material no longer hold. As such, each aspect of nanoparticle behaviour must be investigated afresh to explore the full extent of their potential. The property of nanoparticles we wish to explore and characterise is impedance. Bulk gold is well known to be highly conductive. If this were to remain the case on the nanoscale, it could be highly effective as a contrast agent for electrical impedance tomography, particularly when combined with tumour targeting.

1. Introduction

To explore the possibility of detecting gold nanoparticles via their impedance response we have carried out initial experiments to determine their conductivity using solutions of gold nanoparticles with diameter under 5nm and colloidal gold, which is comprised of much larger particles.

For use in cancer research, gold nanoparticles should preferably be less than 5nm in diameter. This is because nanoparticle diffusion across biological membranes, and consequently their distribution in the body, is size dependent. Nanoparticles less than 10nm will be able to migrate from the blood stream into tumours. Furthermore, nanoparticles less than 5nm can pass the blood-brain barrier, permeate blood vessels and be dialyzed in the kidney allowing unwanted particles to be flushed out of the body [1], [2]. This means that colloidal gold is too large to access tumours after intravenous injection or to be passed through the kidneys, potentially limiting its applicability in the treatment of cancer. It is included here to maximise sensitivity and explore any size-dependence of gold nanoparticle conductivity.

2. Methods
2.1. Gold Particle Solutions
Two gold nanoparticle solutions were used (Midatech Ltd, UK). The first was comprised of a 1.6nm diameter core of approximately 102 gold atoms. These gold nanoparticles (GNPs) are coated with approximately 43 glutathione (gsh) ligands such that the total gsh-GNP diameter approaches 5nm [3]. The second solution was comprised of larger citrate encapsulated colloidal gold particles.

2.2. Impedance Measurements
Impedance measurements were made using a Solartron 1260 impedance analyser (Advanced Measurement Technology, UK) across a frequency range of 1Hz to 1MHz with an applied voltage of 1V. Previous experiments (data not shown here) in which an aliquot of GNP solution was added to saline solutions of known impedance had proved insufficiently sensitive to detect any impedance change from the GNPs. Consequently, a test rig was designed and built in-house to hold a sufficiently low volume to examine the gold particle solutions directly without the need for any surrounding solution so as to maximize sensitivity to the impedance response of the nanoparticles.

2.2.1. Test Rig Construction and Calibration. A well to hold 200µl aliquots of solution was created by overlapping glass microscope slides. 0.5mm thick silver electrodes, across which the voltage was applied, were inserted at either end of this well. Contact was made at two points along the length of the well to facilitate a four-electrode impedance measurement [4]. Prior to investigating the unknown impedance properties of the various gold particle solutions, the rig was calibrated to ensure linearity between the measured impedance and the conductivity of commercially available known-conductivity solutions (Hanna Instruments, UK). Five solutions with conductivities ranging from 8.4mS/m to 8S/m were used in the calibration process. The solution temperature was recorded and the corresponding conductivity was determined from the solution’s technical sheet. A linear fit was performed to determine the geometric factor for the rig. This was in turn used to estimate the absolute conductivity of the gold particle solutions.

2.3. Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES)
Upon completion of the impedance measurements, ICP-AES was carried out on the solutions to determine their gold atom concentrations and convert these to molar concentrations. The molar conductivity of the solution was determined by taking the ratio of the solution’s estimated conductivity to its molar concentration.

Figure 1. Calibration curve for the test rig used to measure the conductivity of the gold particle solutions. The measured conductance (blue points) was fitted to the conductivity, with a goodness of fit of 0.99999 (black line).

3. Results
The acquired impedance data was converted to conductance. Data above 100kHz was excluded to minimize any errors that could be introduced by the effects of stray capacitance.
Figure 1 shows the average conductance for each of the five calibration solutions versus the temperature-corrected conductivity (0.0079 S/m, 0.1332 S/m, 0.4711 S/m, 1.215 S/m, and 7.52 S/m at the measured temperature of 22°C) along with the linear trend line derived from fitting to these data.

Figure 2 shows the measured conductance of the gold nanoparticle solutions compared to that of highly pure deionised (DI) water and moderately pure DI water. The highly purified DI water is an aliquot of that used to manufacture the gold particle solutions and was therefore taken as a baseline with which to compare the increase in conductance caused by the gold particles. The glutathione coated GNPs show a 24-fold increase in conductance while the colloidal gold particles result in a 150-fold increase. The conductance measured for two of the known conductivity solutions are also presented to indicate the equivalent absolute conductivity of the gold nanoparticle solutions.

![Figure 2. Comparison of the conductance between the gold particle solutions, DI water and two known conductivity solutions.](image1.png)

The molar concentration of gold atoms found using ICP-AES was 0.49 mM for the colloidal gold solution and 11.78 mM for the glutathione coated gold nanoparticle solution. The estimated molar conductivities, with respect to gold atom concentration, are 219 mS/m²/mol for the colloidal gold and 1.49 mS/m²/mol for the glutathione coated gold nanoparticles. These values are compared to those of published values for common electrolytic ions [5] in figure 3.

![Figure 3. Comparison of the estimated molar conductivities of the gold particle solutions with the molar conductivities of common electrolytic ions found in the body.](image2.png)
4. Discussion
The typical concentration of GNP solutions is so small that measuring their effect on bulk impedance is at the detection limit for typical systems. The presence of other charge carriers, e.g. the ions in saline solutions or any residual impurities in deionised water samples, can dominate the impedance response and is therefore critical in determining whether or not there is sufficient sensitivity to detect the effect of the gold particles on bulk impedance. By using a rig designed specifically to look at small solution volumes (200µl) sufficient measurement sensitivity was achieved to investigate the conductivity of the gold nanoparticles. Although in absolute terms the conductance of these solutions is very low, the presence of the gold nanoparticles did result in significant amplification of the conductance with respect to baseline. The low absolute conductance is a reflection of the low concentration of gold nanoparticles in the solutions. However, the molar conductivities of the gold atoms in the solutions compare favourably with those of typical electrolytic ions found in vivo and is in fact many times greater in the case of the colloidal gold particles.

5. Future
In future we wish to explore the mechanisms behind the conductivity of the gold nanoparticles as well as their effect on bio-impedance within a cellular environment. Key factors in determining the impact of gold nanoparticles on bio-impedance in vitro and in vivo, where the number of mobile ions will be large, will be the amount of cellular uptake and the resultant concentration of gold nanoparticles that can be achieved. Their effect may well also depend on what ligand is used to coat the GNP, e.g. charged or uncharged, and on which cellular compartment takes up the gold nanoparticles, e.g. whether they are internalized or remain on the cell surface. Understanding these mechanisms may allow us to exploit properties of the gold nanoparticles in cancer detection and/or treatment.

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