A nanomagnet for biomedicine

In an interview with *International Innovation*, Associate Professor Yuko Ichiyana discusses her fascination with nanoparticles, the development of a novel mass spectrometry technique and the exciting potential applications of her current research.

**What is it about magnetic nanoparticles (MNPs) that captivates you?**

The make-up of everything around us is established upon the supposition that the number of atoms is greater than the Avogadro constant – the number of constituent particles found in one mole of a substance. However, this notion collapses with nanometre-sized particles, leading to interesting phenomena and peculiar characteristics, such as quantum size effects and quantum magnetic tunnelling. I am particularly interested in MNPs because they have the potential to be used in many areas, such as for media recording technology and biomedical applications.

**Can you outline your research goals and how you are striving to achieve these?**

My team aims to use an innovative method to develop MNPs for future biomedical applications in areas such as drug delivery systems, imaging materials and hyperthermia treatment. However, to achieve this we must overcome several obstacles: firstly, it is hard to maintain ferromagnetism at the nanoscale; secondly, magnetic particles are ceramic insulators, which makes it difficult to attach drugs to them; and thirdly, an observation and evaluation system for nanosized materials has not yet been established. Therefore, in order to reach our objective, we must optimise magnetic parameters and introduce a novel method for developing MNPs specifically within the biomedical field.

**In what way has the process of synthesising functionalised nanoparticles (NPs) assisted the mass spectrometry (MS) technique that you have developed?**

Today, the ionisation mechanism is still unknown and thus we are continually

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**Pioneering potential**

Scientists at *Yokohama National University*, Japan, are driving magnetic nanoparticle research forward in order to develop innovative biomedical technologies.

**IN THE PAST** decade, an increasing number of scientists have become interested in the potential of using nanoscale materials for a wide range of technological advances. Various unique behaviours and properties are exhibited in nanoscale materials that are not present on the macroscale; for example, when a particle size is reduced to the nanometre realm, the electronic properties are altered – a result that is known as the quantum size effect. Physical properties – including mechanical, thermal and catalytic characteristics – can also be transformed, with changes such as a vastly increased ratio of surface area to volume.

Research on magnetic nanoparticles (MNPs) – nanoparticles that can be influenced through using a magnetic field – has become particularly active in recent years. When optimised effectively, MNPs demonstrate a marked change of properties that can influence their magnetic interactions. These novel properties have led scientists to suggest the use of MNPs in biomedicine, magnetic resonance imaging, magnetic particle imaging, data storage and much more.

A research team within the Graduate School of Engineering at Yokohama National University, Japan, is harnessing the potential of MNPs for developing innovative nanomedicine technologies. The project is run by scientists across a broad range of disciplines, including physics, biology, medicine, electrical engineering and home economics, who meet several times a year to collaborate on new ideas and support one another in complex nanotechnology issues. Led by Associate Professor Yuko Ichiyana, the researchers are using a novel method for synthesising MNPs, which they are endeavouring to use in future biomedical applications such as drug delivery systems, imaging materials and hyperthermia treatment.

**THE WET CHEMICAL METHOD**

An important part of Ichiyana’s research is focused on multiferroic materials, which have a range of electric, magnetic and structural properties that could be used in the emerging field of spintronics. At present, the synthesis of multiferroic materials involves complex processes such as high-pressure synthesis, pulsed laser synthesis or spark plasma sintering. Instead of using these laborious conventional methods, Ichiyana’s team tested a unique method for creating MNPs in a more efficient way, as she explains: “In recent years, we have developed a novel preparation method of MNPs, which is already a Japanese patent. This wet chemical method involves mixing aqueous solutions of transition metal chlorides and sodium metasilicate nonhydrate to gain MNPs.”

While multiferroic properties found in CuFeO have been widely explored in recent years, the expected multiferroic properties found if iron were replaced with manganese to form CuMnO have been barely acknowledged. By adopting the new wet chemical method, alongside an improved sintering process, the researchers were capable of synthesising single-phase...
trying to elucidate this by accumulating experimental data. An indicator of the ionisation mechanism would be, for example, transfer of electrons in the transition of metal particles, vacancy in metal oxides structure and cation adsorption capability.

When establishing our MS technique, we were influenced by a method that won a Nobel Prize in Chemistry in 2002. We noticed that cobalt nanoparticles were included in the matrix for the MS analysis and so tried to use our functionalised MNPs for matrix-assisted laser desorption/ionisation. Luckily, we found that our functional MNPs exhibited excellent ionisation ability and that it is possible to detect both low and high molecular levels using the same matrix. Furthermore, our functional MNPs have magnetic behaviour, so we can introduce them into cells by an external magnetic field.

What major challenges have you faced during your research?

Biomedical application is an interesting and important research area; nonetheless, there are many issues to tackle when conducting such research. For our study, the in vivo experiments were expensive and hard to perform and even after these tests we are still not sure whether the material is biocompatible. It takes time to solve each problem one by one, and it is difficult and time consuming to receive permission for clinical trials from the Ministry of Health and Welfare.

Looking ahead, what is the potential of MNPs for practical applications?

MNPs have potential in areas such as cancer therapy, gene introduction and analysis, magnetic resonance imaging improvements and MS imaging, and will eventually lead to progress in ‘theranostics’ – therapy and diagnostics. In the near future, we hope to achieve magnetic hyperthermia treatment for cancer therapy.

CuMnO, nanoparticles with diameters of 64 nm. This method was also successful in synthesising other multiferroic materials such as gadolinium-doped BiFeO₃, in which magnetic properties of the material were effectively enhanced.

FROM CATIONIC COATING TO COMBATING CANCER

For MNPs to be used in biological applications, it is crucial to find a way to successfully join them with biological molecules, such as amino groups. Experiments with inserting magnetic particles into living cells have been conducted – and most studies so far have coated MNPs with cationic reagents, which have a positive charge, in order to attract them to the surfaces of target cells, which are negatively charged. However, in Ichiyanagi’s study MNPs were able to enter target cells without cationic coating. To achieve this, the outer surface of the MNPs were covered with amorphous silicon dioxide, which allowed for amino-silane coupling – the bonding of organic and inorganic materials. The researchers tested this pioneering approach with iron-based MNPs due to their strong magnetisation, even at room temperature, and were successful in introducing them into living cells.

Such promising findings have driven the researchers to explore the process’s potential in new medical applications. Ichiyanagi’s team is now focusing its research on magnetic hyperthermia treatment, a novel cancer therapy that uses MNPs. “We believe it is imperative to develop certain treatments, such as magnetic hyperthermia therapy, as soon as possible,” Ichiyanagi stresses. It is hypothesised that by taking advantage of the heat produced in materials within a magnetic field, cancer cells – which are more sensitive to heat than normal cells – can be destroyed. The researchers have put this theory into practice through conducting in vitro tests on human prostate and breast cancer cells and evaluating the MNPs’ hyperthermia effects. The researchers’ experiments have so far been successful, and Ichiyanagi hopes that magnetic hyperthermia cancer therapy will soon become an effective biomedical application.