31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Plasmonic Magnetic Nanoparticles for Biomedicine

Sara A. Majetich, *Member, IEEE*, JitKang Lim, and Robert D. Tilton

***Abstract*—Core-shell nanoparticles containing both iron oxide and gold are proposed as a new tool for *in vitro* biosensing applications. The surface plasmon resonance of gold was used to track the positions of individual particles smaller than the optical diffraction limit. With a large magnetic field gradient from a tip made of a soft magnetic material, particles can be collected and later released.**

Magnetic nanoparticles are used in cell separation [1] and as contrast agents for magnetic resonance imaging [2], and they have potential uses in magnetically guided drug delivery [3] and cancer treatment through magnetic field-driven hyperthermia [4]. Magnetic nanoparticles could also be used as guided sensors or delivery agents within living cells. Achieving this requires the ability to position and image individual particles within biological media. Here we review a previously described approach that enables particles to be "seen" using their surface plasmon resonance while being guided magnetically.

The preparation of iron oxide-core, gold-shell nanoparticles has been reported previously [5, 6]. The starting point is the synthesis of highly monodisperse iron oxide nanoparticles. The particles were transferred from organic solvents into water through surfactant exchange, and 1-2 nm gold clusters were reactively bound to the particle surfaces. The composite particles can be used either in their seeded form, or with a complete Au shell grown by electroless deposition onto the gold seeds [6].

At this point the particles form a stable dispersion in deionized water, but flocculate in 0.15 M phosphate buffered saline (PBS) solution that is commonly used with biological media. Additional polymer species must be attached for stable dispersion, which is quantified by the hydrodynamic diameter distribution measured by dynamic light scattering (DLS). Compared with bare iron oxide nanoparticles, the gold-coated particles form more stable dispersions in PBS when coated with adsorbed polymers [7].

The motion of individual particles can be monitored in real time using optical microscopy. The surface plasmon resonance of the gold scatters light with high efficiency, so that dark field optical microscopy can be used for detection [6]. Fluorescence microscopy is an equally valid approach if appropriate molecular tags are attached to the particle surfaces [8].

The magnetic force on a monodomain particle is proportional to its volume, while the viscous drag force scales with its diameter. Viscous drag forces hinder the ability to magnetically guide small nanoparticles. In addition, random Brownian forces introduce significant diffusion. Magnetophoretic and drag force calculations predict the particle velocity as a function of the magnetic field gradient and the particle shape and size. For small particles, nanorods are shown to have advantages over nanospheres due to reduced Brownian motion [7]. Spherical Au-coated iron oxide nanoparticles can be magnetically guided using a mu-metal tip attached to a solenoid [9]. When the solenoid is energized to saturate the tip magnetization, nearby particles are captured. When the field is turned off, they diffuse away.

These particles have been introduced into HeLa cancer cells. With an appropriate polymer coating they are shown to be non-toxic. The particles can be moved by an external magnetic field within the living cells.

Manuscript received April 23, 2009. This work was supported in part by the U.S. National Science Foundation under Grant CBET-0853963, and a Philip and Marsha Dowd Fellowship (J. K. L.).

S. A. Majetich is with the Physics Department, Carnegie Mellon University, Pittsburgh, PA 15213 USA (phone: 412-268-3105; fax: 412-681-0648; e-mail: sara@ cmu.edu).

J. K. Lim is with the Chemical Engineering Department, Carnegie Mellon University, Pittsburgh, PA 15213 USA (e-mail: jitkangl@landrew.cmu.edu).

R. D.. Tilton is with the Chemical Engineering Department, Carnegie Mellon University, Pittsburgh, PA 15213 USA (e-mail: tilton@landrew.cmu.edu).

REFERENCES

[1] K. E. McCloskey, J. J. Chalmers, and M. Zborowski, "Magnetic cell separation: characterization of magnetophoretic mobility". *Anal. Chem.*, vol. 75, pp. 6868-6874 (2003).

[2] H. Pardoe, P. R. Clark, T. G. St. Pierre,, P. Moroz, and S. K. Jones, "A magnetic resonance imaging method for measurement of tissue iron concentration in liver arterially embolized with ferromagnetic particles for magnetic hyperthermia of tumors", *Mag. Reson. Imaging*, vol. 21, pp 483-488 (2003).

[3] J. Cao,Y. Wang, J. Yu, J. Xia, C. Wang, D. Jin, U. Hafeli, "Preparation and radiolabeling of surface-modified magnetic nanoparticles with rhenium-188 for magnetic-targeted radiotherapy", *J. Magn. Magn. Mater*., vol. 277, pp. 165-174 (2004).

[4] R. Hergt, W. Andrä, C. G. d'Ambly, I. Hilger, W. A. Kaiser, U. Richter, and H. G. Schmidt, "Physical limits of hyperthermia using magnetic fine particles", *IEEE Trans. Mag.* Vol. 34, pp. 3745-3754 (1998).

[5] J.-K. Lim, R. D. Tilton, A. Eggeman, and S. A. Majetich, "Design and Synthesis of PLasmonic Magnetic Nanoparticles", *J. Magn. Magn. Mater.* Vol 311, pp. 78-83 (2007).

[6] J.-K. Lim, R. D. Tilton, A. Eggeman, F. Lanni, and S. A. Majetich, "Synthesis and Single Particle Optical Detection of Low Polydispersity Plasmonic Superparamagnetic Nanoparticles", *Adv. Mater.* Vol. 20, pp. 1721-1726 (2008).

[7] J.-K. Lim, R. D. Tilton, and S. A. Majetich, (manuscript in preparation).

[8] J.-K. Lim, D. X. Tan, F. Lanni, R. D. Tilton, and S. A. Majetich, "Optical Imaging and Magnetophoresis of Nanorods", *J. Magn. Magn. Mater.* Vol. 321, pp. 1557-1562 (2009).

[9] J.-K. Lim, F. Lanni, R. D. Tilton, and S. A. Majetich, (manuscript in preparation).