Cellular Level Magnetic Hyperthermia for Cancer Therapy

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Background

Nanoparticles (NPs) that could respond to an external alternating current (AC) magnetic field are termed magnetic nanoparticles (MNPs), usually with the size of <100nm. They could generate heat because of the irreversible magnetization process under AC field condition. On the other hand, cancer cells are more sensitive to elevated temperature, due to higher metabolic rates, than healthy cells. Enough elevated temperature (>42℃) for enough time (~30min) could induce apoptosis in cancer cells while healthy cells remain [1]. This leads to the idea of using MNPs to generate such localized heat to kill cancer cells, termed magnetic hyperthermia (MH). It has become a promising alternative/assistive cancer therapy since last decades with some clinical trials in vivo [2]. However, once associated with cells, the AC magnetic response, as well as the heating response, of MNPs change dramatically compare with MNPs in suspensions due to the complex biological environment. Therefore, investigating the cellular level AC magnetic response of MNPs mimicking the in vivo environment, although not seen much progress due to technical limitations, is a necessity to explore the hidden mystery. Moreover, cellular level MH where MNPs are either inside or on the membrane of cells could potentially increase the efficacy and thus reduce the dosage and side effects compared to the direct tumour-injection methods seen in most clinical trials.

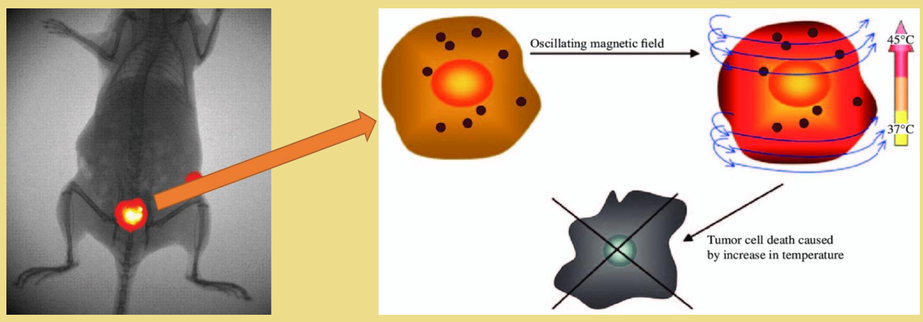

Figure 1. Magnetic hyperthermia concept. [3][4]

Results

As shown in Figure 3, AC hysteresis evolves from minor to major loops with increased field amplitude for all samples. Nanoparticle size has a dominant effect on the width of AC hysteresis loops as shown from Figure 3(a) to (c) regardless of whether the nanoparticle cores are composed of magnetite (Figure 3a, b) or maghemite (Figure 3c). Comparing AC loops measured under the same field amplitude but different frequencies (Figure 3a, d), a slight increase in width at the highest frequency (508 kHz) is observed.

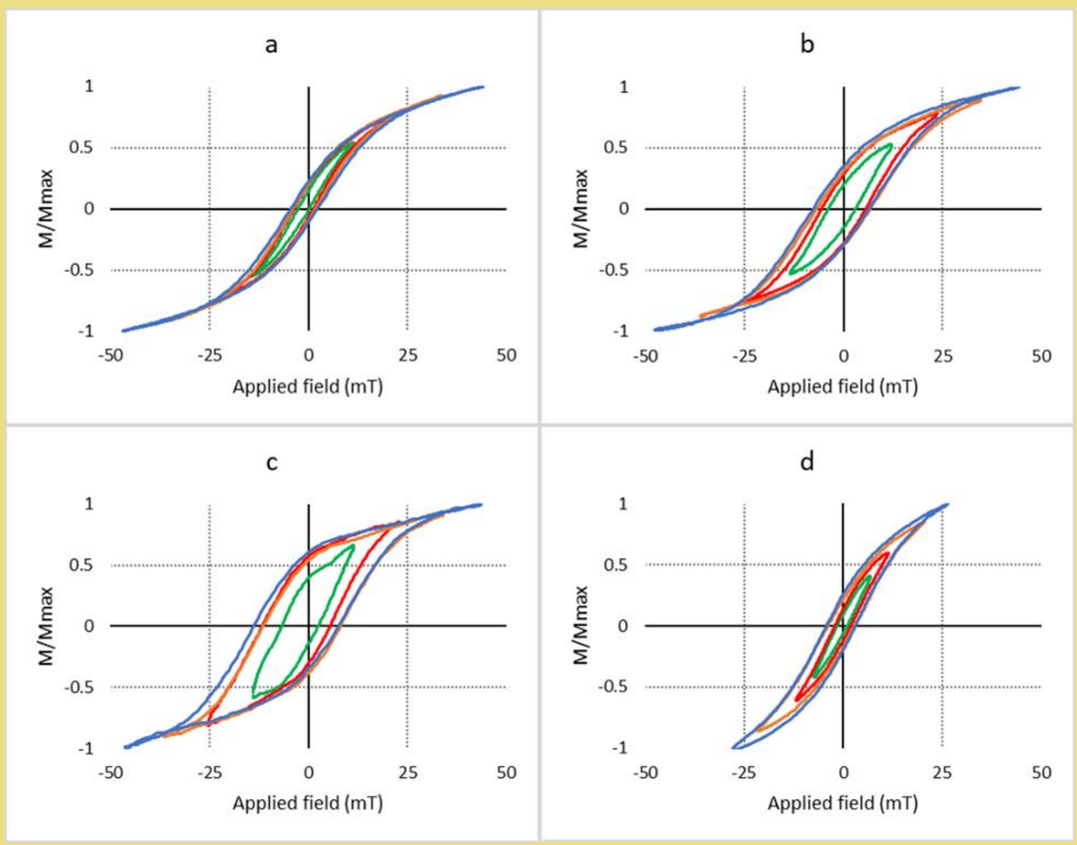

Figure 3. AC hysteresis loops measured with the microscope. (a) Magnetite NPs with core size of 8.5nm under 129.2kHz. (b) Magnetite NPs with core size of 10.5nm under 129.2kHz. (c) Maghemite NPs with core size of 17.4nm under 129.2kHz. (d) Magnetite NPs with core size of 8.5nm, same as in (a), under 508.2kHz. Different loops on each plot show four different AC magnetic field amplitude used.

Method

This project utilizes a home-made magneto-optical microscope (Figure 2) that is capable of measuring the AC magnetic response of samples with high spatial resolution (<0.5μm) which is comparable to the size of MNP aggregations within cells. It determines the AC magnetization of samples by the faraday optical rotation instead of conventional inductive pick-up coils which are hard to scale down with reduced sample size. This microscope is also capable of conducting magnetic mapping and fluorescence lifetime imaging, advantageous for simultaneous biological structural and functional investigation. The heating response of MNPs could be quantified by specific absorption rate (SAR)—heating power per mass. It could be calculated by SAR = A*f, where A and f represent the AC hysteresis loop (AC magnetization with the field) area and magnetic field frequency used respectively [3]. In this work, the effect of field frequency, amplitude and particle core size on the AC hysteresis of two different nanoparticle suspensions (magnetite and maghemite) using the microscope were carefully investigated.

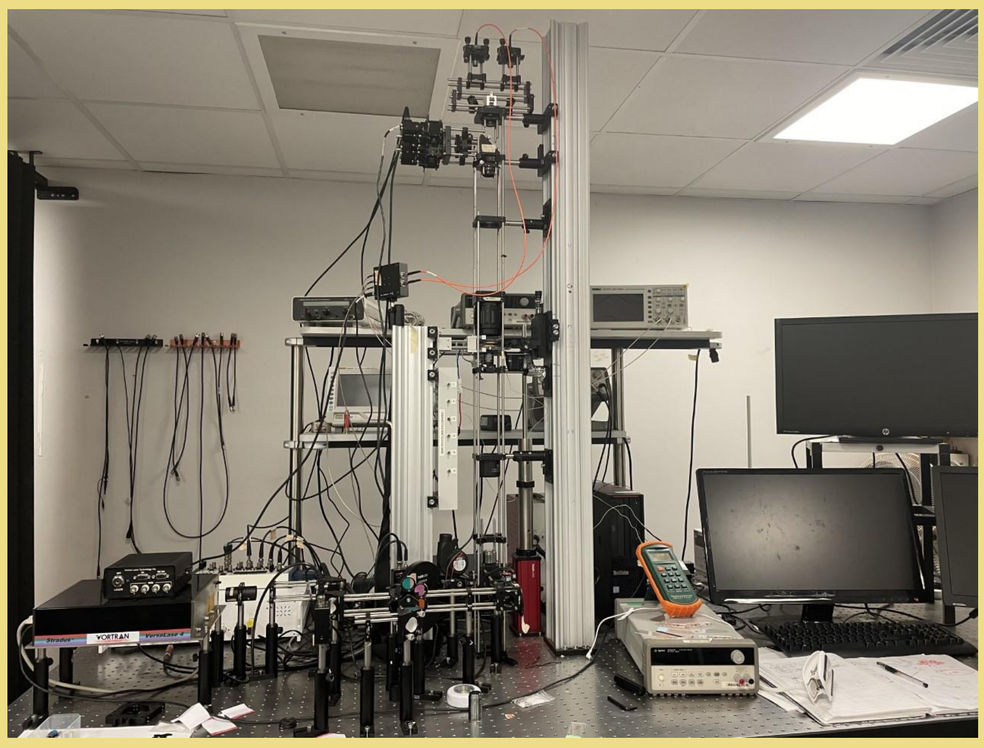

Figure 2. A photo of the home-made microscope.

Conclusion

Above results validate the AC magnetic response measurement of MNPs by this home-made microscope based on magneto-optic methods. Also, effect of field frequency, amplitude and particle core size on the AC hysteresis of two different materials were illustrated. Next step will look at the AC magnetic response of MNPs associated with cells and compare that with the results shown here to investigate the differences.

References

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