Characterization of Two Phase Magnetic Nanoclusters for Oncologic Hyperthermia

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Abstract

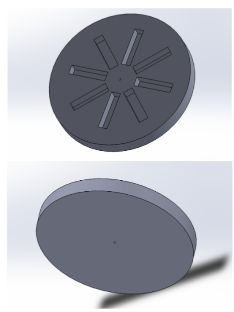
Magnetic nanocluster hyperthermia is an experimental concept applied to an established technique. The concepts of hyperthermia follow the same logic as the body's natural immune response, the fever. By raising the temperature of portions of the body, some harmful cells will die off. Hyperthermia is usually found as an option for treating malignant tumors. Normally, clinical hyperthermia treatments involve microwave radiation of the targeted area. However, this radiation can easily penetrate deeper than needed and radiate outwards, affecting a larger area; both of these events can cause damage to the surrounding tissues.

This issue of precision stands to be solved through the proposed project. Metallic nanoclusters were formed and then exposed to an oscillating magnetic field. This should cause them to vibrate and their friction should raise the temperature to approximately 40C. By localizing the application of the nanoclusters and carefully modulating the magnetic field, the researchers hope to maximize the precision of the hyperthermia.

Over the course of this project, the team has established confluent 3T3 cell lines, fabricated a magnetic field generator, and completed metric testing to assess the viability of these nanoparticles in hyperthermia applications on targeted cells.

Magnetic Field Generator Design

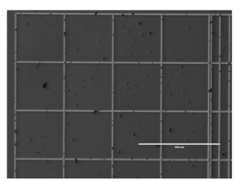
The magnetic field generator (MFG) was designed using SolidWorks to be an interface between the neodymium magnets and the DC motor. It was then 3D printed at the UNH Makerspace using polylactic acid (PLA) filament.



Magnetic Field Generator Model

Nanocluster Synthesis

Following the procedure outlined by Vamvakadis et al.(1), 7.5 mg of both $MnFe_2O_4$ and $CoFe_2O_4$ nanoparticles were added to 6 ml of cyclohexane. This solution was then added dropwise to 30 ml of 19.5 mM sodium dodecyl sulfate (SDS). This was then heated and agitated until all of the cyclohexane had evaporated. This resulted in a solution of ~30 ml of 2.5×10^6 nanoclusters per ml.

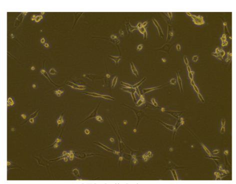


Nanoclusters on a Cytometer

Cell Culture

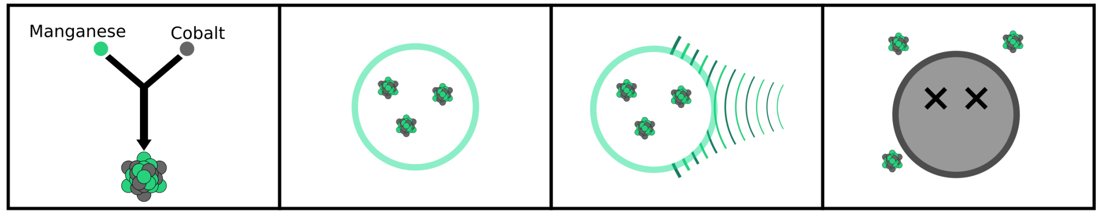
3T3 cells were cultured over the course of a month in a culture of Dulbecco's Modified Eagle Medium (DMEM) with trace amounts of fetal bovine serum (FBS) and a penicillin // streptomycin blend. They were fed every 2-3 days and divided when they reached confluency

Although they have not been used at this point in the project, the cells will be used once the nanoclusters are able to raise the temperature high enough to cause cell death.



3T3 Cell Culture
4 - 13 - 19

Methods



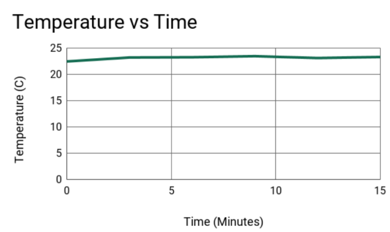
Nanocluster Synthesis | Nanocluster Introduction | Magnetic Oscillation | Cell Hyperthermia

A 12 V DC motor was used to spin a magnetic field generator containing 8 neodymium magnets (1/8" x 1/8" x 3/4"). These magnets were aligned in an alternating fashion, such that, when spun, an alternating magnetic field could be formed at ~ 26 hz. 1ml of MnCo nanoclusters at 2.5×10^6 c/ml were exposed to this magnetic field to force them to oscillate. This oscillation should lead to friction and an increase in temperature of the solution. The temperature was measured using an IR camera at 3 minute intervals.

Results

Over a series of three 15 minute test runs, it was found that the oscillation of the nanoclusters was unable to increase the tempereature of the solution in any meaningful way.

The tests were conducted using a number of MFGs and test volumes.



This lack of heating could be due to any number of test factors. However, the team has narrowed it down to one of three: the magnets being weaker than expected, the concentration of nanoclusters being too low or the nanoclusters being improperly formed.

Future Testing

In order to increase the change in temperature the team will be sythesizing an entirely new batch of nanoparticles, using a sonication probe in lieu of a stir bar. This will both increase yield and quality, while reducing the size distribution of the clusters. There may also be an attempt to purchase more powerful magnets.

Once the nanoclusters are functional to the point of causing apoptosis, there will be two distinct avenues of testing available.

The first, flood testing, will consist of coating an entire plate in nanocluster solution and then exposing it to the magnetic field. This will allow us to determine the degree of control that we have over the temperature and it will allow us to determine how even the temperature distribution is over the area of the plate.

The second type of testing, point testing, will use cultured plates and precisely deposited droplets of nanoclusters. This will allow us to measure the area of apoptosis depending on the concentration and volume of nanoparticle solution.

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(1) Magnetic hyperthermia efficiency and MRI contrast sensitivity of colloidal soft/hard ferrite nanoclusters. Vamvakidis K, Mourdikoudis S, Makridis A, Paulidou E, Angelakeris M, Dendrinou-Samara C DOI: 10.1016