Characterization of magnetic nanoparticles with potential applications in cancer hyperthermia

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• **Hyperthermia** – artificial heating of tumor cells, long studied as an alternative or supplement to chemotherapy
• Externally applied heat damages healthy tissue
• **Magnetic nanoparticles (MNPs)** heated inside the body by the application of an alternating magnetic field
• Triggers cell death with only 4-5 degrees heating

A glioblastoma tumor in the parietal lobe. Metastatic brain cancers could potentially be treated by MNP hyperthermia.

Image: Mayfield clinic
Vector sum is the "magnetization"

MNPs each have a net magnetic dipole from the effects of the internal electronic structure.

The dipoles align in the presence of a field applied by an electromagnet.

There is some tendency for the dipoles to "stick" in one direction after the electromagnet is turned off.
Hysteresis loops

Gives magnetization as a function of applied field and magnetic history ("hysteresis") of the material.

"Sticking" effect in dipoles causes open loop.

Area inside loop is equal to energy loss, most in the form of **heat**, an important design consideration for hyperthermia.

Shape exaggerated for magnetic nanoparticle.
Technical challenges

- Instrumental – large solenoid needed to deliver alternating magnetic fields (kHz), with huge power consumption (MW)
- Biomedical – must be able to target to cancerous cells
  - Biocompatible
- Chemical – narrow size and shape distribution, scalable
Technical challenges – Chemical

– Magnetic, electrostatic, and intermolecular forces may cause clumping and settling out of solution

– A surfactant is needed to stabilize the MNPs by electrostatic or steric repulsion

![Citric acid surfactant](image)
Synthesis

- Three iron oxide nanoparticle systems synthesized at the University of Kentucky by coprecipitation of Fe$^{+3}$ and Fe$^{+2}$ in ammonium hydroxide
- Iron oxide is biocompatible
- “CART” sample reduced in the presence of citric acid at room temperature
- “IS80” sample reduced in the presence of citric at 80°C
- “8080” made by a two step synthesis; first reduced in NH$_4$OH at 80°C then reduced in citric acid
Small changes in synthesis conditions affect bulk magnetic properties!
Torque curves

\[ T = M_T \cdot H \cdot \sin(\Theta_m - \Theta_H) \]

- \( M_T \): total magnetization, the vector sum of the parallel and perpendicular signals
- \( H \): applied field
- \( \Theta_m \): magnetization angle = \( \tan^{-1}(Y/X) \)
- \( \Theta_H \): field angle, determined by physical orientation of magnet

Graph showing the relationship between torque and angle.
IS80 dilution series anisotropy

Black: 1:1
Blue: 1:2
Red: 1:4
Torque curve model fitting

\[ K_1 \sin(\Theta) + K_2 \sin(2\Theta) + K_4 \sin(4\Theta) \ldots \]

- \( K_1 \) = unidirectional anisotropy constant
- \( K_2 \) = uniaxial anisotropy constant
- \( K_4 \) = bidirectional anisotropy constant

We can “pull out” quantitative information about the behavior of magnetic nanoparticles in solution from the model coefficients.
Uniaxial anisotropy energies (K2)

Black: IS80
Blue: 8080
RED: CART
Unidirectional anisotropy energies (K1)

Black: IS80
Blue: 8080
RED: CART
Why are there different signal strengths for equal masses of magnetic material?

- Crystallinity – easy axis of magnetization
- Size effects – fewer surface spins
- Collective behavior – reduces magnetization energy

Left: the crystalline structure of Fe₃O₄
Hysteresis loop model fitting

- **The Langevin Function:**
  \[ M = N \mu \left( \coth \left( \frac{\mu H}{k_B T} \right) - \frac{1}{\frac{\mu H}{k_B T}} \right) \]
  - \( N \) = number of atoms per unit volume
  - \( \mu \) = magnetic moment per particle
  - \( H \) = applied magnetic field
  - \( k_B \) = Boltzmann’s constant
  - \( T \) = measurement temperature

Models magnetic systems that are approximately paramagnetic

Deviation from Langevin function may indicate interparticle interactions
Percentage difference between IS80 dilutions and Langevin

Black: 1:1
Blue: 1:2
Red: 1:4
IS80 hysteresis loops at 5K, 50K, 100K, 200K, and 300K
In review:

• Minor changes in synthesis conditions can affect magnetic properties that change value as a MNP hyperthermia agent

• Collective behavior present in nanoparticles
  -- Relevant to functionalization of nanoparticles
  - Good candidate for SANS study
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Questions?