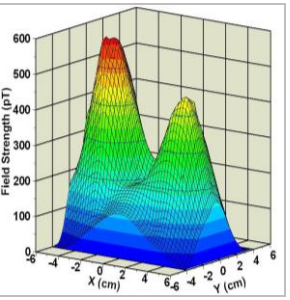
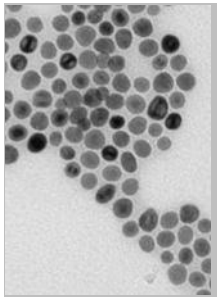
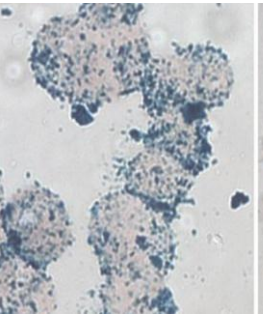
SAND2011-9333 C

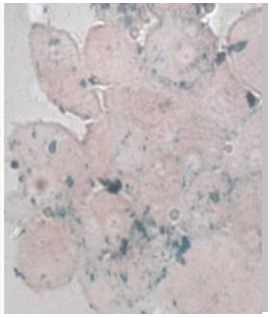
Maximizing the Sensitivity of SQUID Remanence Based Cancer Detection by Optimizing Superparamagnetic Nanoparticles

SAND2011-9333C









Dale L. Huber, E. J. Cooley, T. C. Monson, D. L. Fegan, N. L. Adophi, H. C. Bryant, H. J. Hathaway, D. M. Lovato, K. S. Butler, T. E. Tessier, R. S. Larson, E. R. Flynn

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SENIOR SCIENTIFIC

The University of New Mexico — UNM School of Medicine — At the UNM Health Sciences Center

U.S. DEPARTMENT OF ENERGY

NNSA National Nuclear Security Administration

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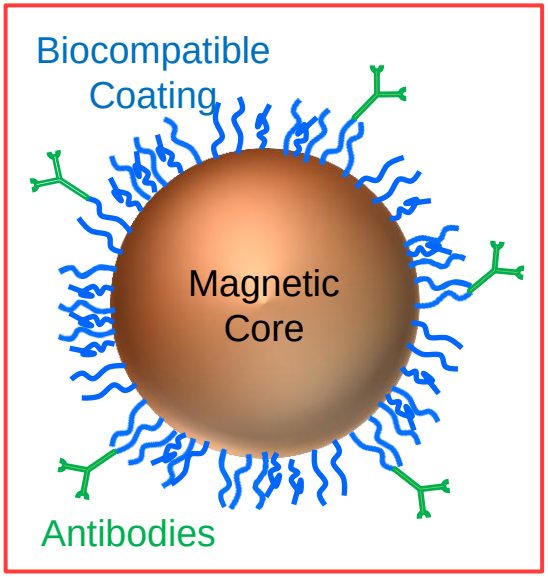
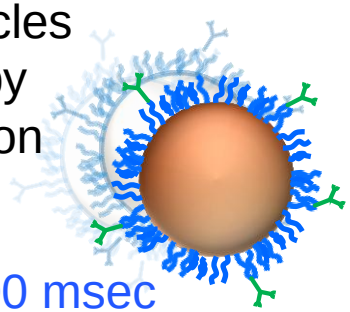
SQUID Relaxometry for Biodetection

- Magnetized superparamagnetic nanoparticles can relax two ways:
  - Néel relaxation, internal motion of the particle spin.
  - Brownian motion, typically much faster than Néel.
- For biodetection, we selectively bind particles to a tissue, magnetize and measure the Néel relaxation of bound particles.
  - Unbound particles relax too quickly to be measured and do not add to background.
  - Detection of a single cancer cell is theoretically possible, since there is no superparamagnetic background in the body.

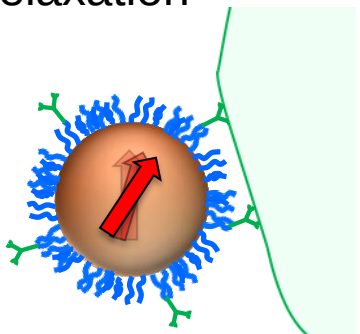


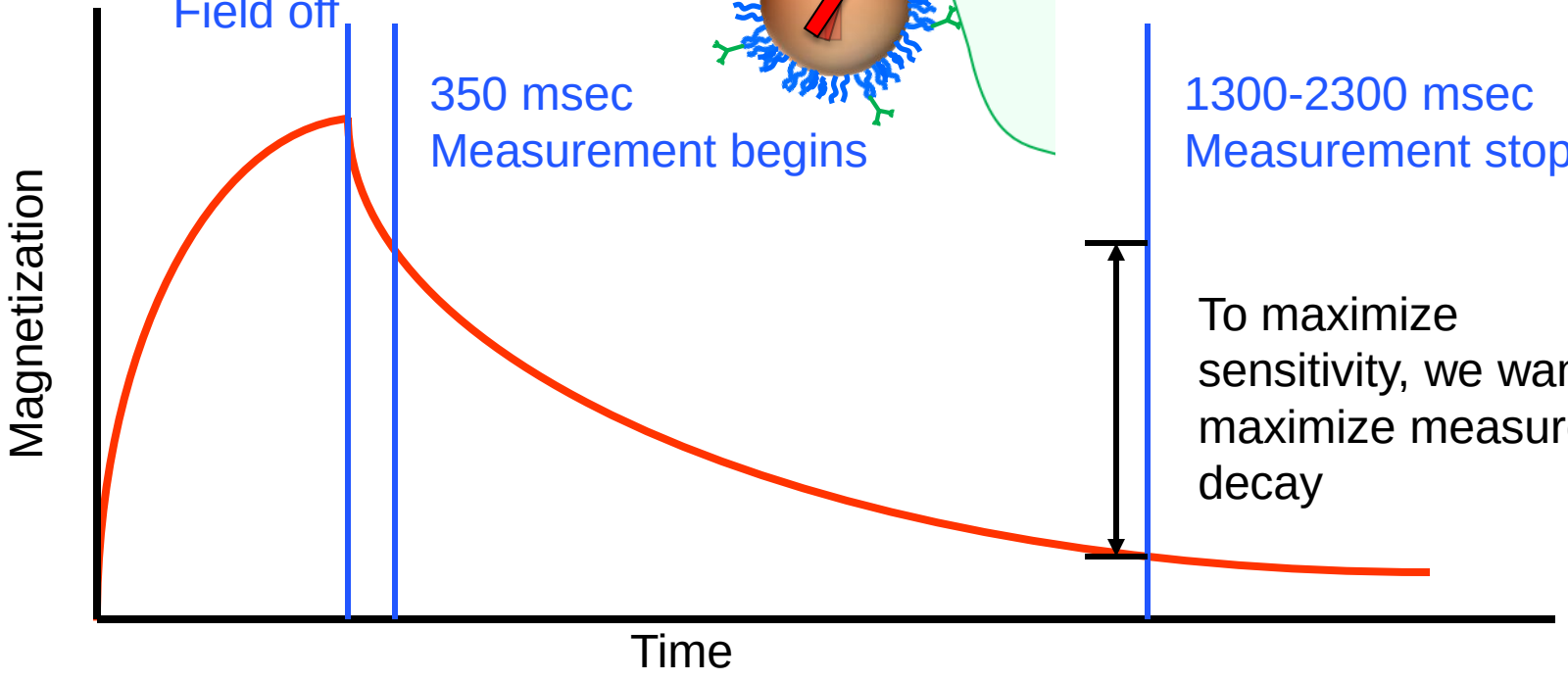
Details of Relaxometry Measurement

Unbound particles relax quickly by Brownian motion



Bound particles relax slowly by Néel relaxation





At 0 msec, a 38G field is applied

Her-2 Is Used as Breast Cancer Marker

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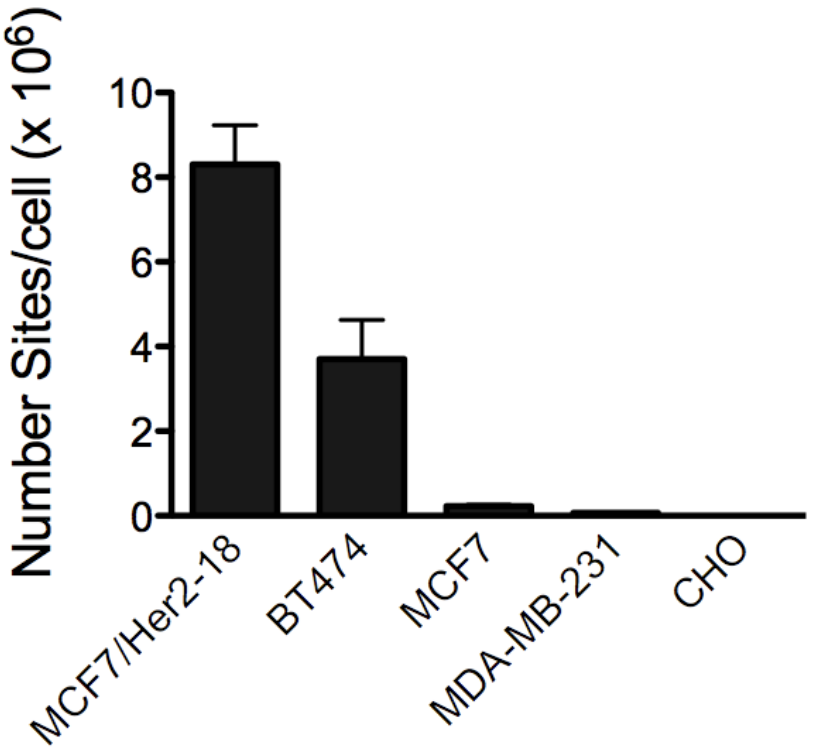
- Nanoparticles are functionalized with anti-Her2 antibody
- Her2 is highly overexpressed in some breast cancers cell lines including MCF7/Her2 and BT474, modestly overexpressed in others (MCF7, MDA-MB), and is absent in the non-breast control (CHO).



Much of this work has recently been published:
Hathaway et al. Breast Cancer Research, 2011, 13:R108
http://breast-cancer-research.com/content/13/5/R108

Comparing Magnetic Detection with Traditional Histology

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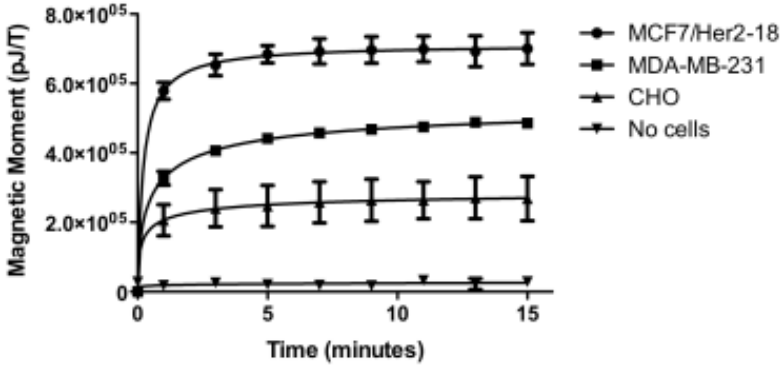
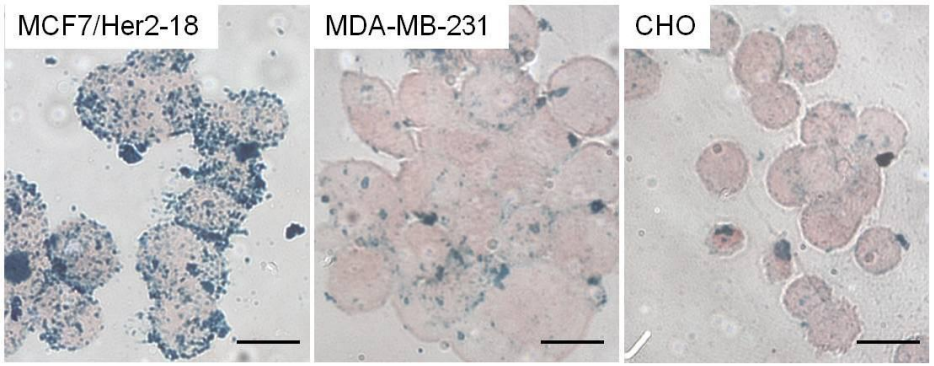
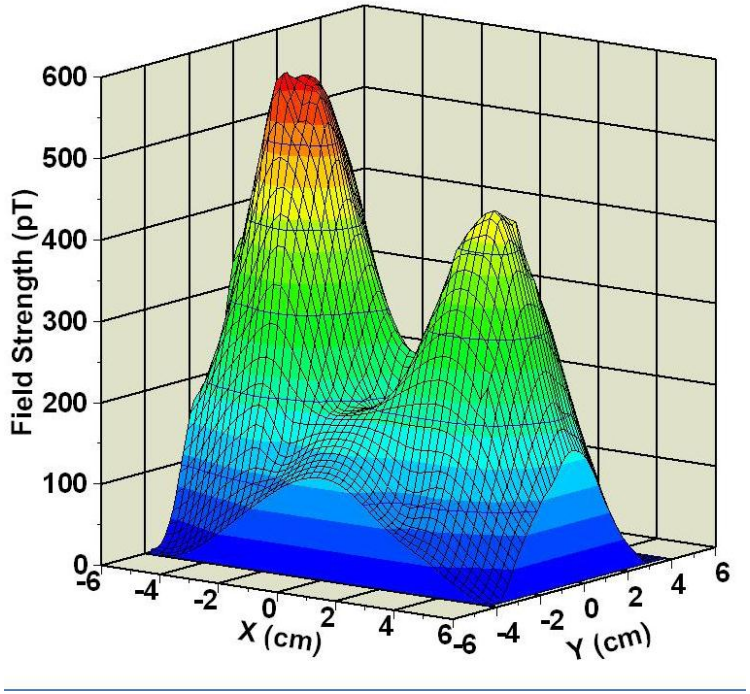
- SQUID relaxometry
  - Moment scales with number of receptor cites.
  - Some non-specific adsorption occurs in absence of receptor.
- Histology
  - Prussian blue staining for Fe^{2+} reveals location of magnetite nanoparticles
  - Prussian blue has enormous amplification allowing nanoparticles to be seen by optical microscopy



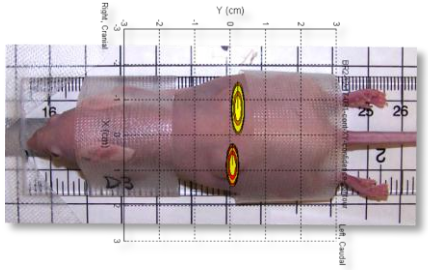


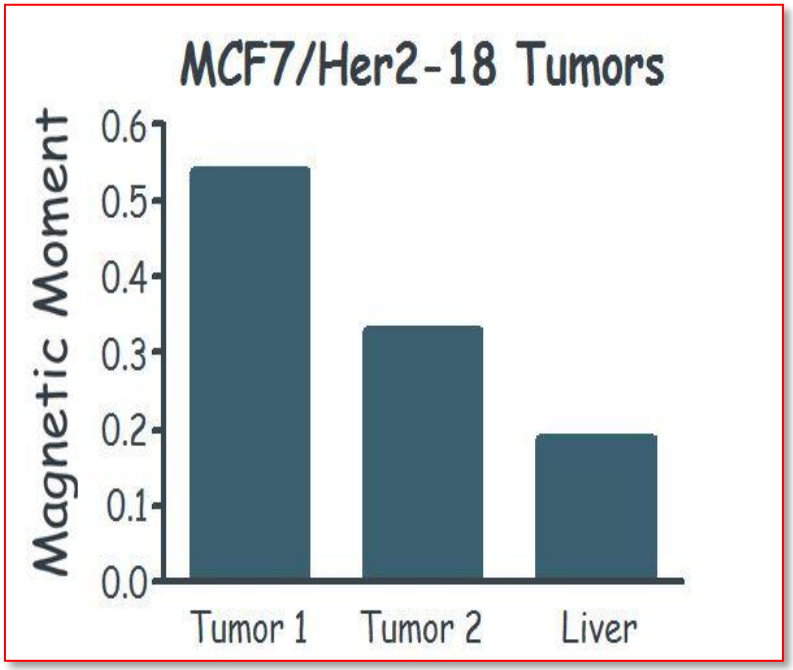
Signal Location in Breast Phantom



In Vivo Detection of Human Breast Cancer in Mouse Model

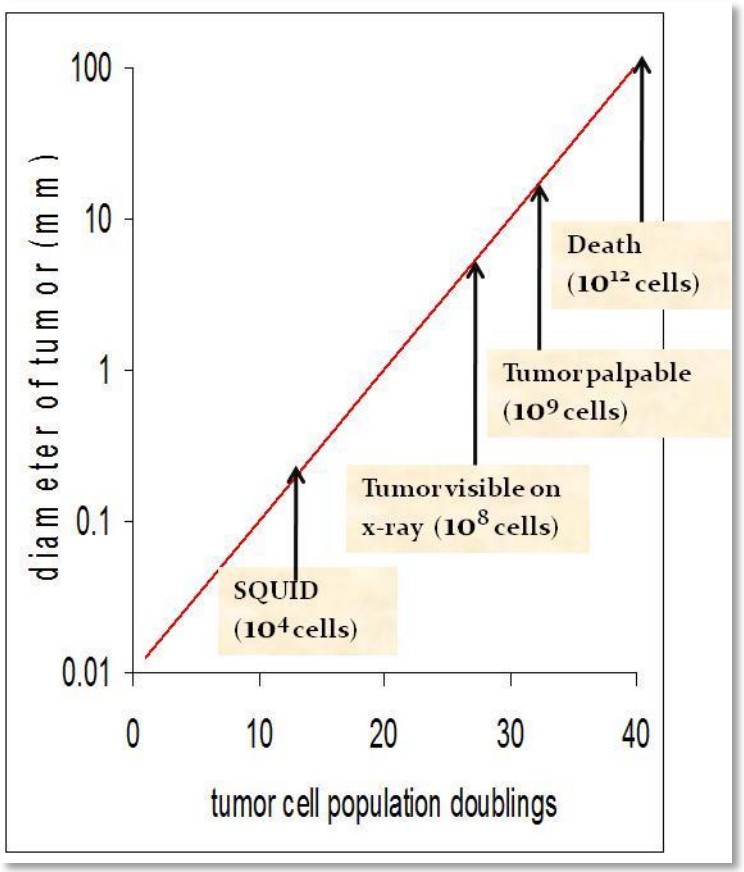
- Nanoparticles are injected into tail vein.
- Moment from two subcutaneous tumors detected.
- Some signal is seen in healthy liver.
- Tumors can be imaged and their size calculated.



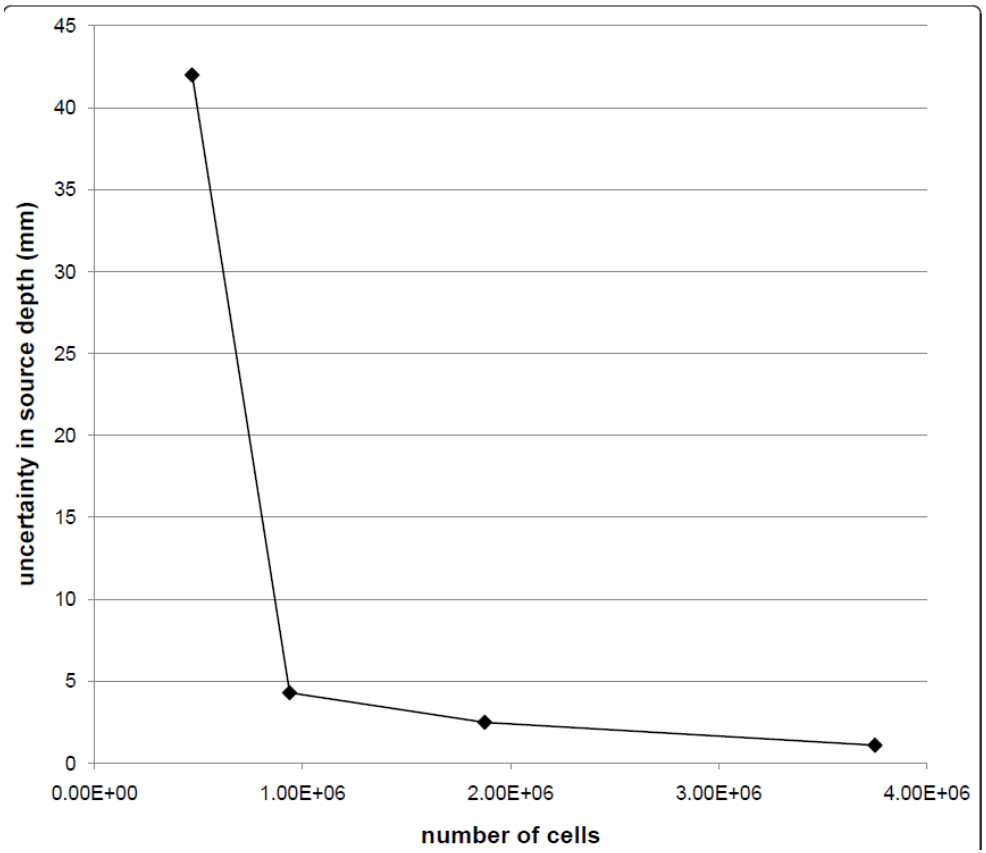


Sensitivity of SQUID Remanence

- Detection Limit

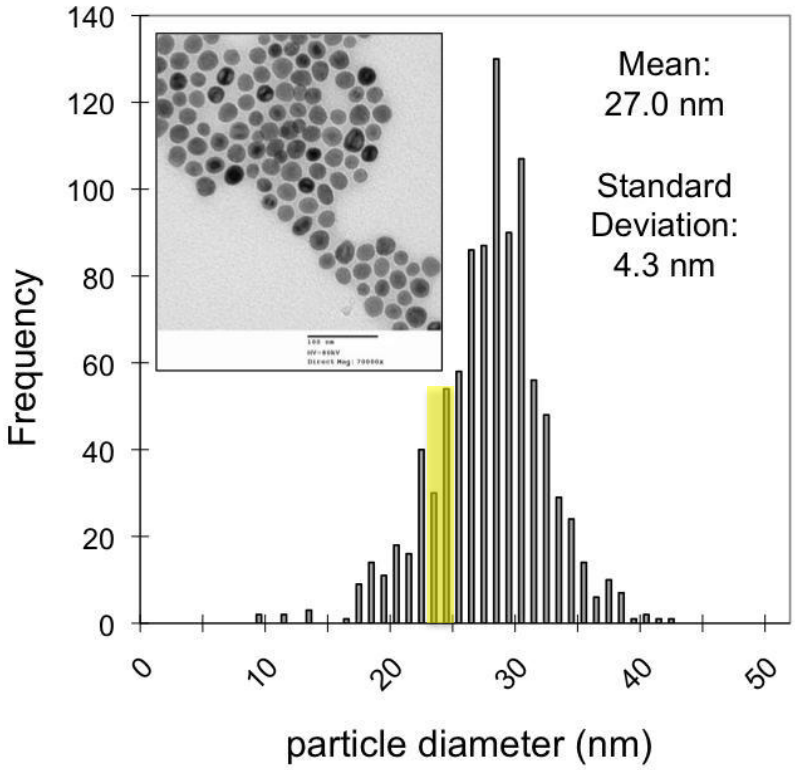


- Imaging Limit



Improving Sensitivity

- Best available commercial particles still leave room for improvement
  - Particle have significant asphericity
  - Mean size is too large
  - Size dispersity could be improved upon.



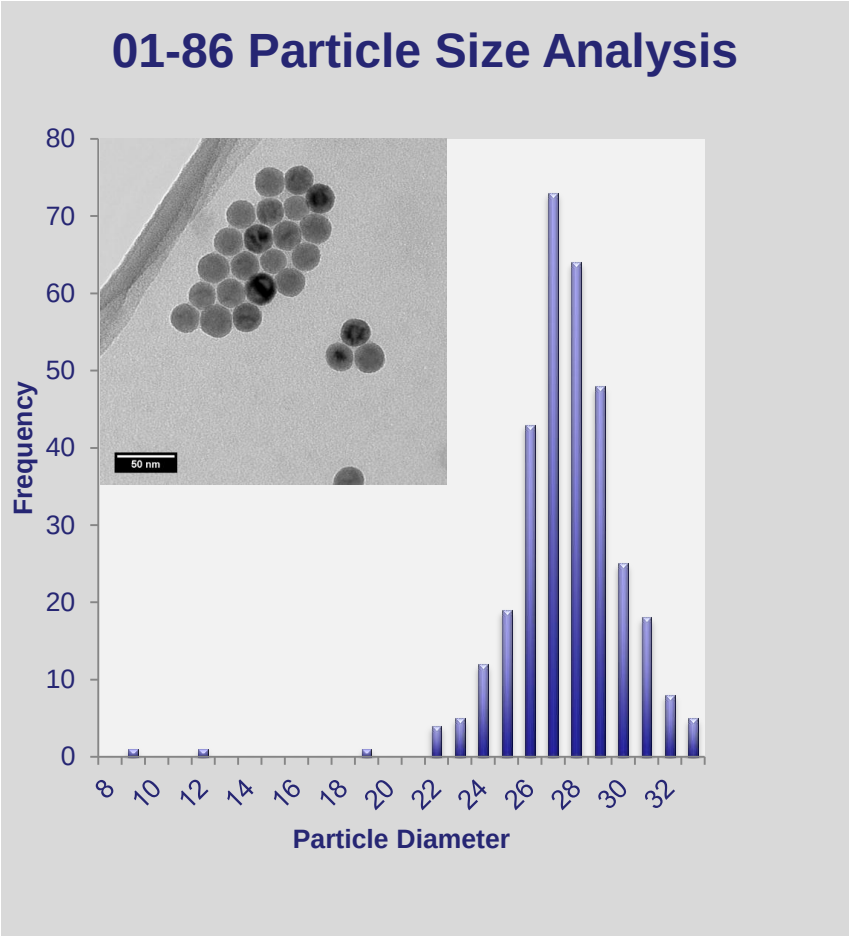
Optimized Particles

Goals:

- Control mean diameter reproducibly
- Minimize size dispersity

Approach:

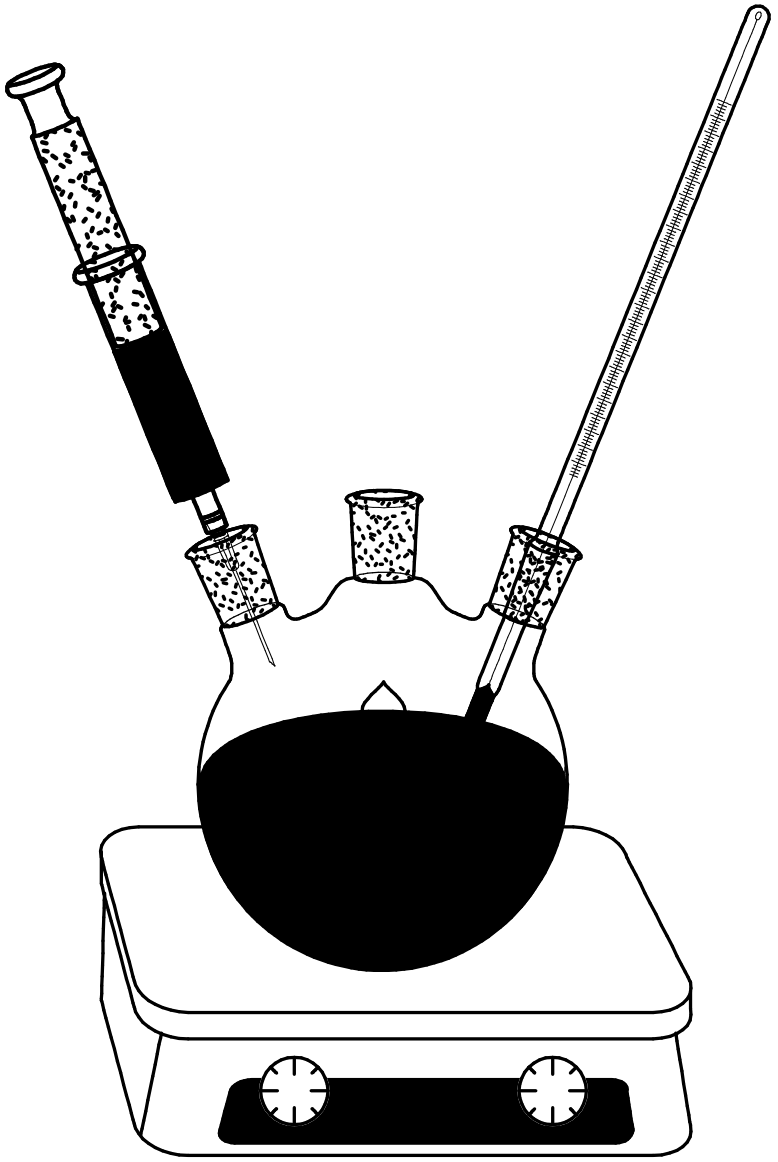
- Developing a new synthesis based upon $Fe(acac)_3$ decomposition
- Improved reproducibility compared to Fe Oleate reactions
- Careful temperature control
- Size control through reaction stoichiometry, not heating rate.



Mean 27.1 nm
Standard Deviation 2.5 nm

Reaction Scheme

- Decompose $Fe(acac)_3$ in high boiling solvent with added surfactant.
- $Fe(acac)_3$ is a crystalline, stoichiometric compound, unlike Fe Oleate.
- We control size with stoichiometry, not heating rates.



Conclusions

- SQUID remanence is already more sensitive than traditional screening approaches.
- Optimizing particle size has the potential for 2 orders of magnitude improvement in detection.
- Minimization of non-specific binding can also have a significant effect.
- A fully optimized particle could theoretically allow detection of a single cancer cell.

Future Work: Microfluidic synthesis

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- Center for Integrated Nanotechnologies (CINT) is developing a microfluidic platform specifically for nanoparticle synthesis.
  - Commercial pumps, fluidic connections
  - Custom temperature controls
  - Custom chips.
  - Focus on size control and surface functionalization

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  cint.lanl.gov