FRONTIERS IN BIOMAGNETIC PARTICLES

June 4-7, 2017

Asheville, North Carolina, USA

CLEMSON UNIVERSITY

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FRONTIERS IN BIOMAGNETIC PARTICLES

June 04, 2017

It is our pleasure to welcome you to the fifth meeting of the Frontiers in Biomagnetic Particles. This three-day meeting will include fantastic talks, presentations, and posters from the leaders in the fields of magnetic nanoparticles for biomedical applications. These experts span a wide range of disciplines, including biology, medicine, chemistry, physics and engineering. In addition to talks, panel discussions, and poster sessions, time is also scheduled for you to explore beautiful Asheville, North Carolina with the new friends and colleagues that we hope you will make at this meeting.

We received many abstracts for this meeting, and the **final program includes 7 invited talks and over 35 contributed talks and many poster presentations.** We are thrilled at the number of distinguished professionals and high quality presentations in the conference. Thanks to you, over the next three days we will hear cutting edge research in the areas of biomedical imaging and sensing, magnetic separations, drug delivery, hyperthermia, and other biomedical applications of magnetic particles.

There are few more perfect places to discuss the cutting edge of magnetic particle research than beautiful Asheville, North Carolina. This 3 day meeting will include fantastic talks, and presentations from the leaders in the field of magnetic nanoparticles for biomedical applications. This conference will bring a diverse group of disciplines together to discuss the frontiers in the characterization and control of magnetic carriers. The program includes invited talks, contributed talks, and posters. A separate session focused on career development for students will also be included. A social event will also be held the evening before the meeting on Sunday June 4, 2017 to greet friends and colleagues, old and new.

We are thankful to all of the contributors to this meeting, including our generous sponsors. We hope that you all have a productive conference and an enjoyable time here in Asheville.

Jennifer Andrew, Mark Bolding, O. Thompson
Mefford Conference Organizers

Sunday, June 4, 2017

18:00	Welcome Reception at The Venue (21 N Market St, Asheville, NC)		

Monday, June 5, 2017

Technical Sessions and Breakfast to be held in main meeting room, The Venue, 21 N Market Street, Asheville, NC

7:30	Breakfast at The Venue		
	Session 0: Opening Remarks (Jennifer Andrew, Mark Bolding and Thompson Mefford)		
8:00			Introduction to Meeting
	Session 1: Imaging and Assay (Chair: Thompson Mefford)		
8:15	**Pothayee**	**USA**	**In vivo imaging of activity-dependent neural precursor cell migration using magnetic microparticle-assisted MRI**
8:55	Vreeland	USA	Specific detection of HER-2 positive tumors in mice using superparamagnetic
9:15	Rivas	Spain	Magnetic Lateral Flow Immunoassay reader for fast, cheap and quantitative analytical screening
9:35	Levy	USA	Magnetomotive Ultrasound Imaging using Super-Paramagnetic Iron Oxide as a Contrast Agent
9:55	Barrick	USA	Magnetomotive optical coherence tomography of endogenous magnetite crystals in magnetotactic bacteria
10:15	Coffee Break		
10:35	**Bakuzis**	**Brazil**	**Monitoring, imaging and treating cancer with multifunctional magnetic nanocarriers**
11:15	Moreland	USA	Low field magnetic imaging agents
11:35	Bolding	USA	MRI-visible Nanoclusters with Elongated Circulation Time and Enhanced Tumor Accumulation
11:55	Panel Discussion with Speakers from Session 1		
12:05	Lunch at the The Venue		
	Session 2: MagMED/Hyperthermia (Chair: John Moreland)		
14:00	**Telling**	**UK**	**Towards an understanding of heating effects and magnetisation response of magnetic nanoparticles associated with live cells**
14:40	Hilt	USA	Magnetic Nanoparticles and Nanocomposites: Tuned Surface Reactivity
15:00	Engelmann	Germany	Hyperthermic Effect of Intra- & Extracellular Magnetoliposomes on Pancreatic Tumor Cells
15:20	Fellows	USA	Glycoconjugate-Functionalized Magnetic Nanoparticles: A Tool for Selective Killing of Targeted Bacteria Via Magnetically Mediated Energy Delivery.
15:40	Break (Poster presenters please hang your poster)		
16:00	Anderson	USA	Why do magnetic nanoparticles form messy clumps? Taking into account the bridging or sticking of ligands
16:20	Livesey	USA	Calculating the variation in hysteretic energy produced inside
16:40	Dhavalikar	USA	Combined MPI - MFH: A promising theranostic platform

17:00	Evans	USA	The Effect of Nanoparticle Concentration on Heating in Magnetic Nanoparticle
17:20	Panel Discusion with Session 2 presenters		
18:00	Poster Session at the The Venue		
19:30	Dinner in town with friends new and old		

Tuesday, June 6, 2017

7:00	Breakfast at the The Venue		
	Session 3: Career Panel - Carlos Rinaldi, Erika Vreeland, Nikorn Pothayee (Chair: Mas Crawford)		
8:00	Career Panel at the The Venue		
	Session 4: Delivery (Chair: Jennifer Andrew)		
9:20	**Pierre**	**USA**	**Magnetoluminescent nanoparticles - combining the dual power of time-resolved luminescence and MRI contrast agents of lanthanide complexes**
10:00	Nakagawa	Japan	Drug-release controlling nanoparticles under exposure to magnetic fields
10:20	Erb	USA	Penetrating Porous Tissue with Magnetic Targeting
10:40	Coffee Break		
11:00	**Tsourkas**	**USA**	**Gold and superparamagentic iron oxide-loaded polymeric micelles for imaging, radiotherapy and the prediction of therapeutic response**
11:40	Panel Discusion with Session 4 presenters		
12:00	Lunch at the The Venue		
	Session 5: Synthesis (Chair: Emilie Secret)		
13:40	**Dravid**	**USA**	**Theranostic Magnetic Nanostructures (MNS) in Biomedicine**
14:20	Davis	USA	Quantitative Measurement of Ligand Exchange on Iron Oxides via Radioanalytical Techniques
14:40	Uhl	USA	Synthesis of Composite Magnetoelectric Particles via Electrospraying for Manipulation of Biologically Relevant Electric Fields
15:00	Break		
15:20	Budi	USA	Tailorable anisotropy in electrospun magnetoelectric nanocomposites
15:40	Hafeli	Canada	Microdroplet Producing Co-Flowing Device for the Generation of Magnetic Microspheres as Embolic Agents for Large Vessels
16:00	Rinaldi	USA	Laying to Rest the Magnetically Dead Layer in Magnetic Nanoparticles
16:20	Panel Discussion with Speakers from Session 2		
18:30	Banquet and Annoucement of Poster Winners		

Wednesday, June 7, 2017

7:30	Breakfast at the The Venue		
	Session 6: Particle Manipulation and Control (Chair: Bolding)		
8:30	**Friedman**	**USA**	**Comparison of different strategies for active transport of magnetic particles in biological fluids and tissues**
9:10	Engelhard	USA	Design and initial characterization of a novel tissue culture tray for the study of magnetically-induced rotary traction of iron oxide nanoparticles
9:30	Chavez	USA	Magnetic field-directed self-assembly and chaining in multiferroic Janus nanofibers
9:50	Unni	USA	Understanding Magnetic Nanoparticle Dynamics in Synovial Fluid Analogues
10:10	Faust	USA	Aligning Alginate-Hydroxyapatite Biocomposites with Magnetic Nanoparticles for Bone Graft Applications
10:30	Coffee Break		
10:50	Monsalve	USA	Poly(Lactic Acid) Magnetic Microparticle Synthesis, Surface Functionalization, and Protein Isolation
11:10	Todd	USA	Correlation of cell volume and toxicity with nanomaterial endocytosis
11:30	Secret	France	Bio-functionalized magnetic nanoparticles for remote control of differentiation and oriented growth of neuronal cells
11:50	Mao	USA	Biocompatible and Label-Free Separation of Circulating Tumor Cells in Ferrofluids
12:10	Panel Discusion with Session 6 presenters		
12:30	Lunch and Closing Remarks at the The Venue		
	Session 7: Conference Closing (Chairs:Jennifer Andrew, Mark Bolding and Thompson Mefford)		

Poster Session: Monday, June 5, 2017

18:00	Poster Session	The Venue	
Poster #	Presenter	Country	Title
1	Anker	US	Multifunctional magnetic nanoparticles for sensing and imaging
2	Chapman	Us	Magnetite Functionalization of Silica-Overcoated Gold Nanorods via Controlled Heteroaggregation
3	Lanier	US	Evaluating the Potential of Commercially Available Magnetic Nanoparticles for Hyperthermia
4	Livesey	US	Interacting magnetic nanoparticles under applied magnetic fields
5	Mair	US	Multi-segmented Magnetic Rods for Loading and Releasing Payloads
6	Oberdick	US	Magnetization Reduction and Domain Formation in Magnetite Nanoparticles
7	Pan	US	Crack Paths in Anisotropic Biomimetic Composites Textured by Magnetic Nanoparticles
8	Rao	India	Nano silver ferrite, a better tool of Target drug delivery than
9	Rich	US	MRI guided drug delivery for location specific neuromodulation
10	Rivera	US	Magnetic nanoparticle thermal therapy to induce mitotic
11	Samia	US	Reactive Extrusion Strategies to Fabricate Magnetite–Polyethylene
12	Sandler	US	Systematic Investigation of Cobalt Doped Ferrites for Increased Energy Conversion in
13	Savliwala	US	Quantitative Exploration of Iron Oxide Nanoparticle Purification Through
14	Singh	US	Magnetically templated hydrogels for peripheral nerve injury repair
15	Todd	US	Finite element analysis of a magnetic cell separation device:
16	Warnock	US	Design and Optimization of a Magnetic Separation Chamber for Filtration of
17	Zando	US	Using Magnetic Nanoparticles for the Design of Calcium
18	Zhao	US	Brownian dynamics simulations of dipolar interacting magnetic nanoparticles

Abstracts

Abstracts for Oral Presentations are provided in the order given, followed by abstracts for Poster Presentations in Alphabetical order.

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17:20	Panel Discusion with Session 2 presenters		
18:00	Poster Session at the The Venue		

In vivo imaging of activity-dependent neural precursor cell migration using magnetic microparticle-assisted MRI

N. Pothayee[1*], G. Zabow[2], S. Dodd[1], J. Moreland[2], A. Koretsky[1]

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[2]Physical Measurements Laboratory, National Institute of Standards and Technology (NIST), Boulder, Colorado 80305, USA.

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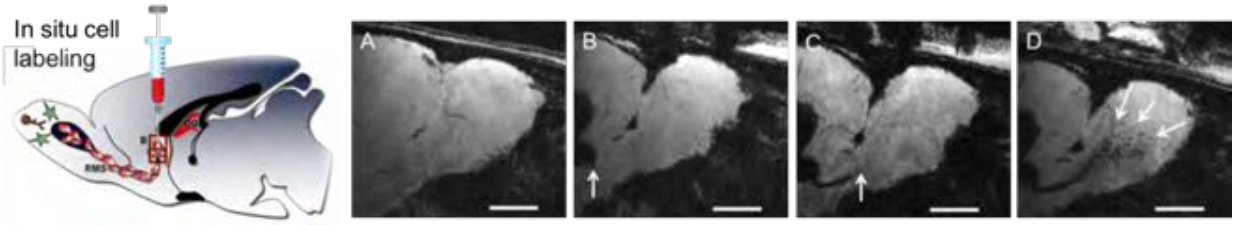
Neural precursor cells or neuroblasts are produced by stem cells in the subventricular zone (SVZ) and migrate along the rostral migratory stream (RMS) to the olfactory bulbs (OB) throughout life. In the OB, these adult born neurons either die or replace existing olfactory interneurons, playing a critical role in the stabilization of OB neural circuitry. Various aspects of the addition of new neurons into the olfactory bulbs have been extensively investigated. However, insight into the dynamics of cell migration rate of migrating neuroblasts has been challenging due to a lack of in vivo tools to monitor the cells in live animals. In this work, using magnetic resonance imaging and in situ labeling of neuroblasts with magnetic microparticles (potent contrast agents), we found that olfactory activity levels alter the migration rate of neuroblasts along the RMS and dictate the extent of integration of these cells into the olfactory bulb.

Another aspect of our work is to investigate the possibility of to make the detection of cells as robust as possible. Our current effort is to develop more uniform particles with higher iron content. These microfabricated particles offer 10- to 100-fold increased MRI T2* contrast. Here we report possibility of using these high magnetic moment microparticles for in-vivo application for MRI tracking of individual cell migration through a rat brain.



Intraventricular injection of MPIOs near SVZ allow migrating neuroblasts to be labeled and detected with MRI in live rats. A) shows MRI image before injection of MPIO. Panel A represents MRI image of rat before MPIO injection. B-D) represent the same animal after injection of MPIOs into the lateral ventricle at different time points, with B = 4 hours, C = 18 hours, and D = 120 hours post-injection. MPIO(+) neuroblasts can be seen as a hypointense track migrating along the RMS into the OB (indicated by arrows). Scale bar = 2 mm.

Specific detection of HER-2 positive tumors in mice using superparamagnetic relaxometry (SPMR)

Erika C. Vreeland[1], Kayla E. Minser[1], Caroline L. Weldon[1], Andrew Gomez[1], Todor Karaulanov[1], William H. Anderson[1], Christopher P. Nettles[1], Dale L. Huber[3], Helen J. Hathaway[2], Christine Warden[1], Blake A. Sims[1], and Giulio Paciotti[1*]

[1]Imagion Biosystems, Inc., Albuquerque, NM, USA
[2]University of New Mexico Health Sciences Center and University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, USA
[3]Center for Integrated Nanotechnologies, Sandia National Laboratories, Albuquerque, NM, USA
**Corresponding email: Giulio.Paciotti@imagionbio.com*

Superparamagnetic Relaxometry (SPMR) is a non-invasive technique that utilizes superconducting quantum interference device (SQUID) detectors to localize and quantify the magnetization of superparamagnetic iron oxide (Fe_3O_4) nanoparticles (NPs) specifically bound to cancerous tumors. In an SPMR measurement, polyethylene glycol (PEG) coated NPs are functionalized with a tumor-targeting monoclonal antibody and injected intravenously. NPs that reach and bind to the target tissue are measured by the MRX™ instrument, while unbound nanoparticles, such as those freely circulating in the bloodstream, are not detected.

Here, we demonstrate the use of SPMR for specific detection of HER2 positive tumors in mice using long-circulating anti-HER2 antibody conjugated PrecisionMRX® NPs in vitro and in vivo. The stability and biofunctionality of conjugated nanoparticles were measured by dynamic light scattering, gel electrophoresis, and ELISA. Specific binding of the nanoparticles was defined by the ability of the native HER2 antibody to competitively block the binding of the anti-HER2 conjugated NPs to HER2 positive cells in vitro and in vivo. Nude mice with xenograft BT474 tumors were intravenously injected with anti-HER2 NPs at a dose of 20 mg/kg of body mass, while 'competition' mice were injected with native anti-HER2 up to 24 hours prior to injection of anti-HER2 NPs. Mice were measured individually on the MRX™ instrument over 4-hours. At 4 hours, blood, tumor, and organs were harvested and analyzed for SPMR signals and anti-HER2 content.

SPMR measurements of mice injected with anti-HER2 NPs were detected in the tumor and liver (the site of NP elimination), as illustrated in Fig. 1. Conversely, in mice dosed with native antibody prior to anti-HER2 NP injection, only the tumor signal was reduced. These results suggest targeted delivery of conjugated NPs to HER2 positive tumors and the utility of SPMR for the sensitive and specific detection of cancer in vivo.

This work was performed, in part, at the Center for Integrated Nanotechnologies, an Office of Science User Facility operated for the U.S. Department of Energy (DOE) Office of Science. Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.

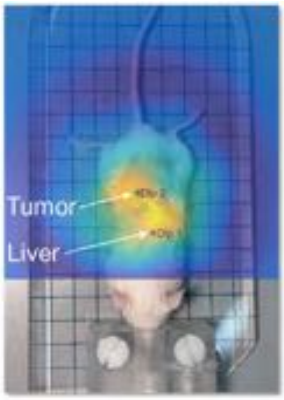


Figure 1. MRX dipole map showing the locations of a BT474 tumor and the liver following injection of anti-HER2 NPs.

Magnetic Lateral Flow Immunoassay reader for fast, cheap and quantitative analytical screening

M. Rivas[1,*], J.C. Martínez-García[1], J. A. García[1], D. Lago-Cachón[1], A. Moyano[1,2], M. Salvador[1], M. Oliveira-Rodríguez[3], M.C. Blanco-López[2]

[1]Dpto. de Física, Universidad de Oviedo, Campus de Viesques, 33204-Gijón, Spain.
[2]Dpto. de Química Física y Analítica, Universidad de Oviedo, C\Julián Clavería 8, 33006-Oviedo, Spain.
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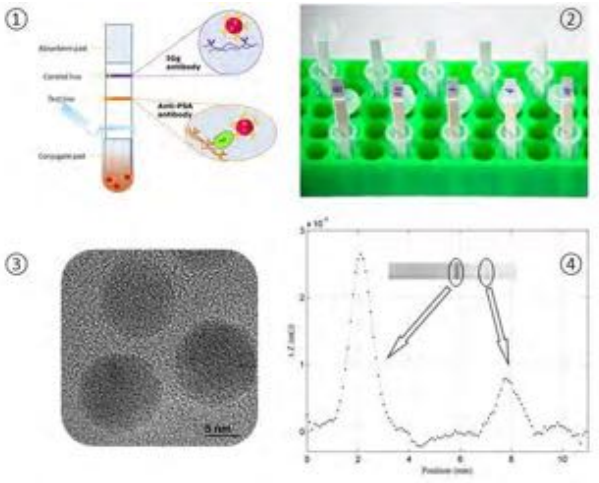
Lateral Flow Immunoassays (LFIA) are based in nitrocellulose strips on which a test line consisting of a reagent is immobilized to specifically capture the bio-analyte contained in the fluid sample which flows along the strip by capillary; the bio-analyte is labelled prior to the flow by some recognition probe (See Fig. 1 and 2). They are often designed for applications in which a presence/absence response is desired. In this case a naked-eye inspection of the test-line is sufficient, which results in an extremely user-friendly, cheap and rapid test, especially suitable for use at point-of-care/need.

However, for many applications quantification of the analyte is a necessity which should be addressed without adding excessive complexity to the method, eluding compromising its main advantages regarding costs, duration, and portability. This challenge leads us to the use of magnetic nanoparticles as labels, which produce a magnetic perturbation to be quantified by the appropriate magnetic sensor. In this work we are profiting from the most significant property of magnetic nanoparticles in superparamagnetic state: the spontaneous oscillation of their magnetic moments due to thermal excitation (Fig. 3 shows a HRTEM image of the Fe_3O_4 particles used for this test). The designed sensor consists of a conducting micro-track carrying radiofrequency current which is sensitive to the rapidly-changing magnetic field produced by the particles. Fig. 4 shows the increase of impedance measured for the micro-track when scanning a magnetic LFIA (performed with a Prostate Specific Antigen PSA concentration 10 ng/mL). The magneto-inductive LFIA reader was tested on PSA levels determination in the range of clinical interest (0-10 ng/mL) obtaining a resolution of 50 pg and a limit of detection of 0.25 ng/mL.



① Scheme of a LFIA; ② Performance of some LFIA of this work; ③ HRTEM micrography of the Fe_3O_4 used as labels; ④ Scanning of a PSA LFIA.

Magnetomotive Ultrasound Imaging using Super-Paramagnetic Iron Oxide as a Contrast Agent

Ben Levy[1,*], Murad Hossain[2], Caterina M. Gallippi[2], Amy L. Oldenburg[1,2,3]

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[2]UNC/NCSU Joint Department of Biomedical Engineering, The University of North Carolina at Chapel Hill, Chapel Hill NC, 27599, USA

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In recent years, nanoparticles have emerged as exciting new contrast agents in a variety of biomedical imaging applications, but ultrasound is not able to contrast nanoparticles due to their extremely-low acoustic scattering. To overcome this hurdle, our lab has developed a Magnetomotive Ultrasound (MMUS) system capable of contrasting Super-Paramagnetic Iron Oxide (SPIO) particles using a commercially-available ultrasound scanner. Our system utilizes two electromagnets, driven to create a proportional sinusoidal displacement in any SPIOs in the imaging region. Ultrasound RF data is collected first with the magnets on, and then again when off to facilitate background subtraction. Then we employ our phase and frequency-locking algorithm to determine which portions of the image exhibit magnetomotion. One application of MMUS that we are pursing is detection of pre-occlusive arterial thrombi. We have shown that platelets which have been loaded with SPIOs and placed within a human tissue-mimicking phantom can be successfully imaged using our MMUS system.[1] Since platelets congregate at thrombi, this technique could be used in the future to detect clots that other imaging modalities cannot detect.

For applications such as targeted thrombosis imaging, the stiffness and size of detected regions will be clinically relevant. We suspect that the MMUS signal contains information about the volume of SPIOs in the imaging region, and the region's elastic modulus. To test this, we built a series of gelatin tissue-mimicking phantoms with SPIO-laden inclusions hidden beneath a simulated artery – a tube through which water is pumped peristaltically at flow rates similar to those found in the human carotid artery. This allowed us to study the effect of simulated pysiological motion from the pulsatile pump on the MMUS signal. Graphite was added to the gelatin to give the phantoms physiologically relevant acoustic attenuation, and alcohol was added to adjust the speed of sound to 1540 m/s. Different gelatin concentrations were used to vary the stiffness over the range found in human tissue. We collected MMUS data with varying inclusion size, elastic modulus, and flow rate.

Our results indicate high MMUS signals for iron concentrations of 2.2 mg/mL, which we estimate may be a level of iron labeling attainable in thrombi *in vivo*. MMUS signals increased for both larger and softer inclusions, as expected. However, we were surprised to find minimal MMUS signal dependence on flow rate, despite increased mechanical vibration at high pump speeds. This suggests that our system is robust to physical motion such as blood flow. These results pave the way for our next step toward clinical applicability in which we will seek to image induced thrombi in *ex vivo* porcine arteries.

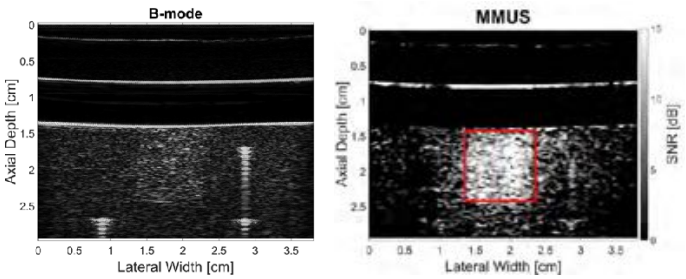

Fig. 1. B-mode (left) and magnetomotive (right) ultrasound images of an SPIO-laden inclusion below a simulated artery with water flowing at 300 mL/min in a gelatin tissue-mimicking phantom. The inclusion is revealed only in the MMUS image. A red outline indicates the known position of the inclusion.

[1] A.G. Pope, ... A.L. Oldenburg, Phys. in Medicine & Biology **58**, 7277 (2013).

Magnetomotive optical coherence tomography of endogenous magnetite crystals in magnetotactic bacteria

Jessica Barrick[1*], David A. Ernst[2], Kenneth J. Lohmann[2], Amy L. Oldenburg[1,3]

[1]Department of Physics & Astronomy, University of North Carolina-Chapel Hill, Chapel Hill, NC 27510 USA
[2]Department of Biology, University of North Carolina-Chapel Hill, Chapel Hill, NC 27510 USA
[3]Biomedical Research Imaging Center, University of North Carolina-Chapel Hill, Chapel Hill, NC 27510 USA
*E-mail: barrickj@email.unc.edu

Magnetomotive optical coherence tomography (MMOCT) is an emerging imaging technique designed to use magnetic iron oxides (MIOs) as contrast agents for optical coherence tomography (OCT) [Oldenburg, *Opt. Lett.* 2005]. OCT is a non-invasive, real-time, ultrahigh-resolution biological imaging modality which produces 2D cross-sectional images from the light back-scattered from the sample. MMOCT is used to specifically contrast objects of interest which have been labeled with MIOs. An electromagnet (placed above or below the sample) produces a sinusoidally varying magnetic field, inducing axial vibration of the MIOs. The movement of the MIOs couples to the highly-scattering surrounding tissue, which is detected as a periodic optical phase shift by the MMOCT system.

Previous MMOCT work has characterized the behavior of exogenous MIOs and their use as contrast agents for *in vivo* small-animal imaging. MMOCT has never been used to image endogenous MIOs. While many species are suspected to contain endogenous magnetite crystals, here we study a species of anaerobic bacteria that contain chains of magnetite crystals (see Fig.1) used for navigation. As a first step toward using MMOCT to search for endogenous magnetite crystals in other animals, we have conducted MMOCT imaging of these magnetotactic bacteria. This will inform our knowledge of how much MMOCT signal can be expected from magnetite crystals in the bacteria, which form chains on the order of hundreds of nanometers in length.

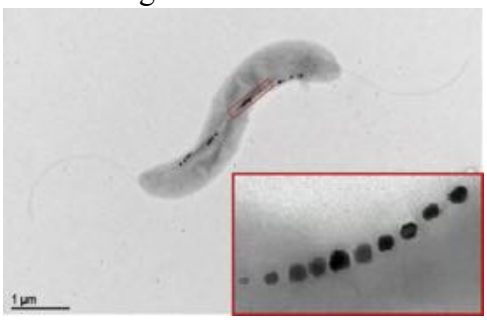

Fig. 1. TEM images of magnetite crystal chains in magnetotactic bacteria (strain AMB-1).

First, we employed tissue phantoms to characterize the MMOCT system's sensitivity to low concentrations of MIO. Phantoms were comprised of silicone containing homogeneous distributions of varying concentrations of Fe_3O_4 nanopowder (Sigma Aldrich, No. 544884). PDMS is diluted with non-cross linking silicone oil in order to match the elastic modulus of soft tissue. We add 4.1 mg/g TiO_2 micro-particles (Sigma Aldrich, No. 22427) to mimic the optical scattering properties of human skin. This platform allowed us to explore different MMOCT data acquisition protocols to optimize the Fe sensitivity of the system, which is currently 200 µg/g.

To image magnetotactic bacteria, we concentrate the bacteria in solution by applying a strong magnetic field. We then centrifuge them, fix them with formaldehyde, embed them in agarose gel containing TiO_2 powder as a light scattering agent, and then perform MMOCT imaging. Preliminary results suggest that there is a significant MMOCT signal from the bacteria compared to control ($p=0.0017$).

Monitoring, imaging and treating cancer with multifunctional magnetic nanocarriers

A. F. Bakuzis[1,*]

[1] *Federal University of Goiás, Institute of Physics, 74690-900, Goiânia-GO, Brazil*

*E-mail: bakuzis@ufg.br

Magnetic nanostructures are of great importance in health issues due to functional tools in labelling, tracking, magnetophoresis, drug delivery, and therapy, among others. A great effort has been made to apply these nanostructures to treat cancer. In particular, magnetic hyperthermia, which consists of heat dissipation by a magnetic material when exposed to an alternating magnetic field, plays an important role in this fight. In this talk we show several results of our group in some of the most important areas of magnetic hyperthermia, namely heat generation, monitoring heat deposition and determining in vivo heat transfer. In vitro and in vivo (intratumoral and systemic delivery) results will be discussed and some cases of complete regression shown. Most of the results will focus on data from a multifunctional magnetic nanocarrier construct developed for long blood circulation time, real-time nanoparticle monitoring, cancer imaging, drug delivery, photothermal therapy and magnetic hyperthermia. Fluorescence molecular tomography (FMT) and alternating current biosusceptometry (ACB) are used for nanoparticle monitoring, biodistribution and intratumoral nanoparticle accumulation due to EPR effect. The kinetics of nanoparticle delivery efficiency are determined and discussed using a three-compartment model. Low field amplitude in vivo magnetic hyperthermia data, within Atkinson's criteria, is presented and some cases of complete or partial regression are compared and discussed using numerical simulations of the bioheat equation. The simulations are performed using the real nanoparticle three-dimensional distribution obtained from FMT, the real tumor shape using ultrasound three-dimensional reconstruction strategy (validated through comparison with microCT data) and animal body photogrammetry approach.

Low field magnetic imaging agents

John Moreland
National Institute of Standards and Technology, Boulder, CO 80303, USA

There are new opportunities for the application of magnetic thin-film structures and nanomaterials as smart tags for in-vivo medical imaging applications. Both microfabrication and chemical synthesis methods have advanced to the point that is possible to mass produce magnetic smart tags with specific geometries, materials, and unique gyromagnetic characteristics. The possibilities for applications of magnetic smart tags is expanding given the immergence of ultra-low field magnetic resonance imaging (ULF MRI) as viable medical imaging modality. I will discuss some of the challenges and prospects for "fusing" magnetodynamic phenomena with ULF MRI.

MRI-visible Nanoclusters with Elongated Circulation Time and Enhanced Tumor Accumulation

Jennifer Sherwood,[1] Megan Rich,[2] Kira Lovas,[1] Jason M. Warram,[3] Mark S. Bolding,[2] and Yuping Bao[1]

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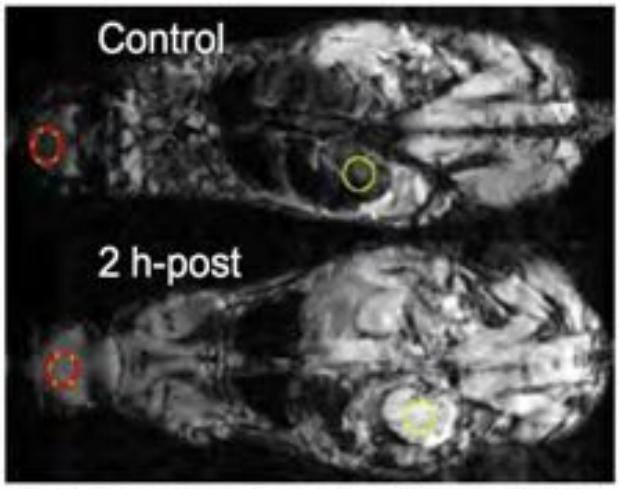
Ultra-small iron oxide nanoparticles have recently been explored as enhancing (T1) contrast agents for magnetic resonance imaging (MRI). However, their small size leads to fast renal clearance and limits their use for vascular imaging or therapy monitoring. Here, we present a state of art approach to forming nanoclusters by crosslinking ultra-small iron oxide nanoparticles with bovine serum albumin. This novel design maintains the T1 performance of the ultra-small nanoparticles, but showed an increased blood circulation of the MRI contrast agents of over two hours. Our breast tumor model study also exhibited enhanced localization of these nanoclusters at tumor sites. The ability to maintain the T1 performance of the ultra-small nanoparticles is significant, because previous studies have shown complete T1 loss or signal decrease upon polymer encapsulation.



T1-weighted MR images pre-injection and 2 h post injection. The red (brain) and yellow (kidney) circles indicate regions of significant enhancement.

Towards an understanding of heating effects and magnetisation response of magnetic nanoparticles associated with live cells

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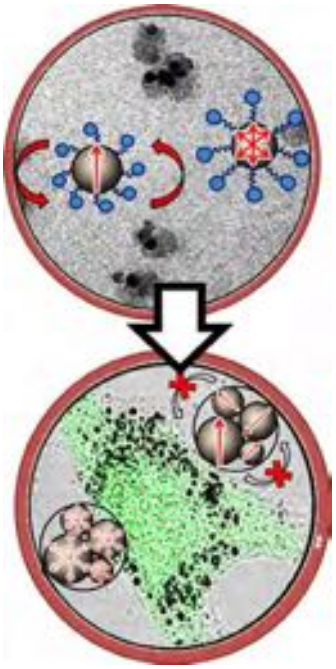
Magnetic hyperthermia is an experimental thermal cancer treatment that uses magnetic nanoparticles to channel the energy from an external high-frequency alternating magnetic field. As heating can only occur where nanoparticles are present, the technique is truly local and significant effects can be obtained by accumulating nanoparticles within tumors. However in order to obtain true cellular level thermal treatment, much recent work has focused on labelling individual cancer cells with magnetic nanoparticles, either by binding them to cell membranes or through internalisation routes such as endocytosis. In principle these particles should then be able to heat the cells directly to trigger cell death. However the results of such experiments to date have been somewhat disappointing because it seems the magnetic and consequently heating properties of the nanoparticles can change once they are associated with cells.

In this talk I will discuss how developing a full understanding of the interactions of nanoparticles with their local environment is essential to achieve effective cellular level heating within real biological systems. Within this context I will describe the results of our recent work using a.c. magnetic susceptometry and magnetometry to probe the high-frequency magnetic response of nanoparticles under different environmental conditions, including in-situ measurements of nanoparticles associated with live cells. I will also discuss how nanoparticle surfaces can evolve when in contact with biological media and how such processes affect their interaction with cells. Our results suggest that the magnetic response and consequently heating efficiency of the nanoparticles is sensitive to a combination of local environmental conditions, and intrinsic physical nanoparticle properties such as magnetic anisotropy.



Magnetic Nanoparticles and Nanocomposites: Tuned Surface Reactivity and Affinity for Medical and Environmental Applications

Trang Mai, Angela Gutierrez, Shuo Tang, Tom Dziubla, J. Zach Hilt
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We apply chemical engineering fundamentals to the rational design, synthesis, and application of novel nanoparticle systems and macromolecular materials. In particular, we are interested in designing and applying advanced materials based on magnetic nanoparticles (MNPs) and nanocomposites. Magnetic nanocomposites are a relatively new class of advanced materials, which have attracted interest as intelligent materials for biomaterial and other applications. In our lab, we are primarily interested in MNPs due to their ability to respond to an alternating magnetic field (AMF) resulting in local energy delivery and potentially localized heating. We have incorporated MNPs into nanocomposites that exhibit new and unique properties such as remote actuation, and the resultant properties of the nanocomposite can be easily tailored by manipulating the composition of the polymer and the nanoparticulate material.

Here, some of our recent activities in the development and application of MNPs and their nanocomposites will be presented. In particular, the application of functionalized MNPs for cancer therapy and environmental remediation will be highlighted. For potential cancer therapy applications, we have been particularly interested in determining the role of reactive oxygen species (ROS) catalytically generated from the surface of iron oxide MNPs, and using a methylene blue degradation assay, we demonstrated that magnetically mediated energy delivery (MagMED) is capable of enhancing the Fenton-like generation of ROS. Here, further studies of the surface reactivity of MNPs and the enhancement of this reactivity with AMF exposure will be presented, as well as the effects of small molecule and macromolecular coatings. These demonstrations illustrate the potential of AMF-induced ROS in cancer therapy. For environmental applications, AMF exposure and the associated energy delivery can be used to carry out various functions. For example, we will present data showing the AMF exposure being used to change the binding properties of an MNP coating.

Hyperthermic Effect of Intra- & Extracellular Magnetoliposomes on Pancreatic Tumor Cells

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Magnetic Fluid Hyperthermia (MFH) offers a potent alternative for the treatment of local tumors. In MFH, magnetic nanoparticles (MNP) are either injected directly into or targeted magnetically at the tumor site, where they are exposed to an oscillating magnetic field (OMF). Driven by the OMF the MNP undergo relaxation and hysteretic processes, generating heat locally. It was demonstrated that local tumor temperatures above 42°C damage cells substantially [1]. Once MNP reach the tumor however, they interact with the local cell environment, binding to cell membranes and being internalized inside cells.

In this study we examined the cytotoxic influence of the environmental temperatures generated in suspension by intracellularly bound and extracellularly unbound MNP during hyperthermic treatment (HT) for either 30 or 90 min. The resulting HT cytotoxic effect was assessed via clonogenic assay (CA). Therefore, samples consisting of MiaPaCa-2 pancreatic tumor cells were incubated for 24 h at 37°C with self-synthesized Fe_3O_4-multicore magnetoliposomes (ML) of different iron concentrations. After incubation, the sample batch was split into two parts: one part was composed of cells with internalized ML and extracellularly dispersed ML, the other part was composed solely of cells with internalized ML dispersed in pure medium. Controls were not treated with ML (Fig. 1a)). ML-internalization was investigated by transmission electron microscopy (TEM) (Fig. 1b). Each sample was subjected to an OMF (36 kA/m, 265 kHz) and temperature was recorded. Subsequently, treated cells were seeded for CA testing and evaluated after 12 days.

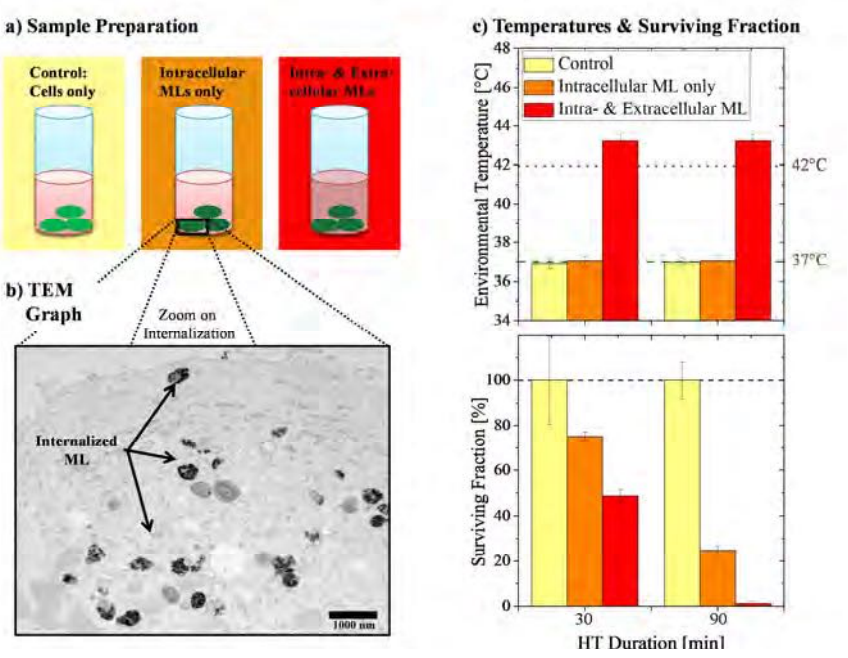

Fig. 1: a) 3 kinds of MiaPaCa-2 cell samples were prepared containing: cells only (control), ML loaded intracellularly and MLs loaded intra- and extracellularly, both latter after 24 h of incubation. b) TEM image of ML internalized in cells. c) Cellular environmental temperatures in suspension (upper row) and surviving fraction (lower row) after (30 & 90) min of HT and an incubation concentration of 225 µg(Fe)/mL ML. Body (37°C) and therapeutic temperatures (42°C) are marked.

Fig. 1c) depicts the environmental temperature around the cells and their surviving fraction after HT for an exemplary incubation iron concentration of 225 µg/mL. For solely intracellular ML no significant heating was observed. For intra- and extra-cellular ML however, the environ-mental temperature reached the therapeutic level (T>42°C). This is explained by the considerably lower amount of ML internalized compared to the extracellularly ML amount. Furthermore, cell survival was significantly lowered with increasing HT duration (comparing 30 min to 90 min), independent of temperature. Our results indicate that temperature and duration, as well as the absolute amount of ML internalized determine the therapeutic efficacy of HT.

[1] Yarmolenko et al., *Thresholds for thermal damage to normal tissues: an update*. Int. J. Hyperth. 27(4), 320-343, 2011.

Glycoconjugate-Functionalized Magnetic Nanoparticles: A Tool for Selective Killing of Targeted Bacteria Via Magnetically Mediated Energy Delivery.

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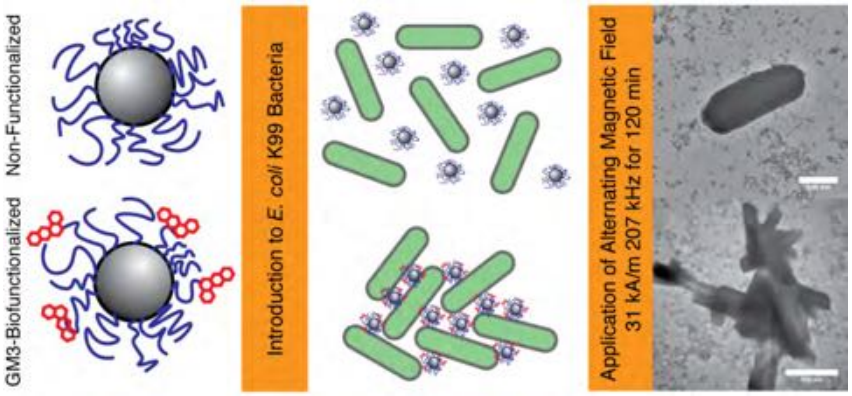

New technologies utilizing nontraditional antibiotic mechanisms are urgently needed to combat the increasingly common appearance of multi-drug resistant bacteria. This work explores the feasibility of using magnetically mediated energy delivery (MagMED) to selectively kill enterotoxigenic Escherichia coli strain K99 (EC K99) in the presence of multi-anchored glycoconjugate-functionalized magnetic nanoparticles. Click ready poly(ethylene oxide)-poly(acrylic acid)-dopamine functionalized magnetic nanoparticles (PEO-MNPs) were synthesized and functionalized with bacteria-specific glycoconjugate Neu5Ac(α2-3)-Gal-(β1-4)Glcβ-sp (GM3-MNPs) for adherence to EC K99. When mixtures containing both EC K99 and the GM3-MNPs were exposed to alternate magnetic fields (31 KA/m, 207 KHz), a clinically relevant 3-log reduction in colony forming units (CFUs) of EC K99 was achieved in 120 minutes. Bacterial selectivity of the treatment was shown using a mixed culture experiment including both glycoconjugate positive EC K99 and glycoconjugate negative EC O157. Targeted cell death of the EC K99 was seen after treatment of the mixed culture with minimal damage to EC O157. Electron microscopy along with live/dead staining assays confirmed membrane damage of EC K99 cells treated with GM3-MNPs and MagMED. Cell death of EC K99 was further supported by the intracellular adenosine triphosphate (ATP) levels which were considerably reduced when incubated with GM3-MNPs and treated with MagMED. These results suggest that GM3-MNPs induced glycoconjugate targeting along with MagMED can be potentially used as a targeted nontraditional antibiotic treatment platform to inactivate/kill bacterial pathogens, with minimal impact on normal microflora and the affected body region/tissue.

Why do magnetic nanoparticles form messy clumps? Taking into account the bridging or sticking of ligands

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[e]Department of Physics, University of York, UK.

When ferromagnetic particles are in fluids, there is the possibility for them to agglomerate due to the long-range magnetic dipole-dipole interactions. Most previous theoretical models predict the formation of chains or rings of nanoparticles that are single particle width[1,2] while many experiments have shown messy, multiple particle width chains and clumps[3]. We calculate agglomeration of ferromagnetic, magnetite nanoparticles using a Langevin dynamics simulation. We use a "stickiness" parameter to model ligand bridging. We compare our homemade fortran code to LAMMPS simulations and find consistent results and similar computation times. We also make analytic estimates for the stickiness parameter and find good agreement between numerical results and the analytic estimate. We characterize the shape and order of agglomerates that form for 100 particles after a 10 ms duration (time steps are 0.1 ns). We find that the stickiness encourages agglomerates to form that are messy loops or multiple particle width chains such as those seen in Fig. 1 (right). We discuss results for particles in an applied magnetic field and particles in no field.

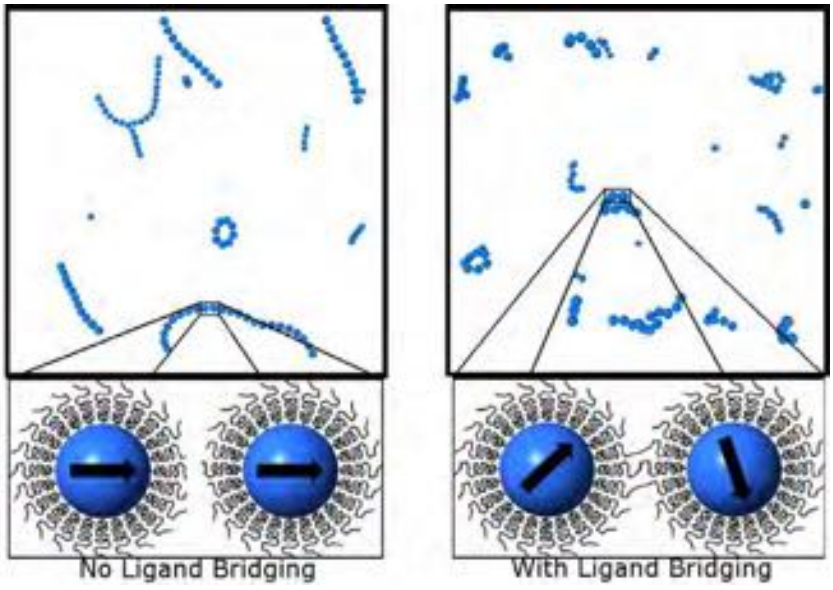

Figure 1: Agglomerates formed when there is no stickiness (left panel) and when ligand bridging causes multiple particle width chains (right panel) for 50 nm diameter magnetite particles in no applied magnetic field after a 10 ms simulation duration.

[1] R. W. Chantrell et. al, J. Appl. Phys. **53**, 2742 (1982).
[2] Z. Wang et al., Phys. Rev. E **66**, 021405 (2002).
[3] S. L. Saville et al. Nanoscale, **5**, 2152 (2013).

Calculating the variation in hysteretic energy produced inside realistic clumps of ferromagnetic nanoparticles

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Dipolar interactions between magnetic nanoparticles can lead to either an increase or a decrease in the hysteretic energy that the particles produce. This energy correlates with the amount of heat the particles can give to the surroundings. The dipolar interactions are important to consider for dispersed particles but especially for particles that have agglomerated or clumped together. Previous theoretical works have studied particles that are clumped in regular – and unrealistic – shapes.[1] A recent work has considered fractal agglomerates within which the easy anisotropy axes of particles are in random directions.[2]

Here we present a more realistic calculation. We have simulated real agglomerates of ferromagnetic, single-domain, magnetite particles using Langevin dynamics calculations with ligand bridging taken into account (see other abstract). Using these agglomerates, we have placed the easy axis of each particle in a direction based on a probability distribution function, which reflects the fact that the easy axis may not coincide with a particle's magnetization direction at finite-temperature. Then we have used Monte Carlo simulations to calculate hysteresis loops. An example of a hysteresis loop for 100 50-nm-diamgeter particles is shown. We find that the hysteretic area is *less* for realistic, disordered clumps (dashed line) than for linear chains (solid lines). We also find that using the probability distribution of easy axes reduces the area substantially for even large particles – where temperature effects are normally assumed to be small – and so this is an important extension to theoretical models.

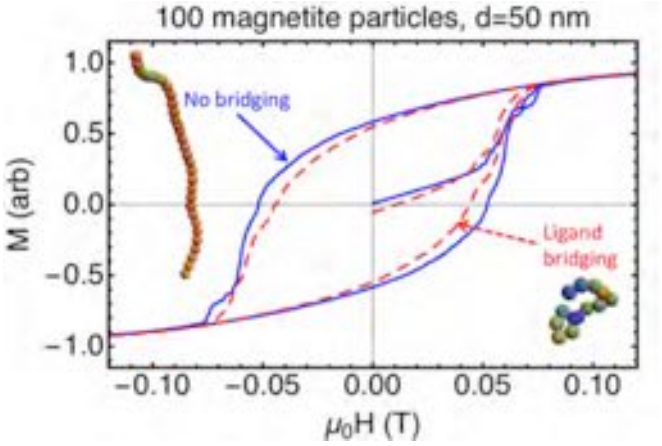

Fig: Hysteresis loops calculated for 100 particles with (dashed) and without (solid line) ligand bridging. Representative agglomerate shapes are shown.

Examples of some agglomerates are drawn on the figure. The colors of particles in the clumps reflect the fact that some particles release more during a field cycle (red) than others (blue) depending on their position in the agglomerate. We discuss the possibility of some particles having a net absorption of energy, rather than releasing energy.

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[1] Saville *et al.* J. Colloid Interf. Sci. **178**, 620 (2014). Serantes *et al.* J. Phys. Chem C **118**, 5927 (2014). Tan *et al.* Phys. Rev. B **90**, 214421 (2014).

[2] Hovorka, J. Phys. D: Appl. Phys. **50**, 044004 (2017).

Combined MPI - MFH: A promising theranostic platform

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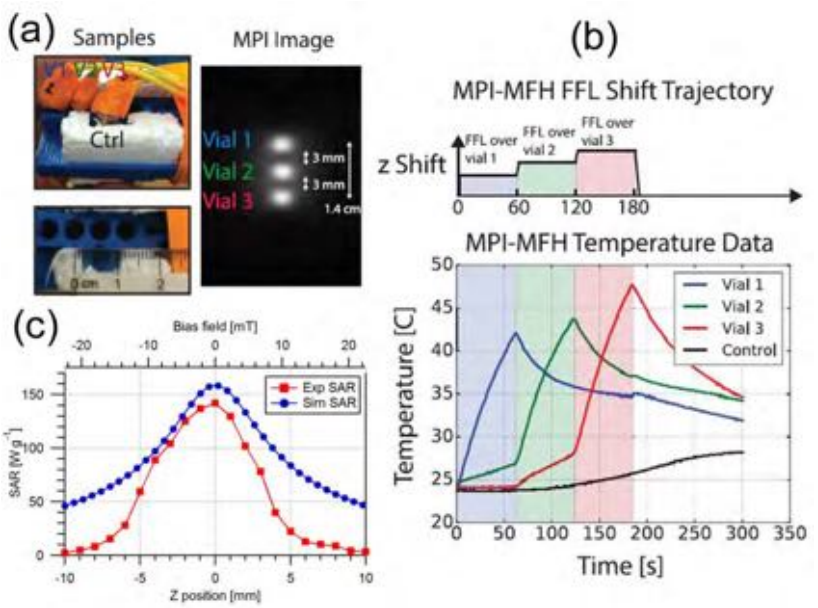
Magnetic particle imaging (MPI) is an emerging molecular imaging technology where imaging signal is provided by the non-linear response of magnetic nanoparticle tracers to a scanned magnetic gradient field. This non-radioactive tracer based technology provides a safer alternative as compared to other radioactive imaging modalities like single photon emission computed tomography (SPECT) and positron emission tomography (PET), and finds application in real-time cardiovascular imaging, cell labeling and tracking.

Magnetic fluid hyperthermia (MFH) is a therapeutic approach which uses magnetic nanoparticles to dissipate heat for treating cancer and for drug delivery. However, non-specific uptake of magnetic nanoparticles in MFH can lead to undesired heating in non-targeted organs. To avoid undesired heating of non-targeted organs, the use of the field free region (FFR) concept from MPI provides a promising solution to deliver heat only in the region of interest.

In this work we utilize the ferrohydrodynamic equations to obtain theoretical predictions of energy deposition by calculating the specific absorption rate (SAR) values and elucidate the effect of MPI field gradient on the spatial distribution of SAR. We also demonstrate experimentally the on-demand heating of magnetic nanoparticle vials which were separated by only 3 mm, using a custom built MPI-MFH setup, along with preliminary results of simultaneous MPI-MFH. The good qualitative agreement observed between experiments and simulations shows potential of this theranostic technology to serve as a basis of future treatment planning and image guided therapy.



(a) MPI image of samples, (b) selective heating of samples using a field free line (FFL) scanning sequence, (c) comparison of experimental and simulation SAR values.(Hensley et al. 2016; Dhavalikar and Rinaldi 2016)

The Effect of Nanoparticle Concentration on Heating in Magnetic Nanoparticle Hyperthermia: An Experimental Model

B.A. Evans

Elon University, Elon, NC, USA

Magnetic nanoparticle hyperthermia (MNH) has shown great potential for cancer therapy, promising a localized therapy which would eliminate many of the systemic side effects inherent in traditional chemotherapy or radiation. Progress toward clinical application, however, has been slow. This is due in large part to the complexity of the physical system: nanoparticle heating depends strongly on particle diameter, magnetocrystalline anisotropy, and interparticle interactions, each of which is difficult to control precisely in large ensembles. The roles of particle diameter and anisotropy are generally well-understood, but there is not yet a strong consensus on the role of interparticle interactions on MNH. Thus, understanding the influence of interparticle interaction on magnetic heating is critical to the clinical application of MNH.

To this end, we have developed a silicone material which contains a well-dispersed suspension of magnetite nanoparticles (Fig. 1) which can be varied smoothly from 0-50% wt. (0-18% v.) without aggregation. This material serves as a well-controlled experimental model for exploring the role of nanoparticle concentration on specific power loss (SPL). We have measured the heating rate (SPL) of the nanoparticles as a function of nanoparticle concentrations ranging up to 10% v. (320 mg/mL) in applied field frequencies of 86, 123, 281, and 460 kHz at field magnitudes ranging from 50-300 G. Our results indicate that SPL is maximized at concentrations of approximately 1% v. (Fig. 2), which is in strong qualitative agreement with theoretical predictions by Carrey *et al.* (2014, PRB 90, 214421). In addition, our results suggest that the optimal concentration is dependent on applied field frequency, with lower frequencies favoring higher-concentration ensembles.

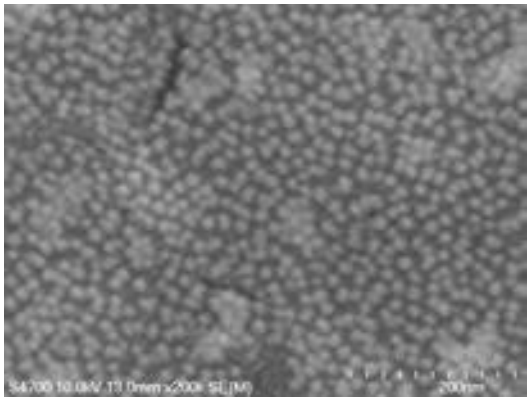


Figure 1: Scanning electron image of the magnetite/silicone composite, showing magnetite nanoparticles (light) surrounded by silicone (dark).

Finally, we show that the frequency-dependence of SPL in our experimental model varies smoothly from the quadratic relationship predicted by the linear response theory ($SPL \propto f^2$) to a diminished dependence of $SPL \propto f^{3/2}$ as the nanoparticle concentration increases (Fig. 3). These results bolster current theoretical efforts and provide insight into new investigations, ultimately leading to better prediction and control of interparticle interactions in MNH.

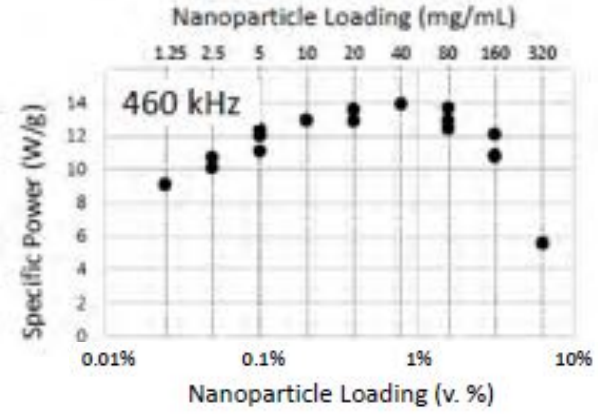


Figure 2: Dependence of SPL on magnetic nanoparticle concentration. SPL is maximized at 1% v., in good agreement with some theoretical models.

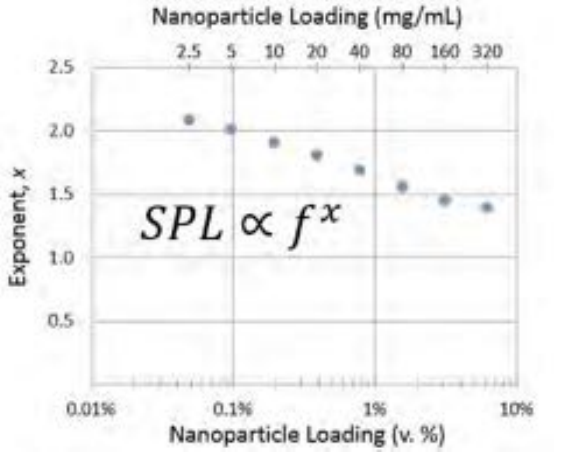


Figure 3: The experimental model shows that the exponential dependence of SPL on applied field frequency (f) is concentration-dependent.

Tuesday, June 6, 2017

7:00	Breakfast at the The Venue		
	Session 3: Career Panel - Carlos Rinaldi, Erika Vreeland, Nikorn Pothayee (Chair: Mas Crawford)		
8:00	Career Panel at the The Venue		
	Session 4: Delivery (Chair: Jennifer Andrew)		
9:20	**Pierre**	**USA**	**Magnetoluminescent nanoparticles - combining the dual power of time-resolved luminescence and MRI contrast agents of lanthanide complexes**
10:00	Nakagawa	Japan	Drug-release controlling nanoparticles under exposure to magnetic fields
10:20	Erb	USA	Penetrating Porous Tissue with Magnetic Targeting
10:40	Coffee Break		
11:00	**Tsourkas**	**USA**	**Gold and superparamagentic iron oxide-loaded polymeric micelles for imaging, radiotherapy and the prediction of therapeutic response**
11:40	Panel Discusion with Session 4 presenters		
12:00	Lunch at the The Venue		
	Session 5: Synthesis (Chair: Emilie Secret)		
13:40	**Dravid**	**USA**	**Theranostic Magnetic Nanostructures (MNS) in Biomedicine**
14:20	Davis	USA	Quantitative Measurement of Ligand Exchange on Iron Oxides via Radioanalytical Techniques
14:40	Uhl	USA	Synthesis of Composite Magnetoelectric Particles via Electrospraying for Manipulation of Biologically Relevant Electric Fields
15:00	Break		
15:20	Budi	USA	Tailorable anisotropy in electrospun magnetoelectric nanocomposites
15:40	Hafeli	Canada	Microdroplet Producing Co-Flowing Device for the Generation of Magnetic Microspheres as Embolic Agents for Large Vessels
16:00	Rinaldi	USA	Laying to Rest the Magnetically Dead Layer in Magnetic Nanoparticles
16:20	Panel Discussion with Speakers from Session 2		
18:30	Banquet and Annoucement of Poster Winners		

Magnetoluminescent nanoparticles – combining the dual power of time-resolved luminescence and MRI contrast agents of lanthanide complexes

Valerie C. Pierre

Multimodal nanocomposite probes - nanoparticle assemblies that enable imaging by two or more techniques have become increasingly prevalent over the past decade. Of these, magnetoluminescent agents are receiving the much attention due to their ability to combine two widespread techniques, magnetic resonance imaging (MRI) and fluorescence microscopy, which are complementary in terms of three-dimensional imaging capability and spatial resolution, respectively. We will describe two approaches to designing magnetoluminescent nanoparticles for dual magnetic resonance imaging and time-gated fluorescence spectroscopy and microscopy. The first includes functionalizing iron oxide nanoparticles with responsive luminescent terbium complexes. The second, involves novel microporous silica nanoshells selectively functionalized with gadolinium contrast agents and bright luminescent europium complexes. The synthesis and contrasting properties of these two sets of multimodal nanoparticles will be discussed.

Drug-release controlling nanoparticles under exposure to magnetic fields

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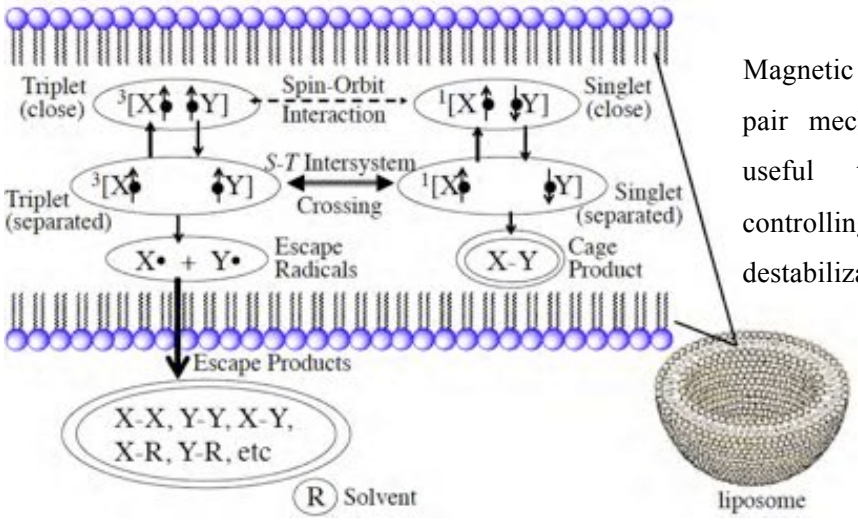
Numerous techniques have been developed to investigate magnetic nanoparticles for biomedical engineering applications to drug delivery systems (e.g., hyperthermia, microembolization, and magnetic resonance imaging diagnosis). However, there are no reported studies of the application of radical pair mechanisms to drug-release controlling under exposure to magnetic fields. So we propose a new drug-release technology using liposomal nanoparticles equipped with magnetic controls.

Magnetic field effects on radical pair mechanisms are known as the one and only phenomenon by which magnetic fields can switch over chemical reaction paths in spite of their low energies. This phenomenon is inferred mainly via *S*-*T* intersystem crossing and magnetic relaxation. Although a radical pair is an extremely short-lived reactive intermediate, it is necessary to prolong the lifespan of the pair for the most efficient magnetic field effects. This can be achieved by introducing pair-forming compounds between the lipid molecules of liposomal bilayers.

In the last decade we have considered applying the mechanisms to DDS methodologies for the best possible balance between clinical performance and low invasivity. For the rapid progress of the methodology, we demonstrated here the liposomal drug-release technology with the pair maehanism. We believe the idea that magnetic fields are extremely suitable for the gentle control of chemical reactions *in vivo*.



Magnetic field effects on radical pair mechanisms are much more useful tools for drug-release controlling rather than membrane destabilization.

Penetrating Porous Tissue with Magnetic Targeting

Randall Erb[1,*], Karlo delos Reyes[2], Rasam Soheilian[1], Hicham Fenniri[2].
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[2] Department of Chemical Engineering, Northeastern University, Boston, MA
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Statement of Purpose: Patients diagnosed with pancreatic ductal adenocarcinoma (PDAC) have a five-year survival rate of less than 7% and a median survival rate of only six months. Current chemotherapy techniques used for treating patients have shown undesirable side effects due to spread of the injected drugs in the body. Recently, it has been shown that Rosette Nanotubes (RNTs) can be effective in delivering therapeutic small interfering RNA (siRNA) to target the mutated KRAS gene in pancreatic cancer cells and knockdown the gene. On the other hand, it is known that magnetic drug delivery offers a non-invasive approach for targeting tumors deep in the body through the remote control of magnetic nanoparticles with external magnetic sources. Such strategies have been implemented by many researchers and have shown enhancements to the concentration of drug in the tumor region.
In this work, we use RNT+siRNA coated Iron oxide nanoparticles to target pancreatic cancer cells *in-vitro* in a two-step process. In the first step, constant magnetic fields are applied to guide aggregates of nanoparticles to the targeted area. This can be explained by the fact that aggregates of nanoparticles have a better transport velocity compared to individual nanoparticles due to hydrodynamic shielding among particles. In the second step, upon reaching the tumor site, we use time dependent magnetic fields to dynamically tune the direction (but not magnitude) of the field to put magnetic nanoparticles into repulsive configurations with neighboring particles driving them into disruption in order to achieve a better diffusion of nanoparticles in porous tissue.
Results: In this work, we have done *in-vitro* experiments where Panc-1 pancreatic cancer cells were cultured at the bottom of a well and Matrigel transwell membrane inserts with 3 μm pore sizes were used as a barrier to replicate the extra cellular matrix (ECM). We have been able to demonstrate that knockdown of cancerous cell genes under rotating magnetic fields is 3 folds higher compared to constant magnetic fields. Furthermore, we have developed theoretical, numerical and experimental frameworks to study particle kinetics under dynamic magnetic fields. Experimentally we have investigated both computer-controlled solenoid setups with low gradients and robotically controlled permanent magnets. Visualization of nanoparticles was enabled with a customized dark-field setup that allowed collection and analysis of real-time behavior.
Conclusions: Here we show that RNT coated Iron oxide nanoparticles can be used effectively as a gene delivery vehicle where pancreatic cancer cells can be targeted locally. Moreover, a method for driving the disassembly of magnetic nanoparticles under dynamic magnetic fields during magnetic targeting is presented. This technique resolves the issues associated with particle aggregation during magnetic targeting implementations. By exploiting dynamic fields, a dynamic energy landscape is generated that can catch particles in repulsive configurations, causing them to break apart. This disassembly process allows the magnetic nanoparticles to travel into the smallest capillaries such as the extracellular channels between tumor cells. In vitro experiments that recreate porous tissue were created that show enhanced penetration of the MNPs with dynamic magnetic fields.

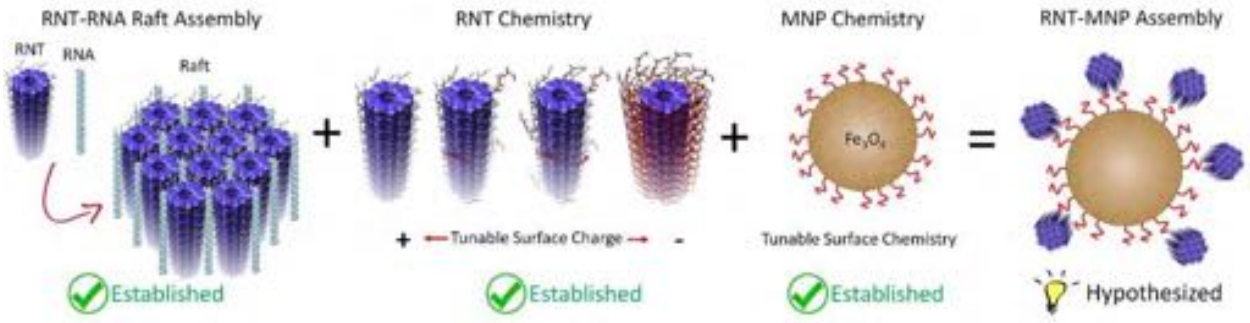

Figure. Developed assembly process of RNTs with siRNA and Iron oxide nanoparticles is shown above.

References: R. Soheilian, Y. S. Choi, A. E. David, H. Abdi, C. E. Maloney, R. M. Erb, "Toward Accumulation of Magnetic Nanoparticles into Tissues of Small Porosity.", Langmuir, 31 (30), 8267-8274, 2015.

Gold and superparamagentic iron oxide-loaded polymeric micelles for imaging, radiotherapy and the prediction of therapeutic response

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Current radiation-based therapies are often limited by the maximum allowable dose tolerated by adjacent healthy tissues. Difficulty in visualizing tumor boundaries often exacerbates efforts to maximize tumor dosage while minimizing the damaging off-target effects of radiation. Here, we describe Gold and Superparamagentic iron oxide (SPIO)-loaded polymeric Micelles (GSMs) (Figure 1A) that were specifically designed to help demarcate tumor boundaries by magnetic resonance imaging (MRI), enhance radiosensitization via a gold-mediated photoelectric effect, and ultimately improve therapeutic index. GSMs were prepared with a hydrodynamic diameter of ~100nm and a transverse relaxivity (r2) of 237$mM^{-1}s^{-1}$. When human HT1080 fibrosarcomma cells were incubated with GSMs and exposed to ionizing radiation, there was a significant increase in DNA double strand breaks compared with cells treated with radiation alone and non-irradiated controls. Intravenous injection of GSMs into tumor-bearing mice led to the selective accumulation of GSMs in the tumors, enabling non-invasive MRI imaging and clearer delineation of the tumor margins (Figure 1B). Subsequent administration of 150 kVp X-ray therapy led to a ninety-day survival for 71% of GSM-treated mice (Figure 1C). In contrast, the ninety-day survival for mice receiving radiation therapy alone was only 25% and it was 0% for mice receiving GSM alone and in untreated mice. In the mice that received GSMs and radiation therapy, a positive correlation was observed to exist between tumor contrast enhancement and the rate of decrease in tumor volume. The combined therapeutic, diagnostic, and prognostic characteristics of this dual-metal nanoparticle micelle system could thus enable a more personalized approach to a patient's cancer therapy and help predict tumor response.

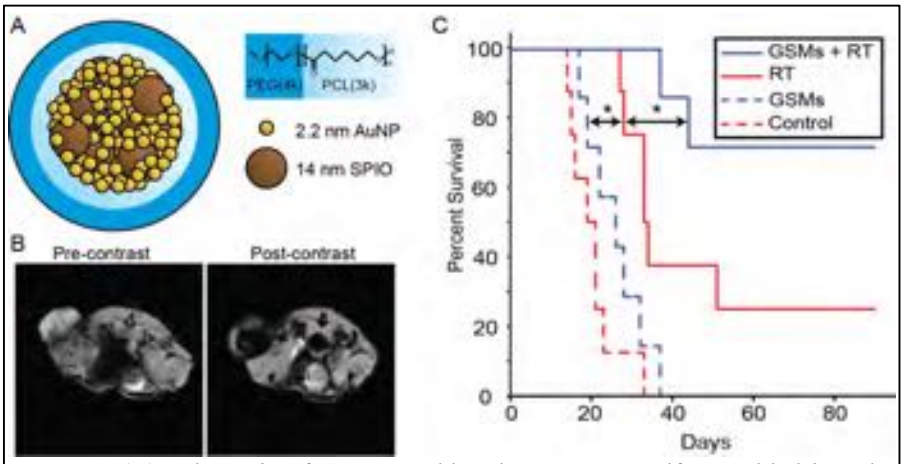

Figure 1. (A) Schematic of GSMs. Gold and SPION are self-assembled into the hydrophobic core of micelles, stabilized with the amphiphilic di-block co-polymer PEG-b-PCL. (B) GSM-enhanced MR imaging nu/nu nude mice with HT1080 flank tumors. (C) Kaplan-Meier survival analysis of HT1080-tumor bearing mice receiving the indicated treatments.

Theranostic Magnetic Nanostructures (MNS) in Biomedicine

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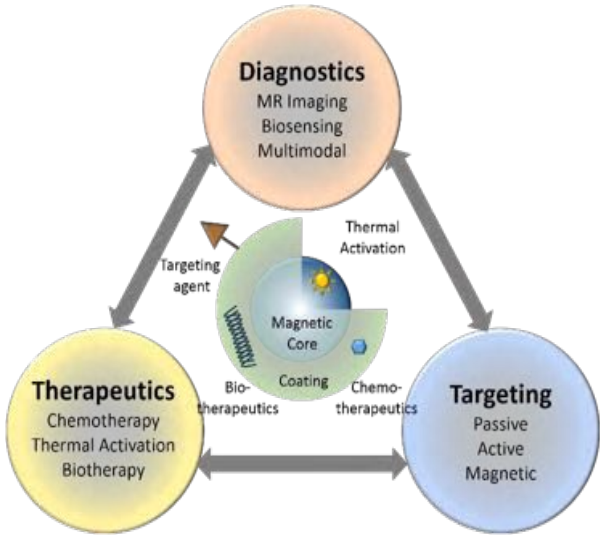
Remarkable advances have been made in biomedicine during the past two decades, ranging from early diagnostics to personalized therapy, that are based on improved genetic, molecular, and nano-scale understanding of the disease. Physical science and engineering in general, and nano-science/-technology in particular, have greatly contributed to these developments through out-of-the-box ideas from perspectives that are far removed from classical biological and medicinal aspects of the diseases.

Multifunctional nanostructures are being used in sensing/diagnostics while nanoscale carriers are able to deliver therapeutic cargo for timed and controlled release, such as at localized tumor sites. Magnetic nanostructures (MNS), have especially attracted considerable attention in combined diagnostics and therapy. A significant part of the promise of MNS lies in their potential for "theranostic" applications, wherein diagnostics makes use of the enhanced localized contrast in magnetic resonance imaging (MRI) while therapy leverages the ability of MNS to heat under external radio frequency (RF) field for thermal therapy or use of thermal activation for release of therapy cargo.

Our collaborative group at Northwestern is engaged in development of innovative MNS-based nanostructure complexes for theranostic application in biomedicine; specifically Alzheimer's Diseases (AD), cancer and cardio-vascular (CV) disease. On one front, we have developed antibody-conjugated MNS (AbMNS) for localization of Aβ oligomers believed to be responsible for the onset of Alzheimer's. Here, we have developed AbMNS for nasal aerosol that seem to pass through the blood-brain-barrier (BBB), and shows high localization with Aβ oligomers in the brain. Cancer targeting of MNS is achieved by invoking surface functionalization of MNS for specific biomarkers, followed by MR imaging and thermal activation with RF field. More recently, we have developed MNS-lipid complexes that show notable efficacy for cholesterol efflux and high loading of hydrophobic drugs. The correlation between optical fluorescence, MR and other complementary techniques demonstrates potential for early diagnostic and localized therapeutic prospects for MNS complexes.

The presentation will cover the emerging MNS platform, their characterization and *in-vitro* and *in-vivo* animal studies of AD, cancer and CV diseases. We believe that MNS-based nanoconstruct complexes have entered a *renaissance* era where intelligent synthesis, functionalization, stabilization and targeting provide ample opportunities for realistic applications in theranostics.

Functional Architecture of MNS Complexes for Theranostics



Quantitative Measurement of Ligand Exchange on Iron Oxides via Radioanalytical Techniques

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[2]Center for Optical Materials Science and Engineering Technologies (COMSET), Clemson University, Anderson, SC
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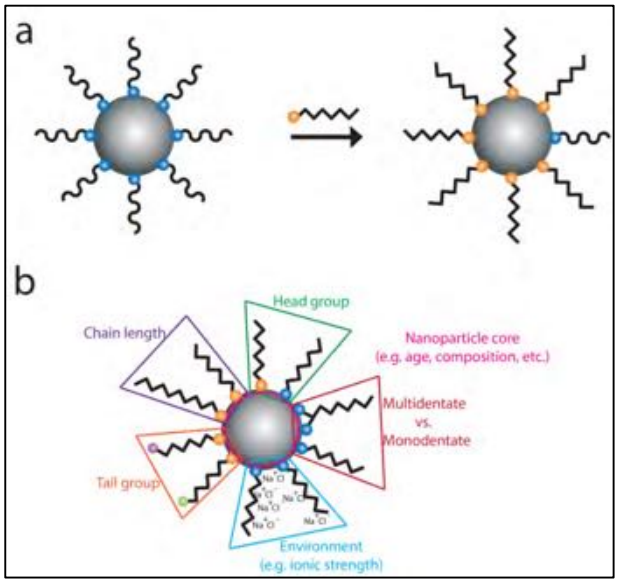
Ligand exchange of hydrophilic molecules on the surface of hydrophobic iron oxide nanoparticles produced via thermal decomposition of chelated iron precursors is a common method for producing aqueous suspensions of particles for biomedical applications. There are many factors which influence ligand exchange including chain length, multidenticity, head group chemistry, and particle aging and oxidation. Despite the wide use, relatively little is understood about the efficiency of ligand exchange on the surface of iron oxide nanoparticles and how much of the hydrophobic ligand is removed. To address this issue, we utilized a radiotracer technique to track the exchange of a radiolabeled ^{14}C-oleic acid ligand with hydrophilic ligands on the surface of magnetite nanoparticles.



(a) Illustration of incomplete ligand exchange. (b) Factors which affect ligand exchange.

Oleic acid coated iron oxide nanoparticles were synthesized via thermal decomposition with trace amounts of ^{14}C-oleic acid on the surface. The particles were modified via ligand exchange with a variety of hydrophilic ligands. The modified particles were measured using liquid scintillation counting (LSC) to determine the activity and ultimately, the total number of ^{14}C-oleic acid chains remaining after exchange. These techniques were used to determine effects of head group chemistry with polymeric ligands and effects of head group chemistry, number of binding groups, and ligand exchange reaction parameters with small molecule ligands. Results revealed catechols displace the most oleic acid during exchange. Furthermore, multidenticity, or multiple binding groups, increases the displacement of the oleic acid.

Davis, K., Cole, B., Ghelardini, M., Powell, B. A., & Mefford, O. T. (2016). *Langmuir*, *32*(51), 13716–13727.
Davis, K., Qi, B., Witmer, M., Kitchens, C. L., Powell, B. A., & Mefford, O. T. (2014). *Langmuir*, *30*(36), 10918–10925. http://doi.org/10.1021/la502204g

Synthesis of Composite Magnetoelectric Particles via Electrospraying for Manipulation of Biologically Relevant Electric Fields

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Electric fields are ubiquitous throughout the body, and are involved in processes ranging from wound healing to neuronal signaling to muscular functions. However, the manipulation of electric fields within the human body typically involves invasive procedures requiring electrode implantation within the body and the use of electrical leads attached to the electrode. Magnetoelectric materials, materials that exhibit a polarization in response to an applied magnetic field, present an opportunity to be able to generate and control biologically relevant electric fields using an externally applied magnetic fields. This is possible because unlike electric fields, magnetic fields are not attenuated by the human body and do not cause bodily harm.

For the purpose of this work, composites of barium titanate and cobalt ferrite will be used to obtain magnetoelectricity. The composite magnetoelectric effect is achieved by coupling a piezoelectric and a magnetostrictive material across a common interface. Thus, as a magnetic field is applied, the magnetostrictive material is strained, which causes a resultant stress in the piezoelectric material, changing its polarization. Conversely, an electric field could be applied in order to achieve a change in the magnetization of the magnetostrictive material. Typically, magnetoelectric composites are created in thin film structures. Our group has previously demonstrated the ability to synthesize magnetoelectric composite nanofibers composed of piezoelectric barium titanate and magnetostrictive cobalt ferrite in the Janus morphology via electrospinning. The nano-size of these fibers increases the ratio of interfacial area to volume allowing for more of the composite to be located at the interface and thus contributing to the transfer of strain necessary for the composite magnetoelectric effect. In addition, the nano-size of these fibers also enables them to be used in biomedical applications as they can be incorporated into biocompatible polymers and used in applications where electrical signaling is beneficial.

Herein, the synthesis of composite magnetoelectric particles is described. These particles are synthesized in the Janus morphology via electrospraying techniques. These particles couple together piezoelectric barium titanate and magnetostrictive cobalt ferrite at the interface between them to achieve a composite magnetoelectric. Due to the increase interfacial area to volume ratio of Janus particles, even as compared to Janus fibers, the composite magnetoelectric effect exhibited by these particles is predicted to be orders of magnitude stronger than that seen in bulk or thin film composites of the same materials. The magnetoelectricity of the particles will be examined qualitatively using vibrating sample magnetometry. Particles will be additionally characterized using scanning electron microscopy, X-ray diffraction, Raman spectroscopy and superconducting quantum interference device magnetometry

Magnetic Field–Induced Cyclization as a Mechanism for Release of Nanoparticle-Bound Substrates

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Introduction: An important attribute of a drug delivery system is regulated spatial and temporal payload release to minimize side effects and possibly to improve therapeutic efficacy. Magnetic nanoparticles (NPs) are appealing in this regard for several reasons, notably for their ability to induce local hyperthermia on exposure to an alternating magnetic field (AMF).[a] We describe here gold–coated magnetic NPs fitted with linker–payload chains that on AMF–induced local hyperthermia release the payload (Figure 1).

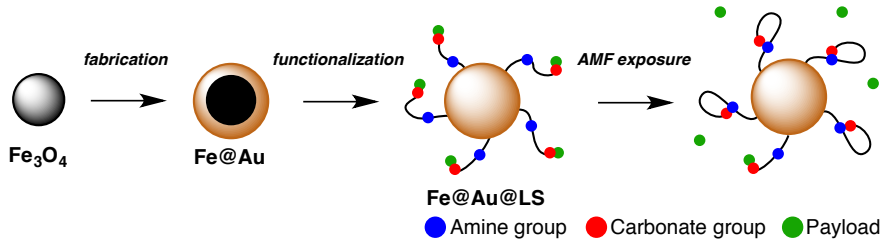

Figure 1. Concept summary for AMF-responsive delivery system.

Methods: We synthesized gold–coated magnetic NPs (Fe@Au) using modified literature procedures.[b] We also prepared and characterized an amine–containing linker system (LS**1**) and a corresponding amine–free linker system (LS**2**). Fe@Au NPs then were functionalized using a 1:1 ratio of PEG-SH to either LS**1** or LS**2** to give Fe@Au@LS**1**-PEG and Fe@Au@LS**2**-PEG, respectively (Figure 2a).[c] AMF-induced payload release studies were performed by exposing NPs to sequences of AMF exposure followed by fluorescence analyses. MALDI was used to confirm the identity of the released payload.

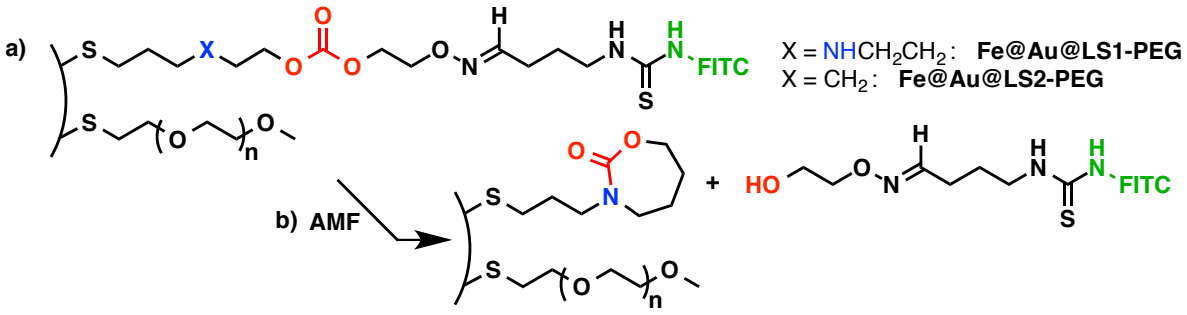

Figure 2. Functionalized NPs containing the fluorescent probe FITC.

Results: Upon exposure to AMF (1X PBS buffer at pH 7.4, 500 A, 30 mins), facile payload release was observed with the Fe@Au@LS**1**-PEG formulation (Figure 2b), whereas minimal payload release was measured with the Fe@Au@LS**2**-PEG NPs. Experimental details will be discussed as well as the control studies using LS**2**.

Conclusion: We demonstrate that a linker system capable of undergoing an intramolecular cyclization in response to heat generated on exposure of magnetic NPs to an AMF can be used for controlled substrate release. The necessity of a nucleophilic element (amine in our case) for release was demonstrated by comparisons to a linker system that lacked this element.

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[a] M Torres-Lugo and C Rinaldi. *Nanomedicine (Lond)*. **2013**. 1689-1707.

[b] L Wang, J Luo, Q Fan, M Suzuki, IS Suzuki, MH Engelhard, Y Lin, N Kim, JQ Wang and C Zhong. *J. Phys. Chem B*. **2005**. 2193-21601.

[c] L Menichetti, L Manzoni, L Paduano, A Flori, C Kusmic, D De Marchi, S Casciaro, F Conversano, M Lombardi, V Positano and D Arosio. *IEEE Sensors Journal*. **2013**. 2341-2347.

Tailorable anisotropy in electrospun magnetoelectric nanocomposites

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Composite materials offer unique opportunities to achieve otherwise unattainable properties, often as the result of unique phenomena that occur at the interface between the phases being coupled. An additional control is the anisotropy of the individual phases and the resultant composite, which can be used to control the magnitude and direction of properties. Here, a method of tailoring anisotropy to enhance magnetic exchange coupling across an interface in composite nanofibers at both the nano- and macro-scale is presented using bismuth ferrite ($BiFeO_3$) and cobalt ferrite ($CoFe_2O_4$) phases. Specifically Janus type nanofibers, wherein two phases are coupled longitudinally, are used to create an anisotropic building block that allow access to both surface and bulk properties of each phase. This novel architecture is linked to an anisotropic interface between the coupled phases, and a model is developed relating fiber composition to interfacial area. The validity of this model is confirmed by measuring the magnitude of the exchange bias between the $BiFeO_3$ and $CoFe_2O_4$ as the composition and thereby the interfacial area between the phases was varied (Figure 1). Next the utility of these anisotropic composites is further extended by controlling the macroscale anisotropy of the collected nanofibers. By incorporating a novel charged electrode set up, wherein four columns flank a centrally charged guide column, the alignment of the final fiber mat could be tailored from randomly dispersed (Figure 2A) to fully aligned (Figure 2B) .

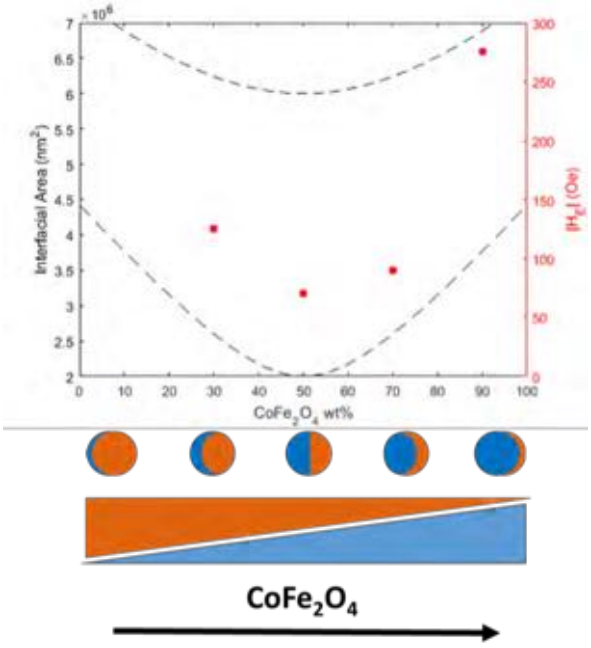

Figure 1. Model of interfacial area of a Janus nanostructure with increasing phase wt.% using a parabolic interface (left axis). The magnitude of measured interfacial phenomena, in this case exchange bias, is overlaid and found to follow the trend predicted by the model (right axis).

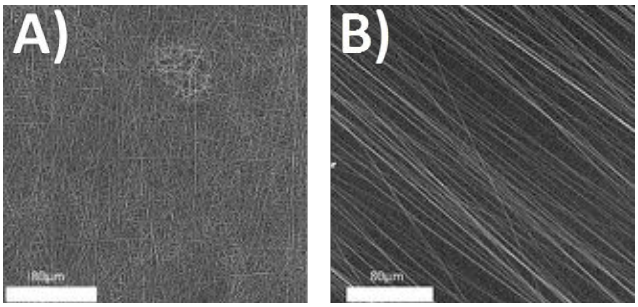

Figure 2. Fiber mats electrospun on novel charged collector A) random mat resulting from no applied charge and B) aligned mat resulting from applied charge.

Microdroplet Producing Co-Flowing Device for the Generation of Magnetic Microspheres as Embolic Agents for Large Vessels

Zeynab Nosrati[1], Sahan Ranamukhaarachchi[1], Alexandre Bigot[2], Francois Michaud[2], Ning Li[3], Sylvain Martel[3], Gilles Soulez[2], Katayoun Saatchi[1], Urs Häfeli[1]*

[1]University of British Columbia, Faculty of Pharmaceutical Sciences, Vancouver, BC, Canada; [2]Clinical Image Processing Laboratory (LCTI), Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), Montreal, QC, Canada; [3]NanoRobotics Laboratory, Department of Computer and Software Engineering and Institute of Biomedical Engineering, Polytechnique Montréal, Montréal, QC, Canada ; *Email: urs.hafeli@ubc.ca

Droplet microfluidics technology has recently been introduced to generate particles for many biomedical applications, including as therapeutic embolizing agents in hepatic, uterine or bronchial arteries. Size and shape of embolic agents is important and must be adjusted to the target vessels. For example, particles of 40-100 µm are used for smaller vessels, while particles from 0.1-1.2 mm are used for large vessels. Magnetic embolic agents can be navigated to the target location (e.g., a tumor) through the blood system with an external magnetic field by a method called Magnetic Resonance Navigation (MRN) technology for applications such as drug delivery, chemoembolization and radiation therapy.

Here we are introducing a high throughput method to produce uniform magnetic PLGA microspheres (MMS) as large vessel embolic agents. Using a simple 3D printed micro-co-flowing device with a central needle inside a teflon tube, an axisymmetric flow was obtained with a central dispersed phase surrounded by a continuous phase (**Fig. 1**). To produce the different required particle sizes, the geometric and flow parameters of the micro-co-flowing device were altered. We used 6 different needle gauges (21G, 22G, 25G, 28G, 30G and 33G) at 3 different flow rate ratios (Qd/Qc = 0.03, 0.003, 0.002) to generate different MMS sizes, while the concentration and viscosity of the dispersed phase was kept constant.

With this method, we were able to generate MMS sized 200-750 µm with narrow size distribution (CV <10%) (**Fig. 2**). MMS morphology, mean particle size and size distribution were quantified from SEM images using Image-J software (for an example of MMS sized 250±25 µm, see **Fig. 3**). The magnetic performance of the MMS was investigated using a vibrating sample magnetometer. The MMS toxicity was studied in HEK293T human embryonic kidney cells by MTT assay and Incucyte tests. MRN experiments with 200-250 µm MMS are currently ongoing in a pig model and will be presented. The preparation of even smaller sizes of the MMS, below 200 µm, are also still under investigation and will be presented as well.

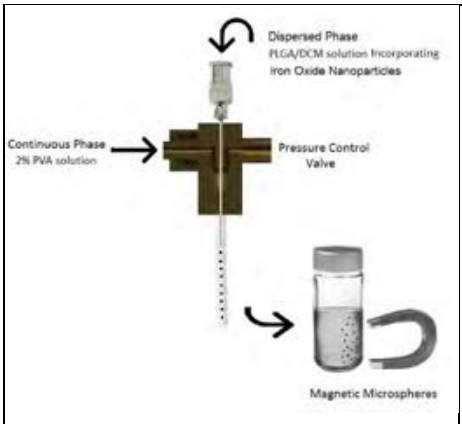

Fig. 1. *3D printed micro-co-flowing device used for the preparation of magnetic microspheres.*

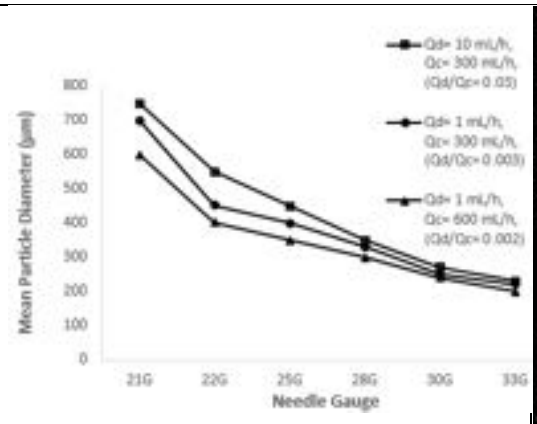

Fig. 2. *Relationship between the needle gauge and mean particle diameter at different flow rate parameters (Q_d: Dispersed phase flow rate, Q_c: Continuous phase flow rate)*

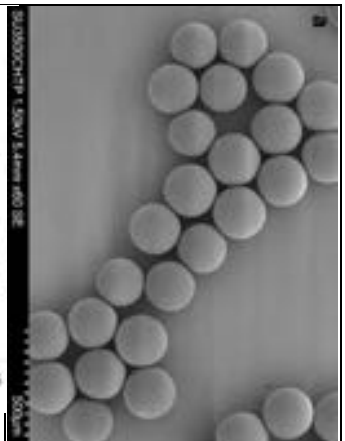

Fig. 3. *SEM image of magnetic PLGA microspheres formulated with 50:50 ratio of lactide to glycolide co-polymers.*

Laying to Rest the Magnetically Dead Layer in Magnetic Nanoparticles

Mythreyi Unni,[1] Amanda Uhl,[2] Shehaab Savliwala,[1] Benjamin H. Savitzky,[3] Rohan Dhavalikar,[1] Nicolas Garraud,[6] David P. Arnold,[6] Lena F. Kourkoutis, [3,4,5] Jennifer Andrew,[2] and Carlos Rinaldi[1,7,*]
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[3]Department of Physics, Cornell University, Ithaca, NY, 14853, USA,
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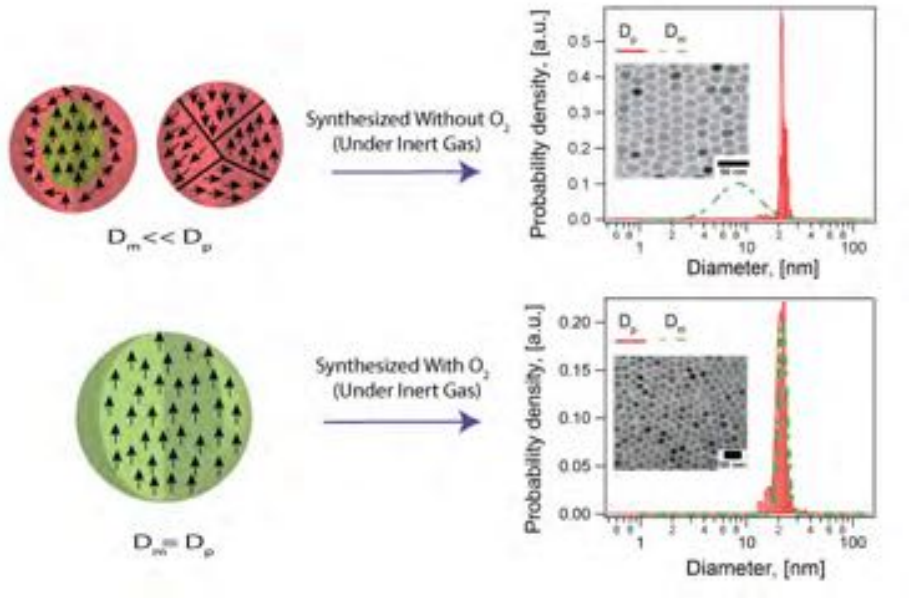
[5]Kavli Institute at Cornell for Nanoscale Science, Cornell University, Ithaca, NY, 14853, USA
[6]Interdisciplinary Microsystems Group, Department of Electrical and Computer Engineering, University of Florida, Gainesville, FL, 32611, USA
[7]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, 32611, USA
[*]Presenter

Decades of research focused on size and shape control of iron oxide nanoparticles have led to methods of synthesis that afford excellent control over physical size and shape, but comparatively poor control over magnetic properties. Synthesis methods based on thermal decomposition of organometallic precursors yield particles with mixed iron oxide phases resulting in poor magnetic properties. One feature of this is the existence of a relatively thick (several nm) "magnetically dead layer" calculated from the difference between the physical and magnetic diameters of the nanoparticles. Guided by the hypothesis that traditional thermal decomposition syntheses are carried out under conditions where oxygen is the limiting reactant, we identified conditions for the safe stoichiometric addition of molecular oxygen as a reactive species.[1] Synthesis of nanoparticles by popular routes, such as the heating-up and extended LaMer methods, with and without controlled oxygen addition into the reactor clearly shows that particles synthesized with controlled oxygen addition have magnetic properties approaching those of bulk magnetite and have thin (< 1 nm) magnetically dead layers, whereas particles synthesized in the absence of oxygen have relatively thick (up to 5 nm) magnetically dead layers, particularly for particle physical diameters above 20 nm. Furthermore, high resolution electron microscopy suggests that particles synthesized with controlled addition of oxygen consist of uniform single crystals with minimal defects. The improved magnetic properties and thin magnetically dead layers lead to improvements in functional particle properties relevant for biomedical applications.

References:

1. Mythreyi Unni, Amanda Uhl, Shehaab Savliwala, Benjamin Savitzky, Roham Dhavalikar, Nicolas Garraud, David Arnold, Lena Kourkoutis, Jennifer Andrew, and **Carlos Rinaldi**, "Thermal decomposition synthesis of iron oxide nanoparticles with diminished magnetic dead layer by controlled addition of oxygen." *ACS Nano*, **11**(2):2284-2303, 2017. [doi: 10.1021/acsnano.7b00609]



Wednesday, June 7, 2017

7:30	Breakfast at the The Venue		
	Session 6: Particle Manipulation and Control (Chair: Bolding)		
8:30	**Friedman**	**USA**	**Comparison of different strategies for active transport of magnetic particles in biological fluids and tissues**
9:10	Engelhard	USA	Design and initial characterization of a novel tissue culture tray for the study of magnetically-induced rotary traction of iron oxide nanoparticles
9:30	Chavez	USA	Magnetic field-directed self-assembly and chaining in multiferroic Janus nanofibers
9:50	Unni	USA	Understanding Magnetic Nanoparticle Dynamics in Synovial Fluid Analogues
10:10	Faust	USA	Aligning Alginate-Hydroxyapatite Biocomposites with Magnetic Nanoparticles for Bone Graft Applications
10:30	Coffee Break		
10:50	Monsalve	USA	Poly(Lactic Acid) Magnetic Microparticle Synthesis, Surface Functionalization, and Protein Isolation
11:10	Todd	USA	Correlation of cell volume and toxicity with nanomaterial endocytosis
11:30	Secret	France	Bio-functionalized magnetic nanoparticles for remote control of differentiation and oriented growth of neuronal cells
11:50	Mao	USA	Biocompatible and Label-Free Separation of Circulating Tumor Cells in Ferrofluids
12:10	Panel Discusion with Session 6 presenters		
12:30	Lunch and Closing Remarks at the The Venue		
	Session 7: Conference Closing (Chairs:Jennifer Andrew, Mark Bolding and Thompson Mefford)		

Comparison of different strategies for active transport of magnetic particles in biological fluids and tissues

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Magnetic nano- and micro-particles are being developed for various biomedical applications including hyperthermia, imaging, mechanical stimulation, toxin extraction, and others. Significant amount of research focusing on such issues as size and surface functionalization has been performed related to bio-distribution of magnetic particles, their sequestration in various organs, cells, and subcellular compartments. Mechanisms of active magnetic particle transport in biological fluids and bodily tissues under the influence of external magnetic field received much less attention so far.

This paper will summarize some theoretical and experimental work comparing two magnetic field actuated transport mechanisms: 1) a locomotion strategy that uses energy delivered through time-varying magnetic field and 2) dragging of particles by forces created through external magnetic field gradients. The comparison will begin by treating the biological fluid as a Newtonian fluid. The possibility of colloidal magnetic particles' locomotion will be demonstrated using a pair of colloidal particles subject to a rotating uniform magnetic field (see Fig. 1A). Comparison with dragging yields a superior scaling properties as the locomotion rate decays linearly with the particle sizes, while the dragging rate decays proportional to the square of the particle size. More complex colloidal particle dynamics, including chaotic motion, will be demonstrated when the number of colloidal particles increases (see Fig. 1B). Subsequently, the analysis will consider media more similar to soft tissues where porosity can play a substantial role. In this case, using the Brinkman model [1] of flow in porous media, it will be shown that scaling advantages of locomotion may be lost as the flow is dominated by the ratio of particle to pore size. Finally, some experimental results will be reviewed suggesting that, among other things, non-linear effects may play an important role resulting in the possibility that AC-modulated transport provides important benefits for magnetic particle dragging.

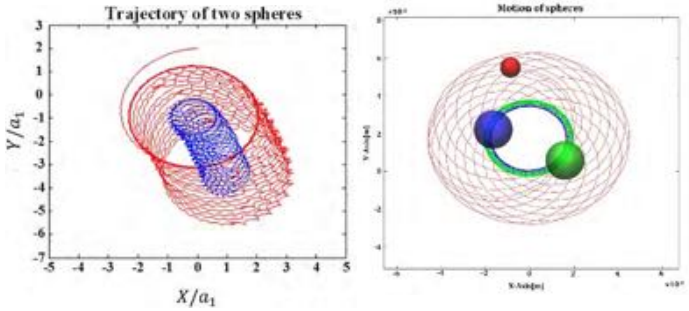

Fig.1. Simulation of magnetic particle trajectories. A) Locomotion of particle pair (radii a_1 and a_2) under rotating magnetic field when the rate of the field rotation changes twice per the pair rotation cycle. B) Chaotic motion of particle triplet under steadily rotating magnetic field.

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Design and initial characterization of a novel tissue culture tray for the study of magnetically-induced rotary traction of iron oxide nanoparticles

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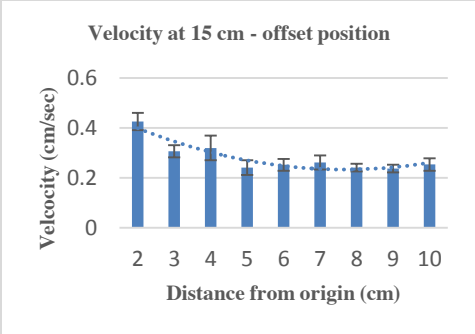
Background: Superparamagnetic iron oxide nanoparticles (SPIONs) have been touted as promising vehicles for enhancing drug delivery for cancer, stroke, and other diseases. To date, successful clinical use has been hampered by the problem of scale, since the attractive force between iron particles and a magnet is inversely proportional to at least the fourth power of the distance. Magnetically-induced rotary traction (MIRT) offers a means to overcome this obstacle. Here, we present data from the use of three-part system which includes: 1) a patented rotating magnet (mini-MED), 2) magnetic microbeads (MBs), which have been optimized for MIRT, and 3) a novel tissue culture tray (MIRT tray), useful for studying the movement and cellular uptake of MBs at clinically-relevant distances.

Methods: MBs and the rotating magnet (mini-MED) were provided by Pulse Therapeutics (St. Louis, MO). MBs consist of single-crystalline magnetite cores (~70 nm), which form aggregates in response to a magnetic field. Here, the field is generated by a neodymium-boron-iron permanent magnet, which is rapidly rotated (3 Hz) in a fixed position, causing MBs to counter-rotate (like meshed gears), and move by means of surface traction. The MIRT tray was designed using CAD software, and produced either by 3D printing, or subtractive manufacturing (milling) of acrylic. The MIRT tray was designed to be compatible with a standard 96-well plate reader, but with lanes (3-5 mm width) instead of wells (see Figure 1). The bottoms of the lanes are semi-circular, in order to mimic luminal surfaces of vessels, catheters, and other biological conduits. Movement of MBs in the MIRT tray was measured at various distances (and relative positions) from the mini-MED, using video photography. MB velocities in phosphate-buffered saline (PBS), tissue culture medium with 10% serum, and 100% serum were determined. Trays were sterilized using ethylene oxide. Human glioblastoma cells were maintained using standard tissue culture technique, before and after being seeded into the lanes of the MIRT tray. Cells grown in the tray were studied using standard (inverted) light microscopy.

Results: MIRT tray position in relation to the Mini-MED was found to greatly affect MB movement, and was divided into 4 categories: pull, push, centered, and offset. Magnetization of the MBs prior to testing greatly increased velocity. MBs moved readily through PBS, culture medium, and serum at distances from 7.5 – 30 cm from the mini-MED. A representative plot is shown indicating MB velocity in the offset position, as a function of lateral distance, at 15 cm from the magnet. Maximum bead velocity at this setting was 0.42 +/- 0.05 cm/sec.



Conclusions: MBs are easily rotated and moved (translated) at physiologic distances, even through 100% serum, by means of surface traction generated by the Pulse mini-MED system. These features show that the Pulse system is an ingenious one for magnetic drug targeting, circumventing the problem of scale by rotating the particles. The MIRT tray is a convenient device which allows SPION translation to be studied in an inexpensive model system. Current investigations with MBs and the mini-MED system are underway in order to evaluate cellular adhesion and uptake, clot lysis, and delivery of therapeutic agents.

Magnetic field-directed self-assembly and chaining in multiferroic Janus nanofibers

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Nanofibers have unique properties and potential application in photonics, nanoelectronics, biosensors, and optoelectronics[1]. Multiferroic nanofibers couple piezoelectricity and magnetostriction, allowing electrical control of magnetism and vice-versa. We report on alignment and chaining in $BaTiO_3$-$CoFe_2O_4$ fibers using magnetic field-directed self-assembly. While chaining has been studied extensively in nanoparticles, similar studies in nanofibers are rare[2]. Methods for aligning nanofibers include electric-field-assisted alignment, magnetic-field-assisted alignment, Langmuir-Blodgett method and microfluidic techniques[3].

Our Janus nanofibers consist of two hemi-cylinders and are produced by electrospinning with a combination of $BaTiO_3$(68% weight) and $CoFe_2O_4$(38%).[4] We grind the fibers to produce random distribution of lengths with an average diameter of 1μm. The nanofibers are then suspended in polyvinyl alcohol using citric acid and sodium hydroxide to provide colloidal stability. Before assembly, the suspended fibers are sonicated and then spin-coated onto glass wafers. We cure the polymer films in an electromagnet as a function of magnetic field strength. The samples are then imaged with bright-field microscopy and alignment and chain length extracted with ImageJ.

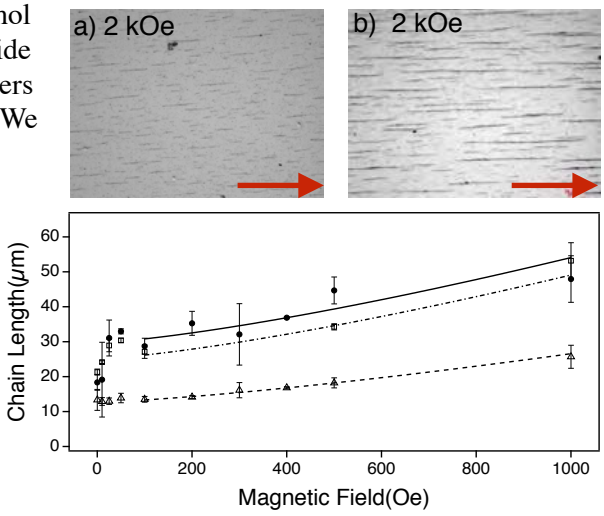

Figure 1.: Sample Pictures: a) highest concentration, b) lowest concentration sample.
Average Chain Length vs Magnetic Field: c)△ is the base sample with the lowest concentration of fibers, □ is two times as concentrated, ● is three times as concentrated, the

Figure 1a-b show images of 2 kOe aligned composites made from weak and strong concentration solutions respectively. Figure 1c shows that average chain length increases with magnetic field. For the weakest concentration, the increase follows the same 4/3 power law observed for nanoparticle chaining (dashed line)[2]. At twice and three times the concentration, chain length increases rapidly at low fields, but above 100 Oe also follows the chaining power law (dash dot and solid lines)[2]. We hypothesize that the rapid increase in chain length at high fiber concentration is a field driven homogenization process whereby shorter fibers agglomerate to form longer fibers, that then chain together in dipolar or tip-to-tip fashion at higher magnetic fields.

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Understanding Magnetic Nanoparticle Dynamics in Synovial Fluid Analogues

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The use of nanoparticles in complex biological environments has motivated study of their dynamics in concentrated mixtures of macromolecules. Synovial fluid, a lubricant found in joints, is one such complex fluid, with macromolecules like hyaluronic acid and lubricin as major constituents that define its structure and function. Fundamental knowledge of how nanoparticles diffuse in synovial fluid would help engineer better drug delivery agents and also improve basic understanding of the structure of synovial fluid. Here, we study the translation and rotation of magnetic nanoparticles in simulated synovial fluids.

Hyarulonic acid (HA) solutions at concentrations where the HA molecules are well separated (i.e., the dilute regime) and where they overlap (i.e., the semi-dilute regime) were prepared as a first approach to mimic the composition of synovial fluid. Cobalt ferrite particles of two hydrodynamic sizes (40 nm, left and 240 nm, right in figure below) coated with polyethylene glycol and a diblock polymer, Polyethylene glycol-Polylactic acid (PEG-PLA) respectively were suspended in these HA solutions to study the effect of particle size on hydrodynamic drag exerted by the complex fluid matrix. The dynamic response of the particles to an applied alternating magnetic field was detected and analyzed to obtain the rotational diffusion coefficient of the particles and, through the Stokes-Einstein relation, the apparent viscosity of the fluid. We found that the average viscosities obtained from nanoscale measurements were similar to that of water and did not correspond to the viscosity of the bulk fluid as measured using a rheometer, for HA solutions in both the dilute and semi-dilute regimes. Control measurements of rotation of the particles in glycerol solutions indicated that the viscosity determined by rotation of the particles in simple fluids was similar to the bulk viscosity.

To complement these measurements, the translation of the magnetic nanoparticles in these synovial fluid analogues was also studied. Magnetic nanoparticles were subjected to an external magnetic field gradient and the extent of translation was monitored by the amount of particles recovered with time. The rate of translation of particles in solutions in the semi-dilute regime was found to be slower than for particles in solutions in the dilute regime, indicating greater viscous drag experienced by the particles in the more concentrated HA solutions.

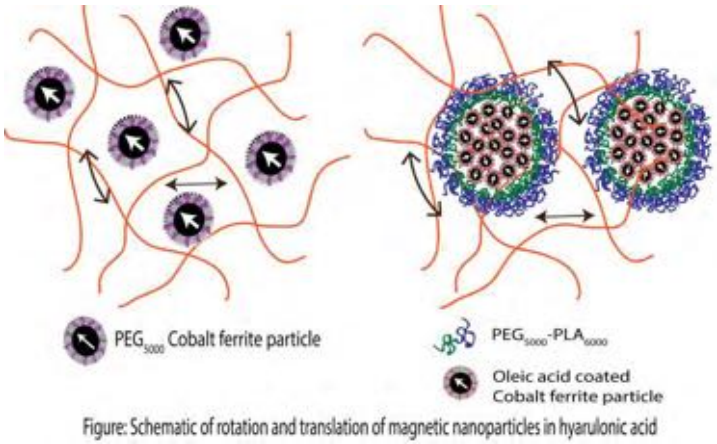

Figure: Schematic of rotation and translation of magnetic nanoparticles in hyarulonic acid

These studies suggest that rotational motion of nanoparticles below 240 nm in diameter is unimpeded by the HA network in these synovial fluid analogues, whereas translation of the particles does appear to be impeded by the HA network, albeit the effect is much less pronounced than expected based on macroscopic rheological measurements. Ultimately, these observations provide insight into the dynamics of nanoparticles in complex biological fluids and can serve to develop novel nanoparticle-based drug delivery and diagnostic technologies applicable in joint diseases.

Aligning Alginate-Hydroxyapatite Biocomposites with Magnetic Nanoparticles for Bone Graft Applications

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There exists a push towards replacing traditional autografts with an injectable and biocompatible synthetic material. Alginate-hydroxyapatite (AH) hydrogel composites are promising candidates for bone tissue scaffolds due to their biocompatibility and osteoconductivity. However, AH hydrogels are inherently weak materials and therefore not yet suited for bone graft applications. Here we suggest decorating the surface of the hydroxyapatite fibers with super paramagnetic iron oxide nanoparticles to magnetically orient the fibers in the direction of the principle stress. This method significantly improves the mechanical properties of fully hydrated samples while maintaining the biocompatibility and osteoconductivity properties of the original scaffold.

Magnetically responsive HA rods were produced through hydrothermal precipitation and functionalization with iron oxide nanoparticles following our previously reported protocol [1]. Magnetic hydroxyapatite rods were added to alginate solutions at varying concentrations (1 to 13w/v%), subjected to magnetic fields and vibration, and cured to form aligned AH composites. Prior to applying the field, low concentration $CaCl_2$ (0.075w/v%) was added to AH solutions in a 1:2 ratio to locally crosslink the polymer and produce a uniform film. The AH solutions were transferred to molds and aligned with 150 Gauss magnetic field and vertical mechanical vibration. The film was then fully crosslinked in 10w/v% $CaCl_2$. This procedure prepares samples with parallel (Pa-AH), perpendicular (Pe-AH), and random alignment (no magnetic field, NM-AH) with respect to the principle stress axis.

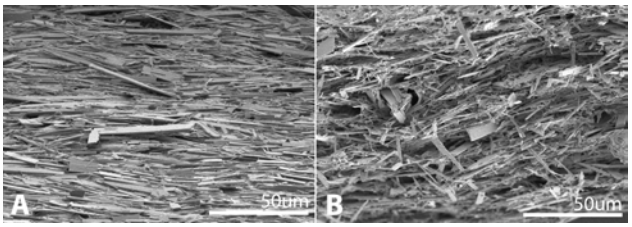

Table 1: Mechanics of 13v% AH films.

Sample	Strength (kPa)	Elongation (%)	Modulus (MPa)
Control	*87.8*	*100*	*0.10*
Pa-AH	244.1 ± 23.6	15.4 ± 1.6	1.93 ± 0.23
NM-AH	206.7 ± 26.1	21.4 ±1.58	1.11 ± 0.12
Pe-AH	154.9 ± 9.7	38.1 ± 4.0	0.51 ± 0.03

Figure 1: SEM images showing AH composites with (a) magnetic alignment Pa-AH and (b) without alignment (no magnetic field, NM-AH) . The aligned composite is mechanically superior.

Comparison of these sample groups provides insight into the strengthening role of magnetically oriented reinforcing fibers within hydrated hydrogel matrices. Nanoparticle surface coverage and rod alignment was confirmed with scanning electron microscopy as shown in *Figure 1*. Film mechanics were measured in the fully hydrated state using Dynamic Mechanical Analysis. The mechanics of the best performing composite, 13v%, compared to a control alginate film is shown in Table 1. By aligning the rods parallel to the applied load, the strength and modulus of the hydrated films was increased to 244 kPa and 1.93 MPa, respectively, compared to 87.8 kPa and 0.1 MPa for the control alginate film. Contrary to traditional discontinuous fiber composite theory, the ductility was increased by aligning fibers perpendicular to the applied load. Wide Angle X-Ray Diffraction (WAXD) was used to investigate fiber alignment at different stages of elongation showing rod rotation during tensile test, the contributing factor to the increased ductility.

In this work, a high strength alginate-hydroxyapatite composite material capable of promoting bone regeneration was developed for injectable bone graft applications. Magnetic nanoparticles allow manipulation of the microstructure to tailor the mechanical properties to increase strength or ductility, depending on the desired final properties. These results show that a high strength alginate-hydroxyapatite is available and a promising material for injectable bone graft applications.

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Poly(Lactic Acid) Magnetic Microparticle Synthesis, Surface Functionalization, and Protein Isolation

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University of Florida, J. Crayton Pruitt Department of Biomedical Engineering[1]
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**Email: amonsalve5@ufl.edu*

Abstract:

Magnetic particles continue to be utilized in novel biomedical applications including the isolation cells, proteins, and nucleic acids. The ease of magnetic particle-based biomolecule isolation has resulted in significant growth in the usage of this technology to study biomedical phenomena. Additionally, short time requirements for biomolecule or cell isolation by means of magnetic particles help to increase the efficiency of the isolation process as well as the maintenance of functionality for downstream assays. The current work aims to synthesize a magnetic particle in an inexpensive fashion in hopes of developing a viable magnetic particle platform for applications such as protein, DNA, or cell isolation. The crucial property of the particles for this application is their fast magnetic separation using a standard NdFeB magnet and easy surface functionalization. To produce the magnetic properties needed to accomplish this task, magnetic nanoparticles were first synthesized using an aqueous co-precipitation. Subsequently, the magnetic nanoparticles were incorporated within a Poly (Lactic Acid) matrix through a double emulsion, solvent evaporation with dichloromethane. The particles were characterized DLS, light microscopy, and SQUID magnetometry. The ability to functionalize the surface was verified through a Ni-NTA functionalization using his tagged proteins in conjunction with flow cytometry.

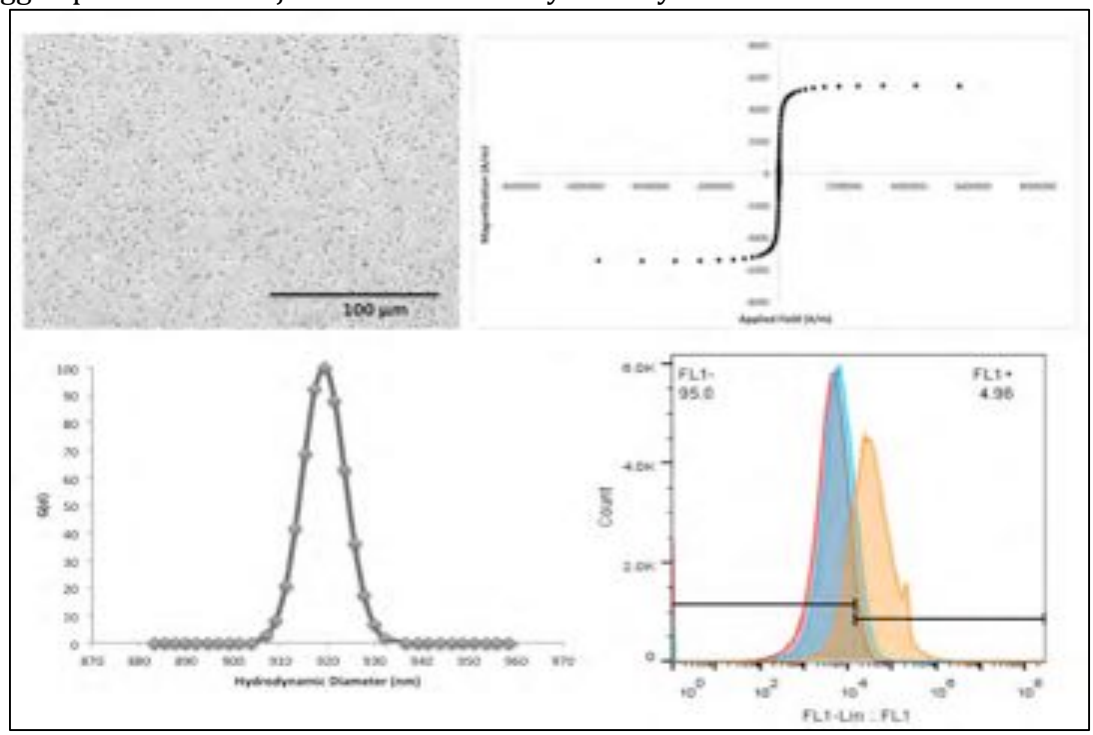

Figure 1:a) PLA magnetic microparticles light microscope image b)M vs. H curve c)Size Distribution d) His-Tagged Protein Isolation

Correlation of cell volume and toxicity with nanomaterial endocytosis: An application of magnetic cytometry

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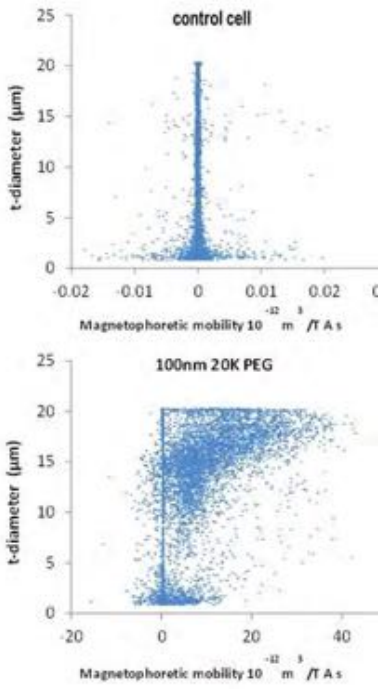
The endocytosis of nanomaterials by a wide variety of cell types is a subject of rapidly rising interest. Magnetic nanomaterials are of greatest interest in this context owing to their in vivo traceability, their potential for guided drug delivery, their use as magnetic imaging contrast media, and their widespread use in cell purification and rare cell detection. Furthermore it is essential to understand the effect on the cell of the endocytosis of magnetic nanomaterials. We investigated the uptake of superparamagnetic iron oxide nanoparticles (SPIONs) by mammalian cells in monolayer culture by exposing Chinese hamster ovary cells, line CHO-K1 which is frequently used in industrial applications, to Chemicell FluidMagD nanoparticles with diameters of 50 and 100 nm and five different surface coatings. Association constants were determined for several conditions on the basis of particle uptake in 24 hours. The amount of particle uptake was determined by measuring the magnetophoretic mobility distributions of treated and untreated cell populations using a Hyperflux™ magnetic particle tracking velocimeter. Cell volumes and viabilities were evaluated on the basis of cell count data from the Hyperflux™ velocimeter and from flow cytometric light-scatter and fluorescence data using an Accuri® C6 Flow cytometer. Cell viability decreased with increasing uptake of SPIONs, which was also manifested as an increase in average cell volume. The maximum cell loss observed was about 50%. Starch-coated and positively charged SPIONs were taken up most effectively, and these led to cell volume increases of several per cent, which, if due to particles only, corresponds to several thousands of SPIONs per cell.



Cell size vs. magnetophoretic mobility. Top: Control. Bottom: Cells treated with positively charged 100 nm SPIONs.

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Bio-functionalized magnetic nanoparticles for remote control of differentiation and oriented growth of neuronal cells

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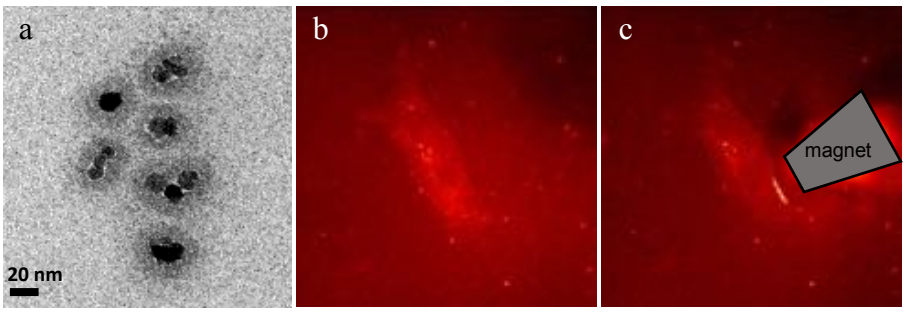
Neurodegenerative disorders, such as Parkinson's, Alzheimer's or Huntington's diseases are among the most common group of medical conditions in the world, and are expected to surpass cancer by 2040.[1] However no cure exists for such diseases at that time. Cell replacement therapy is among the most promising approach to treat neurodegenerative disorder. In the work presented here, part of the MAGNEURON European project,[2] we used magnetic nanoparticles that are bio-functionalized to trigger neurons' differentiation and growth along the direction of use of the external magnet gradient. Mature neurons would in term be re-implanted in the patient brain to replace degenerated neurons.

To this goal, maghemite (γ-Fe_2O_3) nanoparticles were synthesized by an inverse co-precipitation process.[3] These nanoparticles were then used to synthesize γFe_2O_3@SiO_2 core-shell nanoparticles with size, charge and magnetization adjusted to obtain a good colloidal stability, render them injectable in cells, and facilitate intracellular motion. These magnetic nanoparticles (MNPs) were then functionalized with a HaloTag ligand in order to interact specifically with proteins able to trigger different pathways in the cell. MNPs were then microinjected in the cell and showed intra-cellular biased diffusion toward the micro-magnet. The magnet can then be used to displace target proteins attached to the MNPs inside the cell, and trigger signaling events such as actin polymerization at particular subcellular localizations.[4,5]



a) TEM image of core-shell MNPs, b) and c) fluorescence microscopy image of a cell injected with MNPs before (b) and after (c) approaching a magnet

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[5] Etoc et al. Subcellular control of Rac-GTPase signalling by magnetogenetic manipulation inside living cells, Nat. Nano (2013) 8, 193-7.

Biocompatible and Label-Free Separation of Circulating Tumor Cells in Ferrofluids

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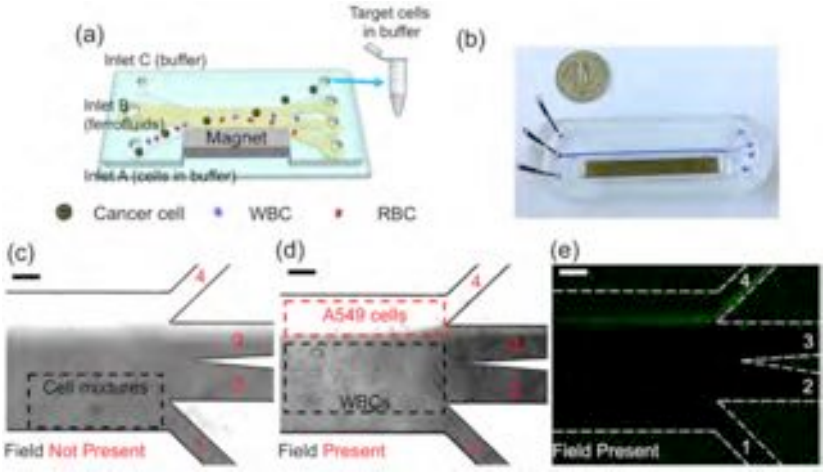
This paper describes a biocompatible and label-free cell separation strategy using ferrofluids in microfluidic devices. Separating cancer cells from whole blood is useful in practical applications such as enriching circulating tumor cells (CTCs) in peripheral blood. Since CTCs occur at a concentration of 1-100 cells every 1 billion of red blood cells (RBCs) and 1 million of white blood cells (WBCs), its enrichment requires the development of a highly efficient and high-throughput separation. Our cell separation is based on cell size difference, and conducted in a custom-made biocompatible ferrofluid that retains not only short-term viabilities, but also normal proliferations of 7 commonly used cancer cell lines. The microfluidic device is designed and optimized specifically to shorten the exposure time of live cells in ferrofluids from hours to seconds, by eliminating time-consuming off-chip sample preparation and extraction steps and integrating them on-chip. This combination of approaches resulted in a live cell separation strategy in ferrofluids. As a proof-of-concept demonstration, a ferrofluid with 0.26% volume fraction was used in a device to separate spiked cancer cells (100 cancer cells/mL, A549 lung cancer cell line and MCF-7 breast cancer cell line) from diluted whole blood at a 0.9 mL/h throughput. The separation efficiencies were 77±6% for A549 cell line, and 84±4% for MCF-7 cell line. Separated cancer cells purity was on the order of 60%. Same spiked cancer cells from undiluted whole blood with red blood cells lysed were also separated at the same throughput. This time, the separation efficiencies were 73±4% for A549 cell line, and 78±3% for MCF-7 cell line, and separated cancer cells purity was between 6-7%. After separation, captured cancer cells showed excellent viability (93.8±1.5%) and normal proliferation.



(a) Schematic illustration of the biocompatible ferrohydrodynamic cell separation strategy. Cell sample, ferrofluid, and buffer are injected into the device without pre-mixing. Cells are only in contact with ferrofluids when they are separated from each other. After separation, larger cancer cells are extracted into the buffer stream, eliminating the washing step. Total exposure time of cells to ferrofluids is estimated to be seconds. (b) Top-view of the proposed device, which consists of a microchannel and a permanent magnet, their relevant dimensions, and labeling of inlets and outlets. (c)-(d) Separation of A549 lung cancer cells and undiluted white blood cells (WBCs).

Poster Session: Monday, June 5, 2017

18:00	Poster Session	The Venue	
Poster #	Presenter	Country	Title
1	Anker	US	Multifunctional magnetic nanoparticles for sensing and imaging
2	Chapman	Us	Magnetite Functionalization of Silica-Overcoated Gold Nanorods via Controlled Heteroaggregation
3	Lanier	US	Evaluating the Potential of Commercially Available Magnetic Nanoparticles for Hyperthermia
4	Livesey	US	Interacting magnetic nanoparticles under applied magnetic fields
5	Mair	US	Multi-segmented Magnetic Rods for Loading and Releasing Payloads
6	Oberdick	US	Magnetization Reduction and Domain Formation in Magnetite Nanoparticles
7	Pan	US	Crack Paths in Anisotropic Biomimetic Composites Textured by Magnetic Nanoparticles
8	Rao	India	Nano silver ferrite, a better tool of Target drug delivery than
9	Rich	US	MRI guided drug delivery for location specific neuromodulation
10	Rivera	US	Magnetic nanoparticle thermal therapy to induce mitotic
11	Samia	US	Reactive Extrusion Strategies to Fabricate Magnetite–Polyethylene
12	Sandler	US	Systematic Investigation of Cobalt Doped Ferrites for Increased Energy Conversion in
13	Savliwala	US	Quantitative Exploration of Iron Oxide Nanoparticle Purification Through
14	Singh	US	Magnetically templated hydrogels for peripheral nerve injury repair
15	Todd	US	Finite element analysis of a magnetic cell separation device:
16	Warnock	US	Design and Optimization of a Magnetic Separation Chamber for Filtration of
17	Zando	US	Using Magnetic Nanoparticles for the Design of Calcium
18	Zhao	US	Brownian dynamics simulations of dipolar interacting magnetic nanoparticles

Multifunctional magnetic nanoparticles for sensing and imaging

*Gretchen Schober[1], Hongyu Chen[1], Unaiza Uzair[1], Fenglin Wang[1], Thomas Moore[2], Qi Bin[3], Dino Sulejmanovic[1], Shiou-Jyh Hwu[1], Thompson Mefford[3], Frank Alexis[2], Jeffrey N. Anker[1,2]**

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Nanoparticles are well suited for drug delivery because they can serve as targeted drug carriers to deliver drugs into cells and tissues. Imaging the nanoparticles in tissue and measuring local drug release is important because heterogeneous environments and drug release can affect treatments. Rare-earth doped inorganic nanophosphors can be detected at high resolution through tissue using X-ray excited optical luminescence to provide high resolution images. In addition, the nanoparticles produce light when in proximity to radioisotope-labeled drugs. The nanoparticles are also MRI contrast agents and can be coated with encapsulated drug and functionalized for cancer cell targeting. We describe the imaging and sensing techniques, as well as methods to improve scintillation efficiency by annealing the particles and increasing crystal domain size. Overall, these nanophosphors have controllable size, shape, magnetic, chemical, and optical properties which can be used for multifunctional sensing and affecting through tissue.

Magnetite Functionalization of Silica-Overcoated Gold Nanorods via Controlled Heteroaggregation

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By assembling different kinds of nanoparticles (NPs), novel optical, magnetic, electronic, or catalytic properties can be integrated in multifunctional NPs that are not available in NPs of a single type. The ability to build multifunctionality within individual NPs is potentially useful in a wide range of applications, including optoelectronics, catalysis, multimodal imaging, drug delivery, sensing, and catalysis. Methods for assembling composite nanoparticles include seeded growth of one kind of NP onto another and linking two or more types of NPs together using chemical (e.g., small molecule linkers, DNA) or physical (e.g., electrostatic attraction, entrapment) means. Each of these methods has advantages and disadvantages, and a need remains to design simple, effective, and broadly applicable methods for preparing multifunctional NPs.

Here we report a method for depositing magnetite (Fe_3O_4) NPs onto the surface of silica-overcoated gold nanorods (SiO_2-GNRs) via nonsolvent-induced heteroaggregation. While the principle of heteroaggregation is well established, it surprisingly underutilized for assembly of multifunctional NPs. Under certain conditions, mixing magnetite (Fe_3O_4) NPs stabilized by oleylamine and dispersed in a nonpolar solvent with SiO_2-overcoated GNRs (SiO_2-GNRs) dispersed in a polar solvent results in controlled deposition of Fe_3O_4 NPs onto the surface of SiO_2-GNRs. The nonsolvent drives the Fe_3O_4 NPs onto the surface of the SiO_2-GNRs through a process known as heteroaggregation, resulting in a Fe_3O_4-SiO_2-GNRs with a satellite/core morphology with a high yield in under 20 minutes. The density of the Fe_3O_4 NP coating can be controlled by varying the ratio of Fe_3O_4 NPs to SiO_2-GNRs. The Fe_3O_4-SiO_2-GNR products maintain the longitudinal surface plasmon resonance of SiO_2-GNRs and exhibit a strong magnetic response, which allows for magnetic separation within x minutes using permanent magnets. As prepared, Fe_3O_4-SiO_2-GNRs disperse in nonpolar solvents (e.g., hexanes, THF, toluene) because of the oleylamine ligands on the Fe_3O_4 NPs that are exposed to the solvent. Fe_3O_4-SiO_2-GNRs can be rendered dispersible in polar solvents (e.g., water, ethanol, methanol) by functionalizing the Fe_3O_4 NP surface coating on the SiO_2-GNRs with poly(ethylene glycol)-catechol. This heteroaggregation approach is simple, effective, and potentially broadly applicable for driving assembly of combinations of NPs with hydrophilic and hydrophobic surface coatings.

Interacting magnetic nanoparticles under applied magnetic fields – how to estimate the local heat dissipation?

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Ferromagnetic nanoparticles interact with one another via magnetostatic interactions. These interactions substantially alter their response to an external magnetic field. The hysteretic heating from a system of particles can be used to perform magnetic hyperthermia treatment or heat-assisted drug delivery, and its magnitude can be estimated by calculating the area of a M(H) loop.

Whilst calculating the global hysteretic heating by a polydisperse, interacting system of particles, we found that some of the smaller particles had what is known as "inverted hysteresis loop" with respect to the external applied field. That is, the M(H) graph is flipped compared to a typical hysteresis loop. This poses the question: although the global heating can be estimated, how does the local heating vary from particle to particle of different sizes, experiencing different local fields?

To understand this phenomenon better, we began by studying a system with just two particles (one large and one small, both ferromagnetic, see the Figure) interacting with each other via dipolar fields and also under the influence of an external field. We performed kinetic Monte Carlo calculations that include the effects of finite temperature and real timescales, and also energy minimization calculations that are similar to Stoner-Wohlfarth theory. We found that when the small particle flips from one energy-well to another during a minor M(H) loop, the large particle has very small changes in its magnetization, as shown by the red lines of the Figure's insert. Although these changes are small, it turns out that they impact the global area under the M(H) curve and must be considered. Our on-going work to calculate how the complicated M(H) loops impact the local temperature will be discussed.

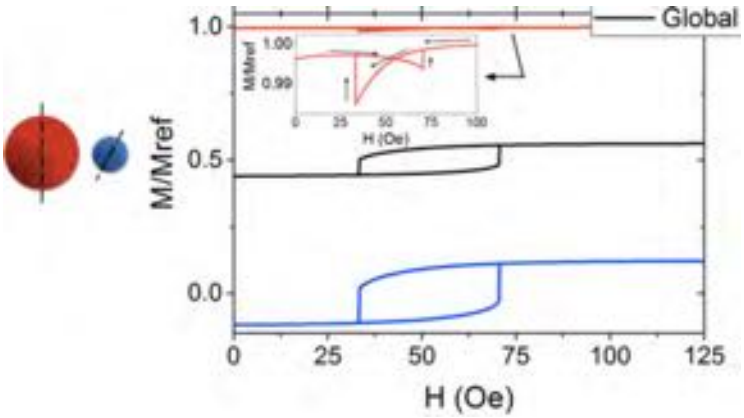

Figure: Minor M(H) loops calculated for a large particle (top, red), a neighboring small particle (blue, bottom) and the global system (black). The two particles are drawn to the left of the graph, with their anisotropy axes shown, and the magnetic field is applied upward.

Multi-segmented Magnetic Rods for Loading and Releasing Payloads

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Introduction: Magnetic particles hold the promise of delivering drugs to specific locations in the body. Multisegmented magnetic rods[1,2] are capable of embodying a spectrum of functionalities, surfaces, and material types. We have previously developed nanorods with orthogonal magnetic domains. Here we demonstrate the addition of a polypyrrole segment for loading a model payload, brilliant green dye. Polypyrrole is a biocompatible[3,4] conductive polymer.

Methods: Multisegmented nanorods composed of nickel, gold, and polypyrrole nanorods are grown via electroplating into the pores of anodized aluminum oxide membranes, followed by etching of the membrane resulting in release of the nanorods. Brilliant green dye is incorporated into the particle as a model payload. Payload release is characterized by ultraviolet-visible (UV-Vis) spectroscopy. Particles can be guided to various regions of a fluidic chamber for location-specific release using an array of six electromagnets.

Results and Discussion: We characterize the nanorods, and validate growth of various segments of nickel, gold, and polypyrrole (Figure 1A). We demonstrate loading and unloading of molecules (Fig. 1B), as well as positional control of nanorod location using an electromagnet array (Figure 1B, inset). Future work incorporating multiple payloads onto individual nanorods may enable the delivery of multiple complimentary payloads via a single particle. Payload delivery via nanorods or nanowires may be useful, as we have devised a method for concentrating such high aspect ratio structures using fast magnetic fields[5].

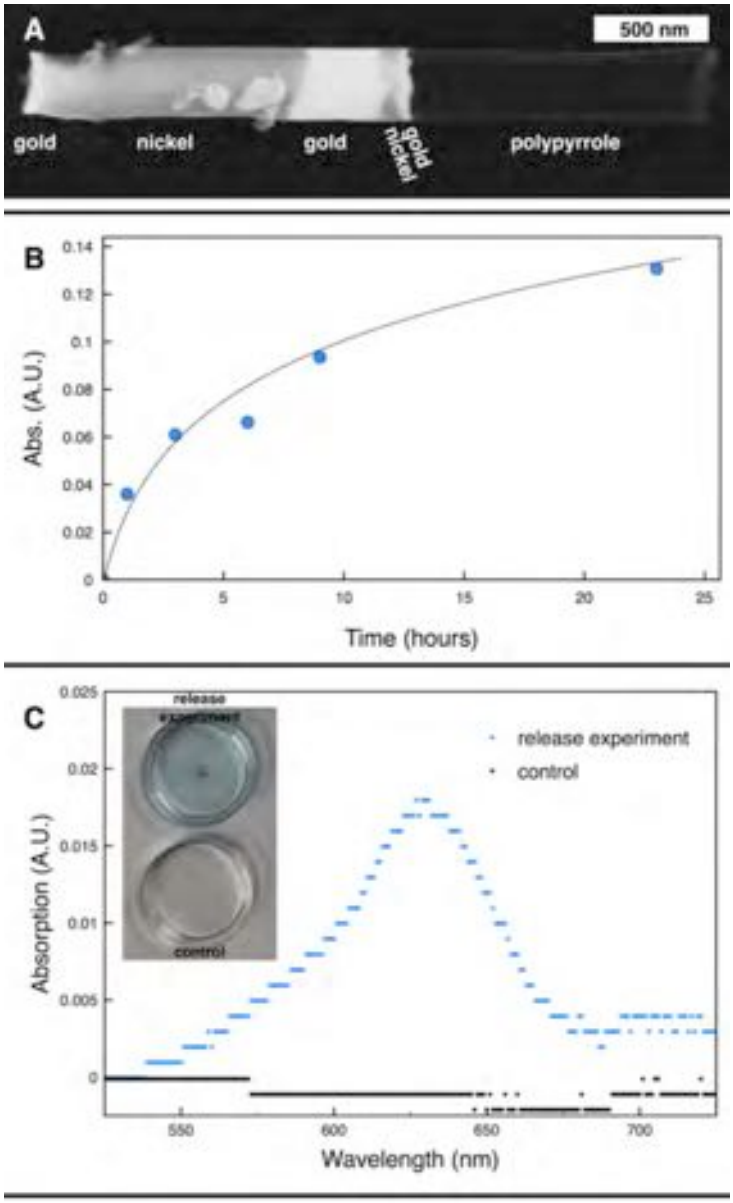

Figure 1: (A) SEM image shows nickel, gold, and polypyrrole segments. (B) Release of brilliant green (BG) over the course of 1 day. (C) UV-vis absorption spectrum for a "control" sample with no rods, and a "release experiment" sample in which loaded rods eluted BG over the course of 22 hours. (C, inset) Image showing "control" and "release experiment" after 22 hours.

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Magnetization Reduction and Domain Formation in Magnetite Nanoparticles: A Comparative Study of Three Common Thermal Decomposition Based Syntheses

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Magnetite (Fe_3O_4) nanoparticles are used for biomagnetic applications such as magnetic particle imaging (MPI) and as contrast agents for magnetic resonance imaging (MRI) because of their intrinsic biocompatibility and high saturation magnetization. Synthesis techniques using thermal decomposition are commonly used to make the nanoparticles because they generate monodisperse particles with uniform shape and material properties. However, the nanoparticles produced by these techniques often have a drastic reduction in saturation magnetization (M_S) from bulk magnetite. This is unfavorable for biomagnetic applications because reduced magnetization generates weaker magnetic signal or contrast. Here, we describe a comparative study between three thermal decomposition techniques using a combination of magnetometry, aberration corrected scanning transmission electron microscopy (STEM) and atomistic magnetic modelling [1]. Magnetite nanoparticles ranging in size from 12-14 nm are synthesized using techniques pioneered by the groups of Sun [1], Colvin [2] and Hyeon [3]. Magnetometry of each particle type shows that Sun-type particles have $M_S = 81 \pm 12$ emu/g (10% of bulk Fe_3O_4) at 10 K while Colvin and Hyeon-type particles have a drastic reduction in magnetization, $M_S = 37 \pm 1$ emu/g and $M_S = 39 \pm 4$ emu/g at 10 K, respectively. STEM revels subtle differences in the internal composition of the nanoparticles synthesized by the different techniques (Figure 1). Colvin and Hyeon-type particles comprise of multiple domains separated by antiphase boundaries (APBs), while Sun-type particles are single nanocrystals. Zero-field-cooled/Field-cooled (ZFC/FC) curves of multi-domain particles show several ZFC peaks compared to a single peak for single crystalline particles. Multiple peaks in the ZFC reflect a range of blocking temperatures for different sized domains. Atomistic magnetic modelling shows that strong antiferromagnetic interactions across the APBs in multi-domain particles drastically reduces the saturation magnetization of the particles. The study suggests that common synthetic techniques are not all equally as favorable for biomagnetic applications.

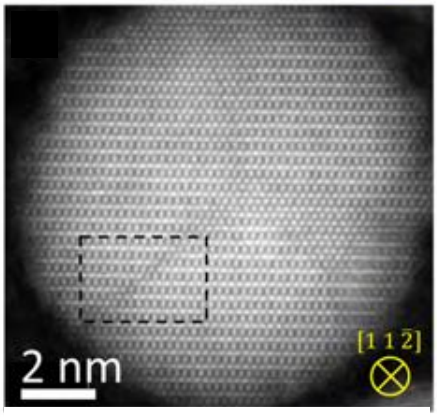

Figure 1. STEM image of multi-domain, Hyeon particle, dashed box shows APB defect interrupting crystalline order.

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Crack Paths in Anisotropic Biomimetic Composites Textured by Magnetic Nanoparticles

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Lightweight biocomposites such as nacre, bone, and bamboo exhibit strong strength and toughness. Although their toughening mechanisms were widely studied, the fracture properties of these biocomposites remain insufficiently understood at a fundamental level due to the geometrical complexity of crack paths in them. It is observed that cracks in homogeneous and elastically isotropic propagate normal to the principle stress axis, while cracks in hierarchically structured composites can strongly deflect from this axis. However, the influence of the anisotropic properties and macroscopic heterogeneities on crack propagation is still not well known. Developing this understanding is the key to elucidating the remarkable toughness of biocomposites and drawing lessons for the biomimetic design of lightweight engineering materials such as bone grafts and implants.

Here we use micron-size alumina platelets coated with super paramagnetic iron oxide nanoparticles positioned in an acrylate – urethane copolymer matrix to mimic the anisotropic structures of natural materials. The reinforcement can be aligned into designed patterns by an external magnetic field. Therefore the anisotropy of the composite can be tuned by controlling the alignment patterns as well as the concentration of the magnetic particles in the matrix. We also use a computational method to approach this cracking behavior to show the crack path found in our experiment can be theoretically and computationally predicted on the size scale of our sample.

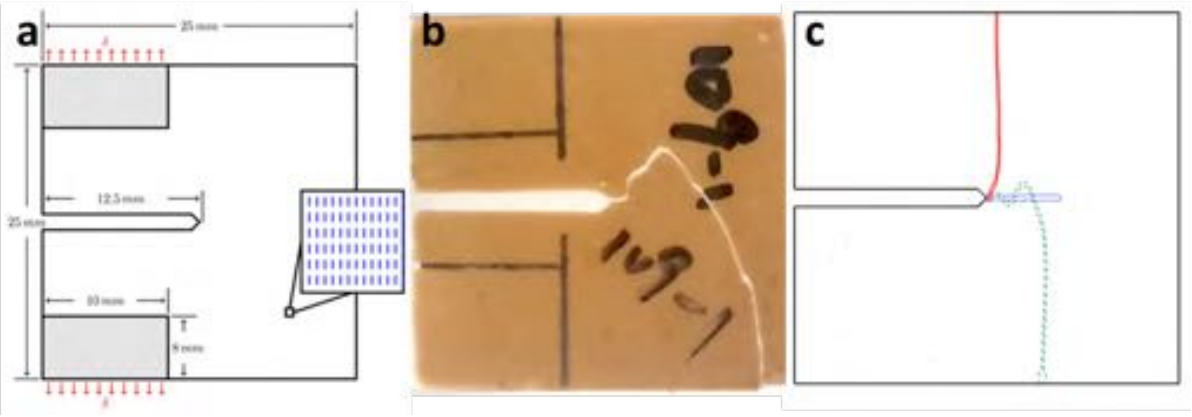

Figure 1: Crack path in biomimetic composite with a 10% volume fraction of particles aligned parallel to the tension axis. a) Sample dimensions, particle alignment pattern (blue) and loading configuration (red). b) Fracture path observed in experiment. c) Fracture path from phase-field simulations for three different anisotropies: relatively low (blue), medium (green), relatively high (red).

Nano silver ferrite, a better tool of Target drug delivery than other antimicrobial nanoferrites

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Abstract

Nanosilver ferrite is synthesised through co precipitation method [1] A new silver coated cobalt ferrite nanocomposite [$Ag@CoFe_2O_4$], was prepared by a two-step procedure. In the first step, cobalt ferrite nanoparticles were synthesized by a co precipitation method followed by combustion method using glucose as fuel . This nano cobalt ferrite was then coated with nanosilver via chemical reduction of Ag+ solution using glucose as reducing agent [2]. nanosilver is synthesized by chemical reduction of Ag+ solution.

The synthesized nano $CoFe_2O_4$, nano $Ag@CoFe_2O_4$, nanoAg and nano $AgFeO_2$compostes were characterized by X-ray diffraction, Scanning electron microscopy/transmission electron microscopy, and vibrating sample magnetometer.

The antibacterial activity of these nanoparticles were investigated against some Gram-positive and Gram-negative bacteria and compared with those of silver nanoparticles and standard antibacterial drugs. it was observed that nano silver ferrite has more antimicrobial action than all other tested nano particles.

As the nano silver ferrite has small particle size (4.5nm), good antimicrobial nature,anti fungal nature super paramagnetic and biocompatibility, so it is concluded that nano silver ferrite is better tool for target drug delivery than other tested ferrites. The detailed study is presented.

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MRI guided drug delivery for location specific neuromodulation

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Abstract

Pharmacological manipulation of neural activity is essential in both the clinic and laboratory, but current methods of drug delivery to the brain have important intrinsic limitations. Many potential neuromodulatory agents delivered systemically do not cross the blood brain barrier (BBB) and can accumulate in off target tissues. Those agents that do cross the BBB have a widespread effect throughout the entire CNS. Thus, potential treatments are confounded by both reduced efficacy and a wide range of side effects. One can overcome these problems by direct injection into the brain, however this requires highly invasive surgeries. To overcome these limitations, we have developed a non-invasive focused ultrasound drug delivery system that allows targeted neuromodulation with fewer off target effects. This system provides an MRI-visible encapsulation mechanism that is both biocompatible and stable and that can carry therapeutic concentrations of a variety of drugs. It allows the drugs to be cleared from the body without releasing a drug payload in non-target tissues. Focused ultrasound (FUS) is used to open the BBB allowing the non-invasive delivery of of the drug carriers into the brain in a location specific manner. In addition, FUS can activate drug release from drug carriers into target tissue and causes a change in MRI contrast confirming location and concentration of drug release to desired tissue.

Magnetic nanoparticle thermal therapy to induce mitotic catastrophe in breast cancer cells

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Taxanes, such as Paclitaxel (PTX), block cells in mitosis causing death of sensitive cells by mitotic slippage/catastrophe. Resistant cells remain in mitotic block longer and resume proliferation after drug concentration decays. It has been shown that the application of short physiological hyperthermia (HT, or heat shock, 1-2 h at 40-42°C) can overcome taxane resistance, killing resistant cells by forcing mitotic exit/catastrophe of PTX-pretreated cells. This holds promise in reversing PTX-resistance in breast cancer. Nanoscale thermal therapy using iron oxide (IO) magnetic nanoparticles (MNPs) provides a potential means to deliver heat to and reverse resistance to taxanes in breast cancer while sparing healthy tissue, because heat can be generated and constrained within the area of interest through a combination of nanoparticle localization and spatial control of the alternating magnetic field (AMF) used to actuate heat release. This potential was tested through experiments conducted with sensitive and resistant human breast adenocarcinoma sub-lines of MCF-7 cells. The half maximal inhibitory concentration (IC_{50}) of the anti-mitotic drug PTX was determined to be 10 nM. Experimental groups consisted of control cells, cells exposed to PTX (18 h), cells exposed to IO MNPs (2 h) for cytotoxicity determination, cells exposed to external heating (2 h) with and without PTX (18 h), and cells exposed to IO MNPs HT (2 h) with and without PTX (18 h). These experiments were conducted in a coil designed to accommodate 8-well strips, allowing n = 8 replicates per condition. IO MNPs were synthesized by the co-precipitation method and conjugated with PEG (poly ethylene glycol). For MNP HT, an iron concentration of 1.5 mg_{Fe}/ml was used, then the 8-well strip was placed inside the induction heater coil and the magnetic field was modulated to achieve a temperature of 42 °C for 2 hours. Metabolic activity of the cells in all samples was analyzed four days after treatment using CellTiter Blue assay, to estimate cell viability. Preliminary results show that MNPs are not cytotoxic and demonstrate that cell viability can be reduced by more than 50% in wild type and resistant cells using both IO MNP HT and the combination therapy of PTX and MNP HT. Further work is underway to fully evaluate the combination of MNP HT and PTX treatment in sensitive and resistant breast cancer cells.

Reactive Extrusion Strategies to Fabricate Magnetite–Polyethylene Nanocomposites with Enhanced Mechanical and Magnetic Hyperthermia Properties

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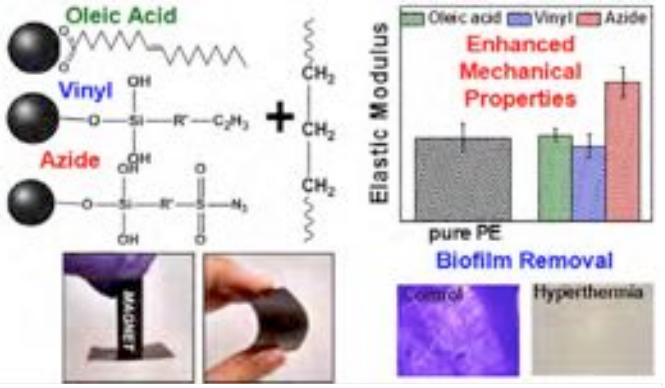

Magnetite-polyethylene nanocomposites prepared via reactive extrusion using silane coupling agents offer enhanced mechanical and magnetic properties.

Biofouling is a major problem in water filtration units, which leads to premature system failure. Conventional treatment methods involving the use of chemicals or high-pressure hydraulics exert mechanical strain on filter materials, leading to shortened service lifetimes. In this study, a novel magnetic polymer nanocomposite is fabricated using a blend of high density/ultra-high molecular weight polyethylene with magnetite nanoparticle (MNP) fillers. The resulting magnetite-polyethylene nanocomposite (MPE-NC) is mechanically robust and can be externally actuated with an alternating magnetic field to generate localized heating that is effective in eradicating bacterial biofilms. The MNPs are functionalized with silane-based coupling agents and crosslinked onto the polyethylene backbone via a reactive extrusion approach, which results in a 2-fold enhancement in mechanical properties of the polymer matrix. Furthermore, the magnetic hyperthermia performance of the MPE-NC is improved 8-fold by replacing undoped magnetite nanospheres with zinc-doped magnetite nanocube fillers, and the magnetic hyperthermia treatment approach is shown to be 12 times more effective in destroying bacterial biofilms compared to a direct heat-treatment method. During hyperthermia treatment, the mechanical integrity of the MPE-NC is preserved, thereby validating the potential of the MPE-NC as a new filter material with high efficiency in biofilm removal and extended durability.

Systematic Investigation of Cobalt Doped Ferrites for Increased Energy Conversion in MagMED

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Magnetically mediated energy delivery (MagMED), formally known as magnetic field hyperthermia, has been a heavily researched area in the magnetic community for many years. The concept being that an alternating magnetic field is applied to magnetic particles. The particles convert the energy of the magnetic field and deliver it locally to the surrounding medium. The efficiency of this transfer is defined by the specific absorption rate of the material which can be measured by placing a sample in an alternating field and measuring the temperature change of the medium over time. The energy produced during this time period is related to both the frequency (number of cycles) and the field magnitude as each field flip can be seen as a minor hysteresis loop with the area of the loop being the energy released in a single magnetization event.[1] To maximize the area in these minor hysteresis loops, two main materials properties can be manipulated. The first being the effective anisotropy which is an intrinsic value based on the material composition and the second being particle volume. The ability to control and change effective anisotropy and particle volume present a unique opportunity to produce materials that can be optimized for maximum power output at a given field and frequency. Traditionally research in MagMED has been centered on iron oxides including the most commonly studied phases, maghemite (γ-Fe_2O_3) and magnetite (Fe_3O_4). Recently, to improve upon the material properties of iron oxides, researchers have begun to consider substituted and doped ferrites. These complex materials show a wide range of magnetic properties, including tunable magnetic saturation, magnetocrystalline anisotropy, and blocking temperature. Coupled with recent advancements in synthesis, and increasing control over both size and morphology of nanoscale colloids, these new materials have been shown to exhibit properties that are greatly improved form those of Fe-ferrites. One of these select materials is cobalt ferrite ($CoFe_2O_4$), which has a much greater effective anisotropy due to the replacement of the Fe^{2+} with the highly anisotropic Co^{2+} ions.[2] By maximizing the effective anisotropy through Co doping, as well as identifying optimal volume for energy release using a novel drip synthesis the optimization of cobalt ferrite based materials for application in MagMED is possible.

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A Quantitative Exploration of Iron Oxide Nanoparticle Purification Through Solvent Precipitation and Size Exclusion Chromatography

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Thermal decomposition synthesis, a popular route for the manufacture of iron oxide nanoparticles, yields a reaction product consisting of a mixture of surfactant-coated nanoparticles, excess surfactant, un-reacted iron oleate precursor, high boiling point solvents, and decomposition byproducts. Separating the surfactant-coated nanoparticles from the rest of the components is an important step in further functionalization for a variety of applications, and is often accomplished by anti-solvent precipitation followed by centrifugation or magnetic separation. Unfortunately, these methods rarely yield a product consisting solely of the surfactant-coated nanoparticles.

Recently, Shen *et al*.[1] recognized this problem in the related field of quantum dot nanoparticle synthesis and reported the use of size exclusion chromatography to separate surfactant-coated nanoparticles from other reaction components. This approach was then adopted for purification of iron oxide nanoparticles by Davis *et al*.[2] Here, we report a quantitative study of the purification of iron oxide nanoparticles by anti-solvent precipitation followed by size exclusion chromatography. Samples taken at points along the purification process were analyzed for iron content by the phenanthroline assay, magnetic content using SQUID magnetometry, and organic content using UV-Vis spectroscopy.

Results show that an initial 'first cut' precipitation step using ethanol as anti-solvent, yields a precipitate containing ~90% of the nanoparticles, concentrated to ~1/5th the original volume. This enriched phase was passed through a size exclusion chromatography column. Analysis of eluent fractions reveals that nanoparticles elute in a fairly tight band, at a concentration similar to that loaded onto the column, with aliquots prior to and after the band almost devoid of iron oxide. Preliminary analysis of the eluent after the nanoparticle band indicates that a large amount of the reaction solvents and unreacted precursors are present. Ongoing work aims to explore the parameters affecting the purification process, such as maximum volume that can be effectively purified by size exclusion chromatography and the effect of the ratio of reaction product to anti-solvent in the initial precipitation step. Success in identifying an optimum wash protocol *via* anti-solvent precipitation followed by size-exclusion chromatography will impact the success of post-synthesis modification of iron nanoparticles for use in biomedicine.

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Title: Magnetically templated hydrogels for peripheral nerve injury repair

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While there are many options currently on the market for peripheral nerve injury (PNI) repair, these devices fail to repair PNI gaps greater than 5 cm. Our hypothesis is that a hydrogel-based scaffold templated with porous microchannels could improve PNI repair for large nerve gaps by mimicking the tubular structure of the peripheral nerve extracellular matrix. These hydrogels are patterned with a process called magnetic templating -- this involves suspending magnetic alginate microparticles (MAMs) in a hydrogel precursor solution, aligning the MAMs in a magnetic field, crosslinking the hydrogel, and finally degrading the MAMs, leaving behind a tubular porous architecture. We have developed a protocol for fabricating MAMs that are uniform in size and composition using microfluidics for improved reproducibility and tunability of the magnetically templated hydrogels. This platform has allowed us to better tune MAM composition and examine corresponding effects on alignment and degradation. Using nano-computed tomography (nanoCT) we can quantify MAM chain length and alignment within the templated hydrogel. Furthermore, we have constructed a setup of permanent magnets capable of magnetically templating long hydrogels (~3 cm). Finally, we have conducted a preliminary *in vivo* study by inducing a 10 mm gap in a rat sciatic nerve to test three implants: magnetically templated hydrogels, non-templated hydrogels, and fresh nerve isografts. With n = 2, the study showed that after 4 weeks, the magnetically templated hydrogel demonstrated an areal density of axons comparable to that of the isograft near the proximal end of the implant. Our results show promise for a microstructured biomaterial that could aid in large PNI repair and other potential tissue engineering applications.

Finite element analysis of a magnetic cell separation device: The importance of magnetophoretic mobility measurements

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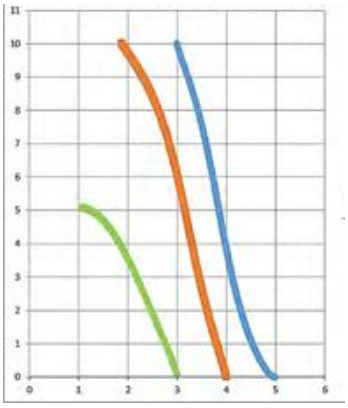
Point-of-care diagnostic devices targeting rare cells circulating in the blood need to be small but capable of processing significant volumes of sample (up to 30 mL) in a short time (less than 1 hour). Magnetic capture of magnetically labeled cells has become a popular method for rare-cell collection, but magnetic force must be balanced against high flow rates. A special 3-stage flowing magnetic capture device was designed and subjected to finite-element analysis accounting for flow rate, flow profile, magnetic field shape, flow-channel size and shape, starting and intermediated cell position, cell magnetization, and capture step. Flow profiles and streamlines were established using ANSYS FLUENT® software. The magnetic field was mapped at the capture magnets, which occupied positions at three stations of the capture device. The path of individual labeled cells was computed on the basis of lateral starting position in a 4-mm-wide flow channel, and it could be determined whether a magnetically labeled cell would be captured at the first, second or third magnetic capture station. The important starting variable is the cell's magnetophoretic mobility, defined as the ratio of the terminal velocity of the particle, v_m, to the gradient of the magnetic energy, $\frac{\nabla B_0^2}{2\mu_0}$,

$$U_m = {v_m}\Big/{\frac{\nabla B_0^2}{2\mu_0}}$$

The units of U_m are m s^{-1}/T A m^{-2} or m^3T^{-1} A^{-1} s^{-1} (meters cubed per Tesla-ampere-second) or m^3/T·A·s. By knowing the magnetic field profile in the separation device the velocity of the cell toward the capture magnet across the flow velocity profile can be calculated in terms of a two-dimensional trajectory, which may or may not lead to the capture of the cell. Therefore, to operate the three-stage capture device successfully the magnetophoretic mobility distribution of the target cell population is determined, and the flow rate through the channel is adjusted to assure cell capture while allowing timely disposition of non-target cells and fluids. To test the resulting predictions a chicken leukemia cell line CRL-211, DT40 was immunolabeled with 2.8 μm diameter Dynal® beads, and the minimum magnetophoretic mobility was determined using a Hyperflux™ velocimeter to be 1.3 x 10^{-11} m^3/T·A·s, and an acceptable flow rate was calculated to be 1.0 mL/min through the 4-mm-wide channel. Under these conditions more than 86% of target cells were captured by the three-magnet assembly. Post-separation mobility distributions showed that magnetically labeled cells were captured and unlabeled cells were not.



Two-dimensional trajectories of cells in a 4 mm channel starting 3, 4 and 5 mm from a 10 mm diameter magnet.

Design and Optimization of a Magnetic Separation Chamber for Filtration of Pro-inflammatory Cytokines During Cardiopulmonary Bypass Surgery

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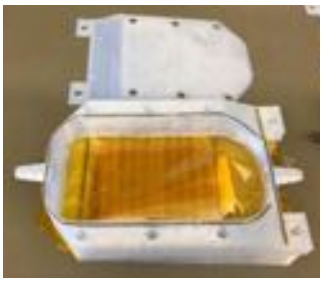
Cardiopulmonary bypass (CPB) is a technique used while the heart is in arrest to maintain the oxygenation and circulation of blood throughout the body. Inflammation inducing cytokines produced during CPB are associated with increased post-surgery morbidity and mortality. This study looks at the development of a separation chamber to incorporate in to the CPB system to remove these cytokines using magnetic particle targeting and capture.

Utilization of 3D printing technology has allowed for rapid prototyping and optimization of the separation chamber. The incorporation of novel, high-gradient magnetic arrays will allow for the separation of cytokine targeting magnetic particles from the CPB system at physiologically relevant flow rates. The chamber was designed to limit cell shearing as well as minimize the distance between the magnetic particles and the magnetic array, by using a sheet flow geometry, so that the capturing force exerted on the particles was maximized.

Preliminary experiments showed that the prototype design was capable of efficiently capturing magnetic particles at physiological flow rates. Side-by-side testing of the capturing chamber and other magnetic separation methods showed that the prototype is capable of filtering a greater amount of particles in a shorter time at a flow rate that is several orders of magnitude greater than similar studies in literature. For example, Earhart et al. developed a magnetic separation device that filtered 0.2 ml of a magnetic particle containing solution at a rate of 1 ml/hr with an efficiency of 37% [1]. Also Inge K. Herrmann et al. achieved a capture efficiency of 75% under a flow rate of 1.5 ml/min, using a total volume of 2.8 ml [2]. Ultimately, simulation of the magnetic filtration process will guide the design of the chamber and ensure that the magnetic force is sufficient to prevent particles from escaping the capture chamber in to the CPB system.

Filtration Test Parameters and Results	
Flow Rate	500 ml/min
Volume Used	80 ml
Filtration Time	10 min
Particles used	Maghemite
Initial Particle Concentration	0.125 mg/ml
Final Particle Concentration	0.0064 mg/ml
Concentraion Reduction	**94.88%**

Before filtration



3D printed chamber

After filtration

Kapton sheet showing captured particles

[1] C. M. Earhart, R. J. Wilson, R. L. White, N. Pourmand, and S. X. Wang, “Microfabricated magnetic sifter for high-throughput and high-gradient magnetic separation,” Journal of Magnetism and Magnetic Materials, vol. 321, no. 10, pp. 1436–1439, 2009.

[2] I. K. Herrmann, A. Schlegel, R. Graf, C. M. Schumacher, N. Senn, M. Hasler, S. Gschwind, A.-M. Hirt, D. Günther, P.-A. Clavien, W. J. Stark, and B. Beck-Schimmer, “Nanomagnet-based removal of lead and digoxin from living rats,” Nanoscale, vol. 5, no. 18, p. 8718, 2013.

Using Magnetic Nanoparticles for the Design of Calcium Phosphate Reinforcement in SLA-Printed Catheter Geometries

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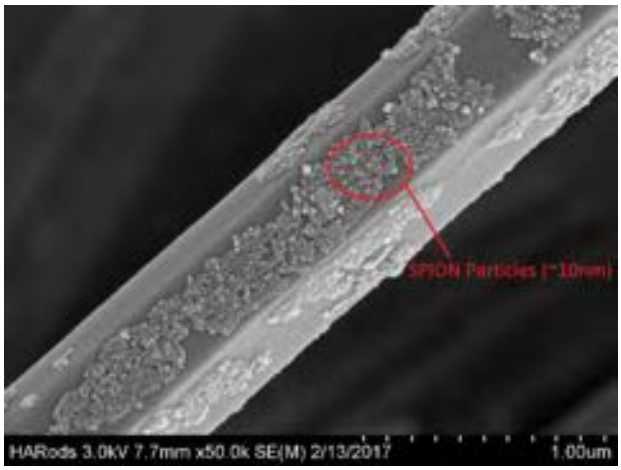
In this work, we investigate reinforcing neonatal catheters with hydroxyapatite fibers labeled with magnetic nanoparticles. The magnetic nanoparticles provide a mechanism for angular control of the fibers within the catheter that is necessary to maximize composite strength. Catheters have a wide range of practical uses in the medical profession, and are instrumental in a variety of medical techniques. However, the dimensions and scale of the catheter must be designed around the needs of the patient. Neonates present especially challenging circumstances requiring small geometries that vary widely patient to patient. Neonatal catheter tubes outer-wall diameters must be scaled-down to accommodate this reality. However, a decrease in the outer-diameter of the tube demands a proportionate decrease in the inner diameter, to limit any decrease in the overall wall-thickness and thereby maintain the strength of the catheter structure. This decrease in inner-diameter results in a diminishing of the catheter's maximum flow rate, which in turn raises the risk of a number of medical complications, including infection and clotting. These issues may be likewise compounded by the catheters exhibiting a kinking instability, in which significant bending of the catheter exhibits a non-linear response and drastically inhibits the flow of liquid through the tube.

To address this important problem, we have developed a new type of manufacturing method to produce patient-specific catheters utilizing stereolithographic 3D printing coupled with magnetic alignment techniques. First, calcium phosphate fibers are coated with 10 nm superparamagnetic iron oxide nanoparticles (SPIONs) to provide an ultra-high magnetic response. These fibers are then mixed with photopolymerizable resins including acrylate/polyurethane mixtures. The precursor solution is then used to stereolithographically 3D print both test coupons and patient specific catheters. Our results indicate an increase in the mechanical strength and stiffness of the reinforced structures that allows for a reduction of catheter wall thickness. A thinner catheter wall thickness without sacrificing mechanics represents the missing paradigm in neonatal catheter manufacturing. Further, our ability to 3D print patient specific catheters means that we can pre-design curves into the catheter to accommodate for the intricate insertion pathways of human veins. This allows us to maintain a circular inner diameter in the inserted configuration, which maximizes flow rates and avoids kinking instabilities altogether.



Brownian dynamics simulations of dipolar interacting magnetic nanoparticles for magnetic hyperthermia

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Suspensions of magnetic nanoparticles subjected to alternating magnetic fields (AMFs) can generate heat, which can be employed to release drugs and kill cancer cells. Prior computational work has explored the effect of particle properties and applied field parameters on the specific absorption rate (SAR) of suspensions of magnetic nanoparticles, including for magnetically blocked particles which respond to a change in field amplitude and direction by physically rotating. Some of this work has considered random initial configurations of particles and the effect of magnetic dipole-dipole interactions. However, most prior work fixes particle positions and as such have not considered the potential role of field-induced aggregation on energy dissipation rates.

In this work, the behavior of spherical single-domain magnetically-blocked nanoparticles in AMFs with and without constant bias fields are investigated through Brownian dynamics simulations accounting for translation and rotation of the nanoparticles, magnetic dipole-dipole interactions, and repulsive interaction potentials. The translation and rotation of the particles is analyzed to obtain measures such as the harmonics of particle magnetization, dynamic hysteresis loops, and specific absorption rate (SAR) as a function of the amplitude and frequency of the AMF, relative strengths of magnetic and repulsive interactions, and the strength of an applied bias field. Results suggest that increasing the strength of dipolar interactions leads the equilibrium magnetization of the magnetic suspension to increase first and then decrease. The results of magnetorelaxometry show that magnetic interactions slow down the characteristic relaxation time of the particles to changes in the field. For low frequencies of the applied AMF increasing interactions result in an increase in SAR for all excitation field amplitudes studied. For intermediate frequencies of the applied AMF strong magnetic interactions reduce the SAR value slightly at low excitation field amplitudes and enhance the SAR value slightly at high excitation field amplitudes. For the highest frequencies considered interactions appeared to lower SAR value slightly at low excitation field amplitudes but had no effect at higher excitation field amplitudes. These results provide theoretical insight into the role of particle-particle interactions on the performance of magnetic nanoparticles for application in magnetic hyperthermia and magnetically-triggered drug delivery.

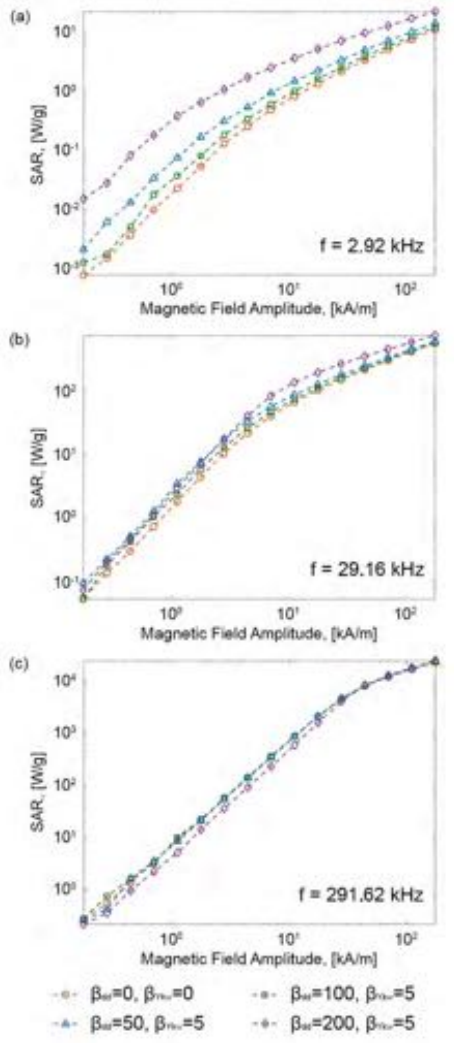

Figure. Specific absorption rates as a function of the amplitude of the AMF for (a) f=2.92 kHz, (b) f=29.16 kHz and (c) f = 291.62 kHz, and various strengths of magnetic (β_{dd}) and repulsive (β_{Ykw}) interactions.