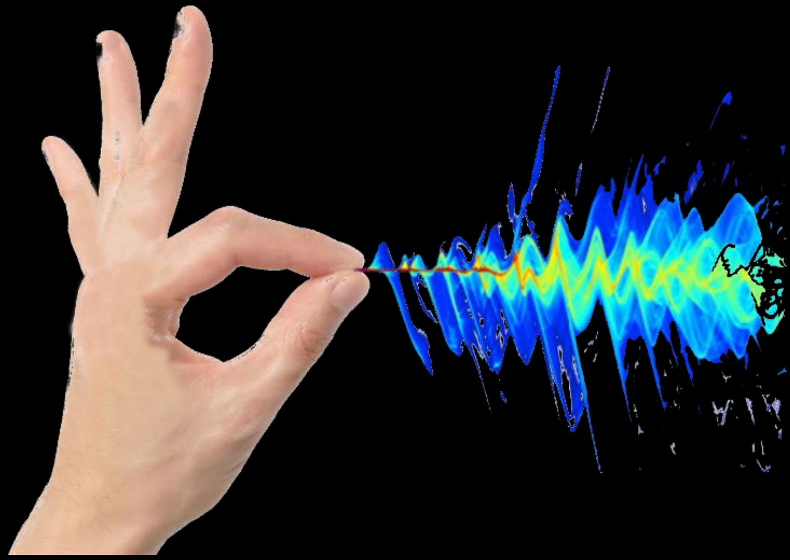
Driving Molecular Transport across Biological Membranes from Magnetic Nanoparticle/Pulsed Magnetic Field Induced Ultrasound



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Kansas State University, Chemistry

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Department of Chemistry

Research Interests: Synthesis and spectroscopic characterization of nanoparticles, magnetic hyperthermia, chemical dynamics

Acknowledgements (KSU)

Graduate students: Dr. Pinard Dagtepe (Boston Turkish Embassy), **Dr. Naween Dahal** (Environmental Health And Safety specialist University of Texas, Austin), **Dr. Christopher Tuinenga** (Adjunct Professor at Elmhurst College), **Dr. Raj Kumar Dani** (Senior Lecturer, Trinity International College, Dillibazar, Kathmandu, Nepal), **Dr. Santanu Roy** (Assistant Professor Dimapur, St John College, Nagaland, India), **Dr. Hongfu Luo** (Toronto/Canada currently seeking employment), **Dr. George Podaru** (Works at Nitech is one of the top Romanian suppliers of high-end technology instruments for general laboratory, diagnostic and research purposes.), **Krisztina Sarosi** (currently PhD student at ELI-ALPS), **Basanta Acharya** (currently PhD student at KSU), **Pratikshya Sharma** (currently PhD student at KSU), **Laszlo Bodnar** (currently PhD student at KSU), **Roland Flender** (University of Szeged/ELI-ALPS co-adviser with Adam Borzsonyi), **Mohammad Sadegh Yazdanparast**(transfer student)

Undergraduate students: Fadzai Fungura (Process Engineer at Intel Corporation), **Curt Hamphill** (Senior Process Engineer at Burns & McDonnell), **Brett Vaughn** (Professional Research Assistant at University of Colorado Denver), **Christopher Lewis** (Laboratory Technologist II at Halliburton), **Alicia Aguirre** (PhD student Iowa State University), **Saralyn Ogden** (Software Engineer, Seattle area), Nathan Young (Kaplan GRE teacher and former engineer at Graphene Frontiers), **Dr. Lorinc Sarkany** (finished PhD University of Tübingen interviewing in Japan for postdoc), **Alec Todd** (not known), **Amanda Baxter** (Ph.D. Candidate at University of Southern California), **Joshua Shipman**(PhD student University of Kansas), **Emery Brown**(graduated from KSU), **Dr. John Moore** (postdoc, University of Barcelona), **Chris Ramirez** (Test Engineer, Washington DC), **Matthew Taw** (Technical Lab Coordinator Louisville, Kentucky Area), **Krisztina Sarosi** (ELI-ALPS), **Daniel Tye** (KSU), **Karan Mehra** (RF Design Engineer at ViaSat Phoenix, Arizona Area), **Zachary Sliefert** (Software Engineer at Decision Resources Group Kansas City, Missouri Area), **Noah Hollinger** (KSU), **Nathan Flesher** (KSU), **Erwin Petracs** (University of Szeged), **Mathew Davis**(KSU)

Postdoctoral trainees: Dr. Pankaj Kanti Mandal (Associate Professor IISER Pune), **Dr. Karoly Mogyorosi** (senior research fellow at ELI-ALPS)

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Johnson Cancer Research Center
USRG
ACS Doctoral New Investigator
NSF EPSCOR, NSF SBIR/STTR , NSF(ELECT, PHOTONICS, & MAG DEVICE), DOE(BES)
European ESFRI project

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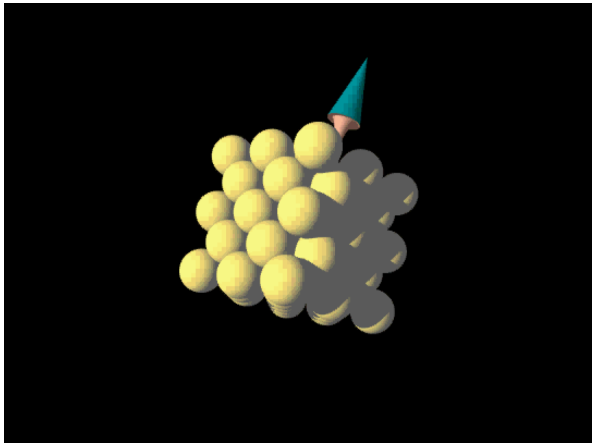
Outline

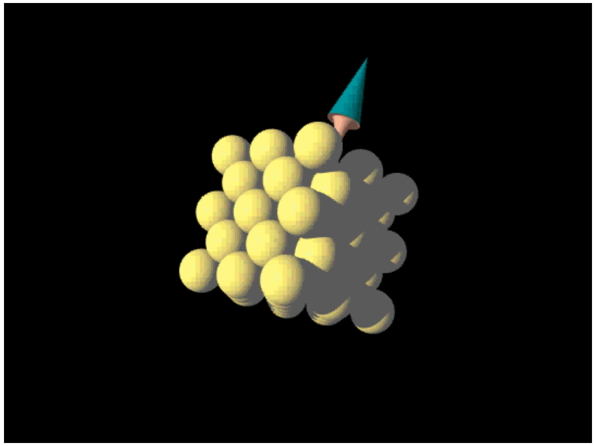
- **Nanoparticles in Magnetic fields:** Using external time dependent magnetic fields to mechanically(ultrasonic waves) manipulate magnetic nanoparticles resulting in new interesting and useful phenomena

Magnetic Hyperthermia with Superparamagnetic Nanoparticles

Brownian Relaxation



Neel Relaxation



Mechanism of Energy disposal

$$\tau = \tau_N^{-1} + \tau_B^{-1}$$

Solvent drag (friction heating)

Electron-electron scattering

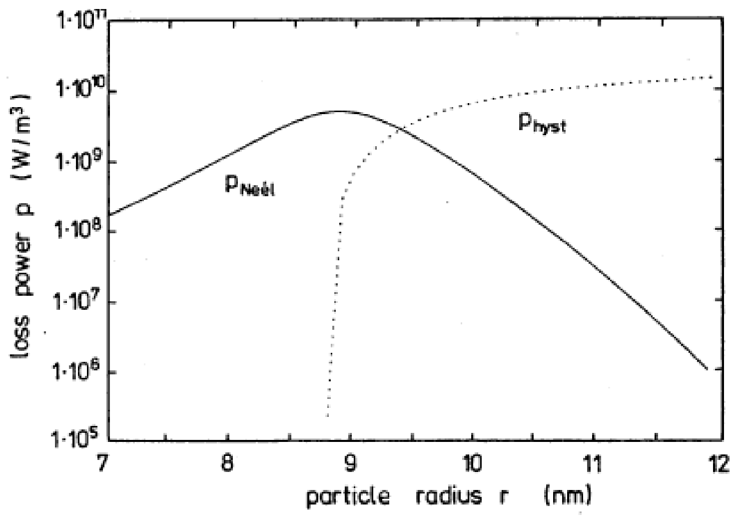


Fig. 7 Dependence of SAR on particle size for magnetite fine powders in rf-field (2 MHz, 6.5 kA m^{-1}): dotted line – hysteresis losses, full line – Néel losses. (Reprinted from ref. 89. © 1998 IEEE.)

Bossmann, S.; Chikan, V.; Dani, R. K., Magnetic Nanoparticles for Biosensing and Cancer Treatment Biosensing and Cancer Treatment with Magnetic Nanoparticles. In Biosensors Based on Nanomaterials and Nanodevices, Li, J.; Wu, N., Eds. CRC Press: 2013.

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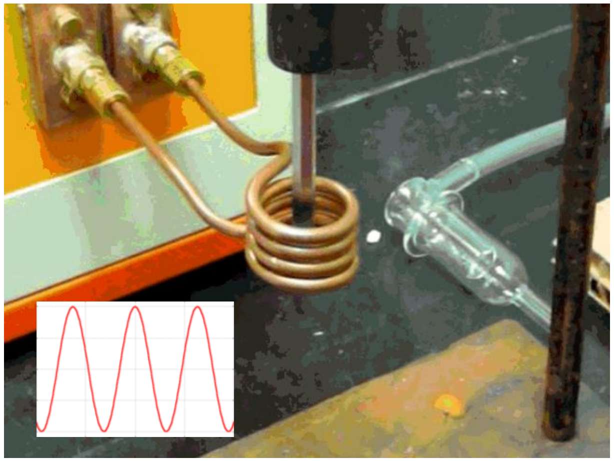
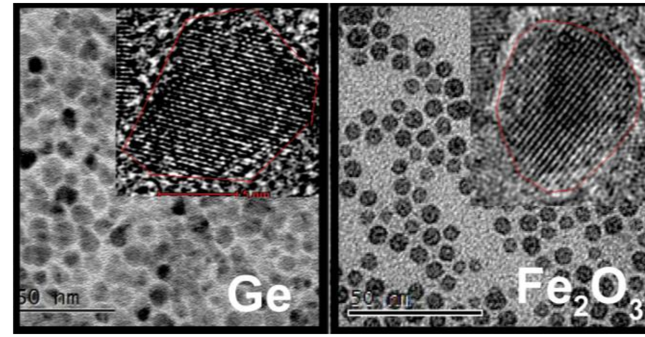
J. Mater. Chem., 2004, 14, 2161–2175

Magnetic Heating

Heating Steel



NP Synthesis-Alternative to hot injection technique



Our Work:
- *ACS Omega* **2018,***3* (5), 5399-5405.
- *Nanomaterials* **2016,***6* (5), 85.
- ACS Omega **2020.**

$$SAR = C\frac{\Delta T}{\Delta t}$$

- Typical SAR values are on the order of few hundred W/g
- The frequency of the AC magnetic is a few hundred kHz (problem non-specific heating and cardiac and muscle stimulation at high frequency)
- Field amplitude is around 10 kA

$$H \cdot f$$

$$4.85 \times 10^8 \text{ A m}^{-1}\text{ s}^{-1}$$

Heating with NPs

(I.A. Brezovich, Med. Phys. mono. 16 (1988) 82)

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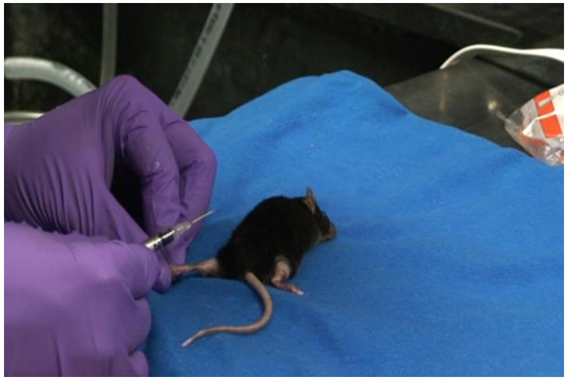
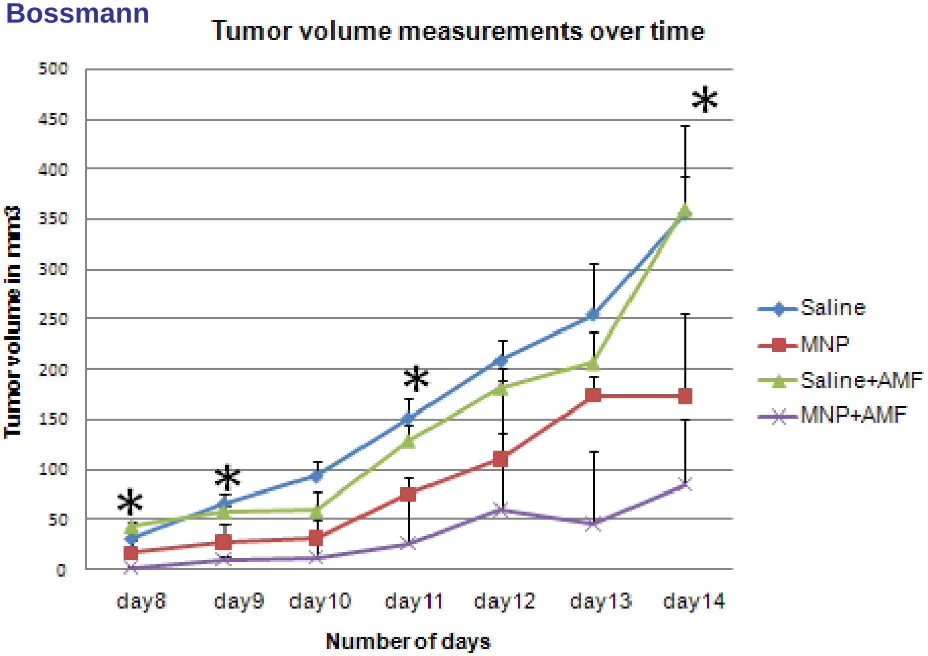
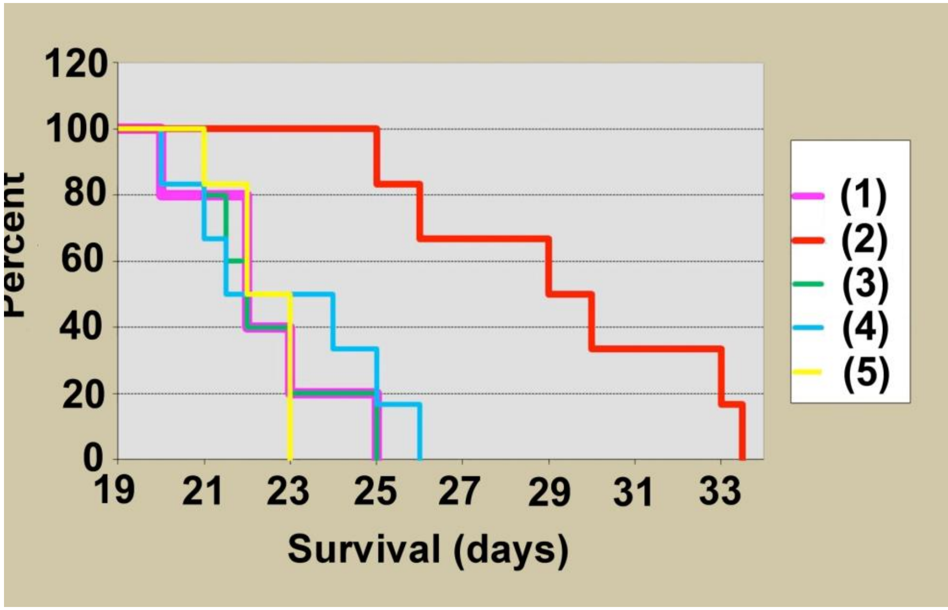
Magnetic hyperthermia treatment of melanoma and pancreatic tumors

Prof Stefan Bossmann

Prof Deryl Troyer







Balivada, S.; Rachakatla, R. S.; Wang, H.; Samarakoon, T.; Dani, R. K.; Pyle, M.; Kroh, F.; Walker, B.; Leaym, X.; Koper, O.; Tamura, M.; Chikan, V.; Bossmann, S.; Troyer, D., **A/C magnetic hyperthermia of melanoma mediated by iron(0)/iron oxide core/shell magnetic nanoparticles: a mouse study.** *BMC Cancer* **(2010)** 10, (1), 119.

Basel, M. T.; Balivada, S.; Wang, H.; Shrestha, T. B.; Seo, G. M.; Pyle, M.; Abayaweera, G.; Dani, R.; Koper, O. B.; Tamura, M.; Chikan, V.; Bossmann, S. H.; Troyer, D. L., Celldelivered magnetic nanoparticles caused hyperthermia-mediated increased survival in a murine pancreatic cancer model. International Journal of Nanomedicine 2012, 7, 297-306.

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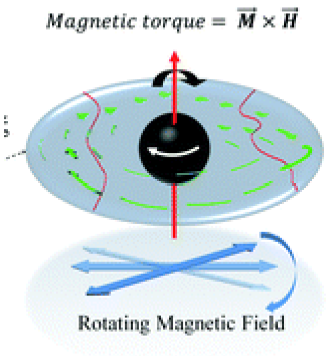
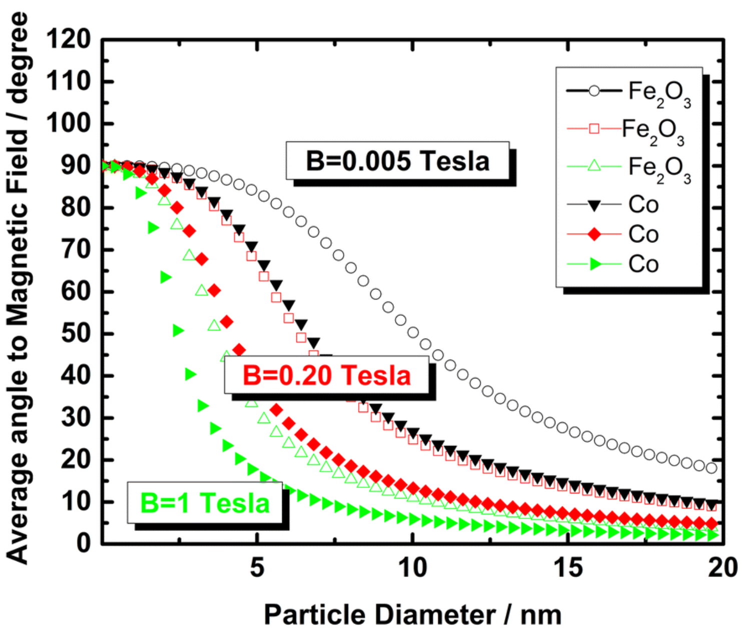
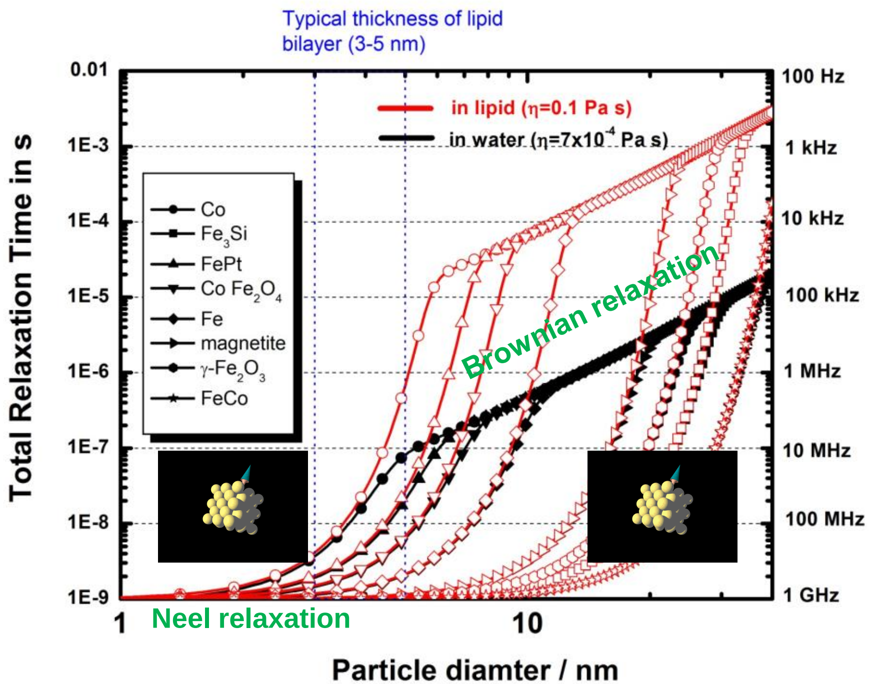


Utilizing mechanical force from the rotation of magnetic nanoparticles





Nanometer sized drill bit

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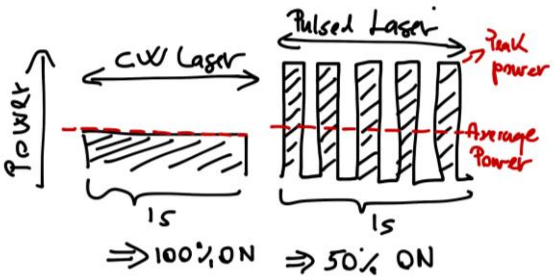
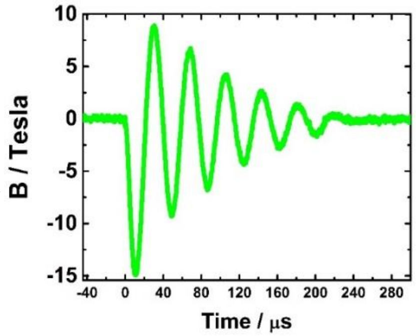
Pulsed Magnetic Fields

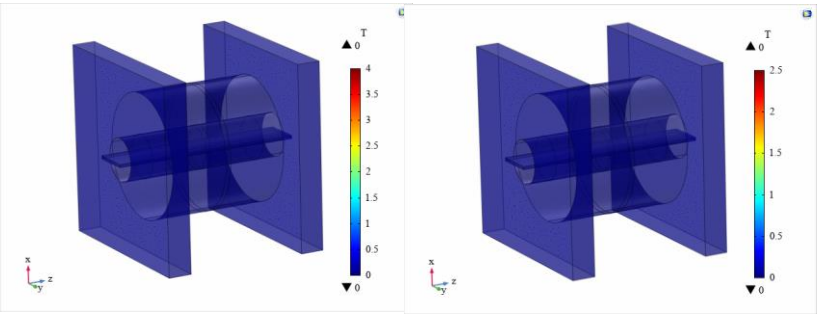
Concept



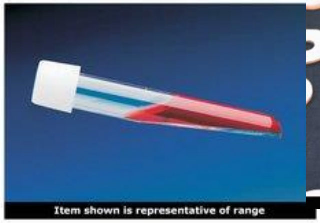
Actual magnetic pulse

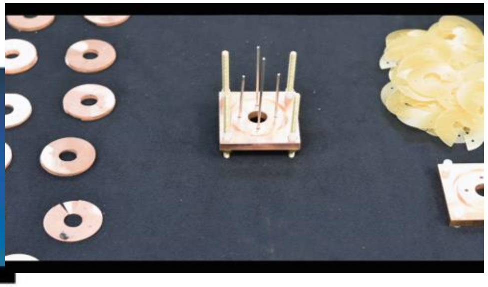


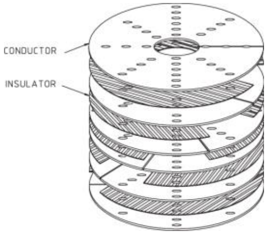
Homogeneous vs. inhomogeneous magnetic fields



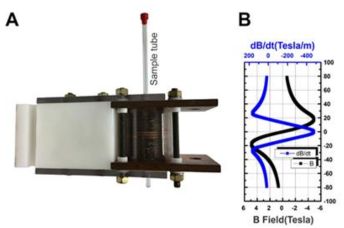
Construction of the magnet, bitter coil



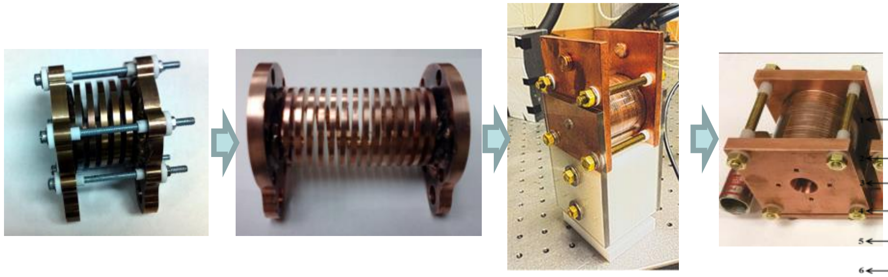




Integration with experiments

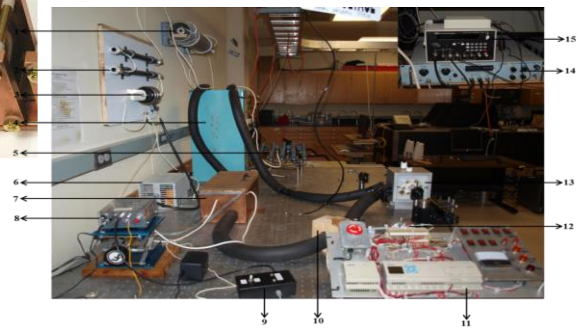


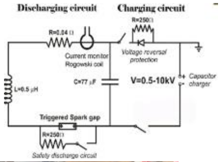
Evolution of magnets in Chikan Lab



Beryllium copper attains the highest strength (to 1,400 MPa (200,000 psi)) of any copper-based alloy

Power delivery system





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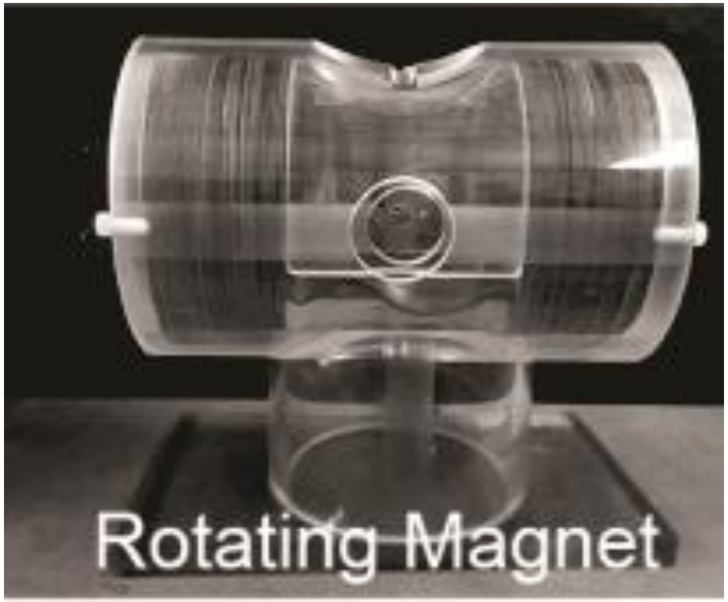
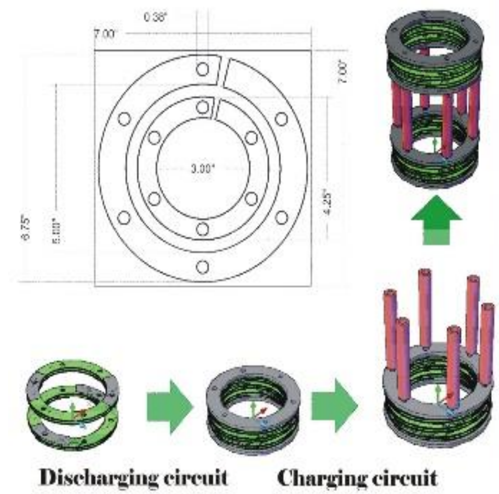
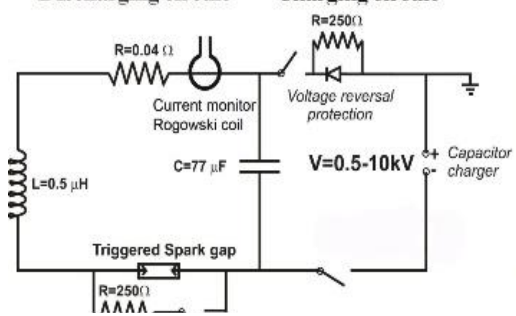
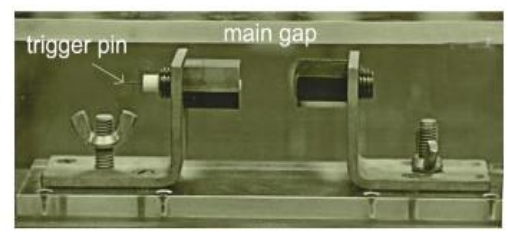
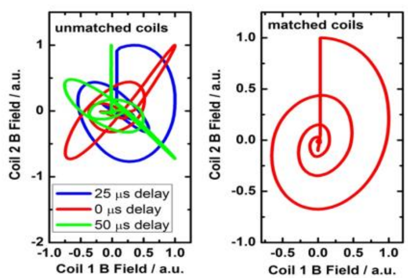
Development of Pulsed Rotating Magnet

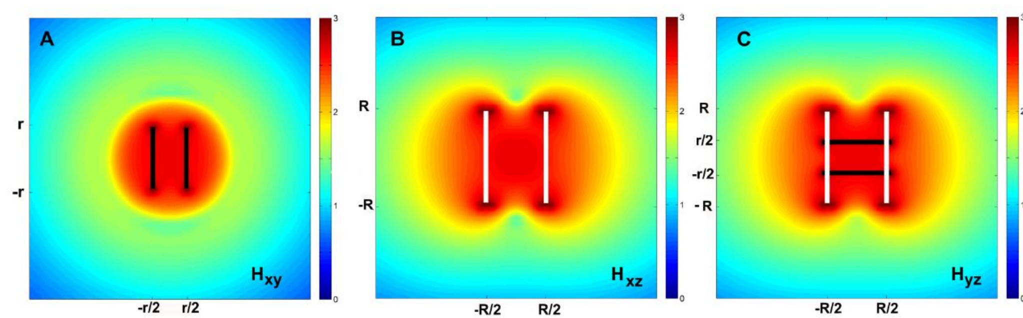












Podaru, G.; Moore, J.; Dani, R. K.; Prakash, P.; Chikan, V., Nested Helmholtz Coil Design for Producing Homogeneous Transient Rotating Magnetic Fields. Review of Scientific Instruments 2015, 86.

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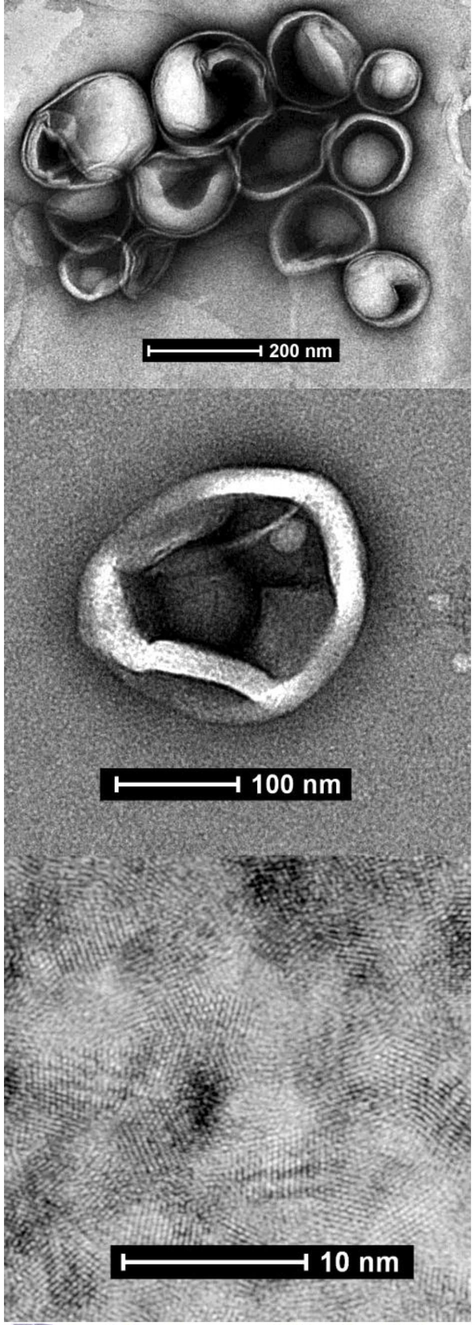
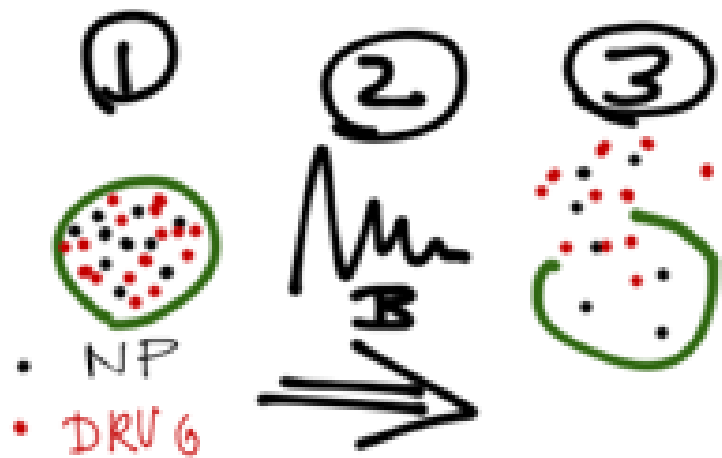
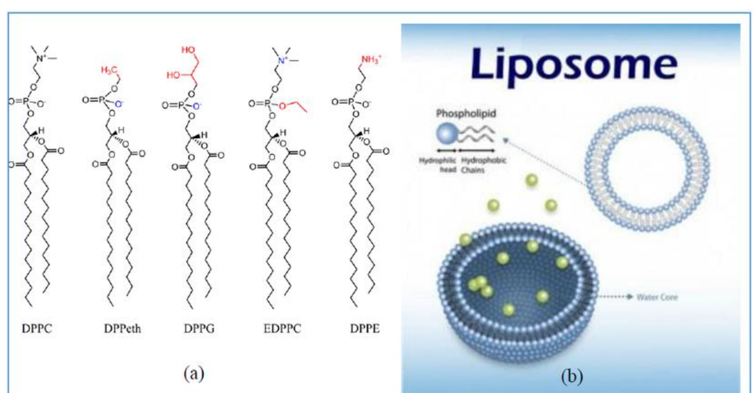
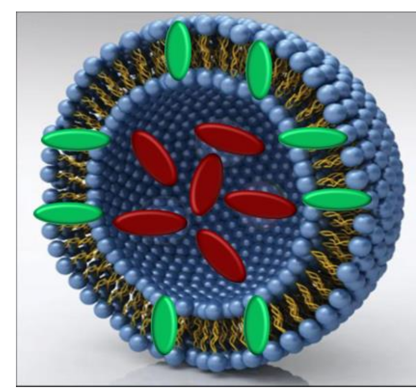


Pulsed magnetic field induced drug delivery from magneto liposomes







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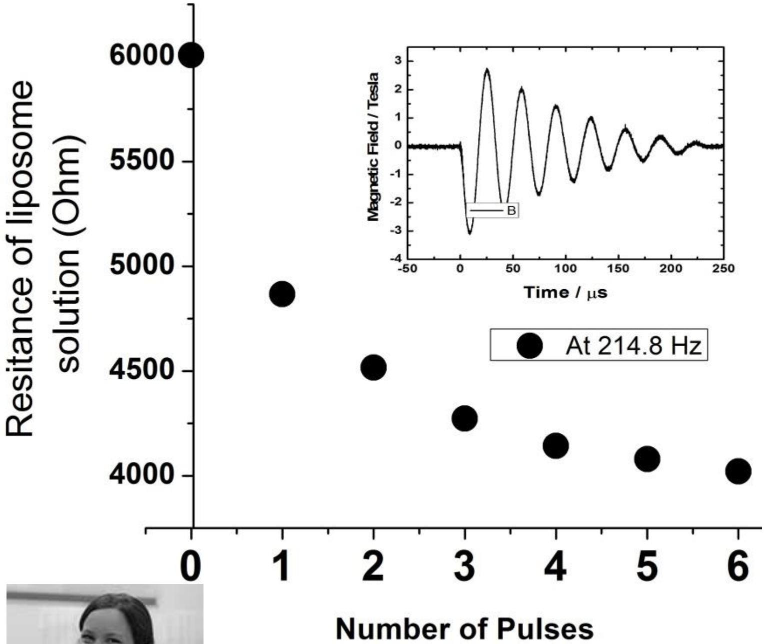
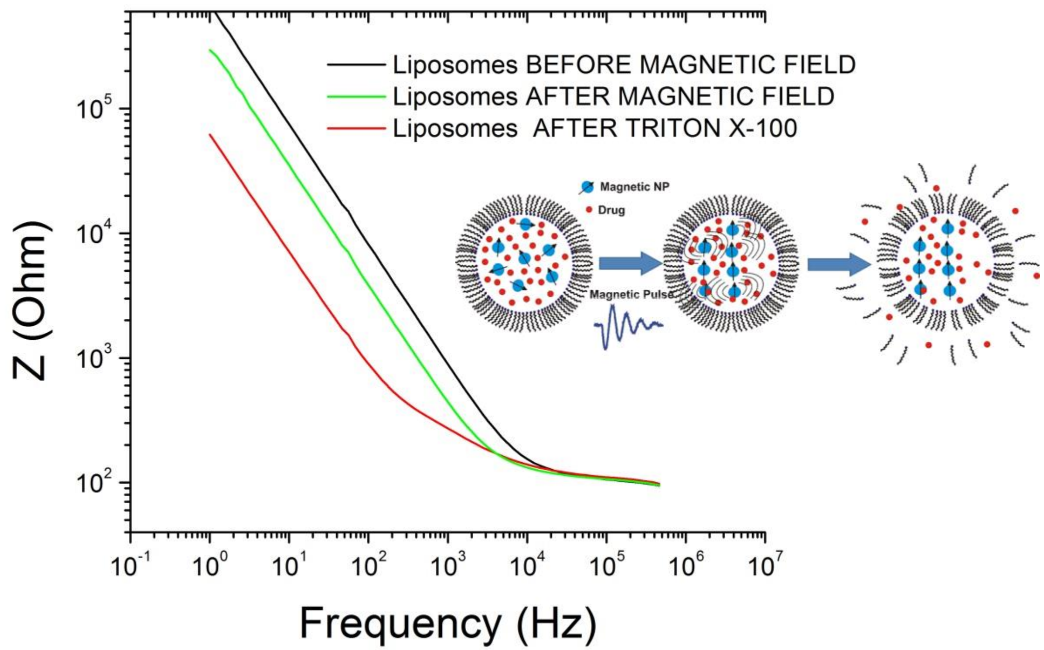
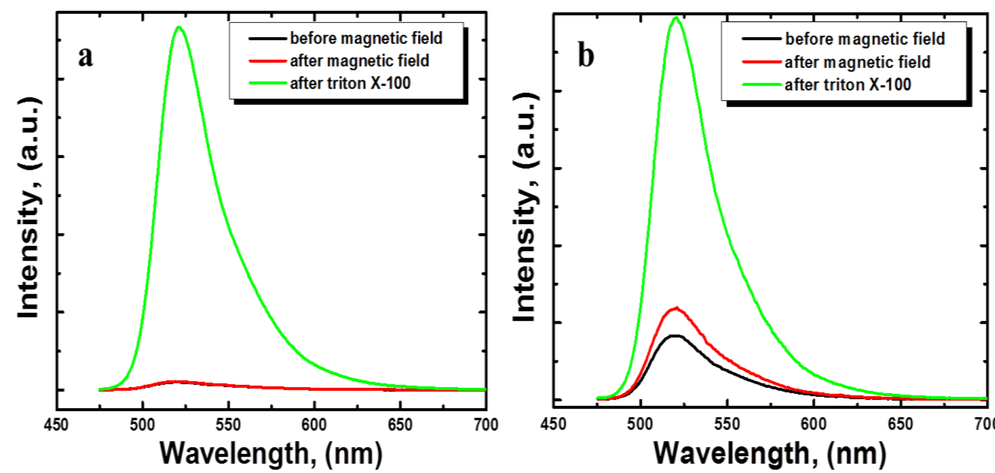
Podaru, G.; Dani, R. K.; Wang, H.; Basel, M. T.; Prakash, P.; Bossmann, S. H.; Chikan, V., Pulsed Magnetic Field Induced Fast Drug Release from Magneto Liposomes Via Ultrasound Generation. J. Phys. B (2014), 118(40), 11715–11722.

AC conductivity of MgSO4





carboxyfluorescein permeability assay



Amanda Baxter

Saralyn Ogden

Conductivity Measurement And Dye release Assay

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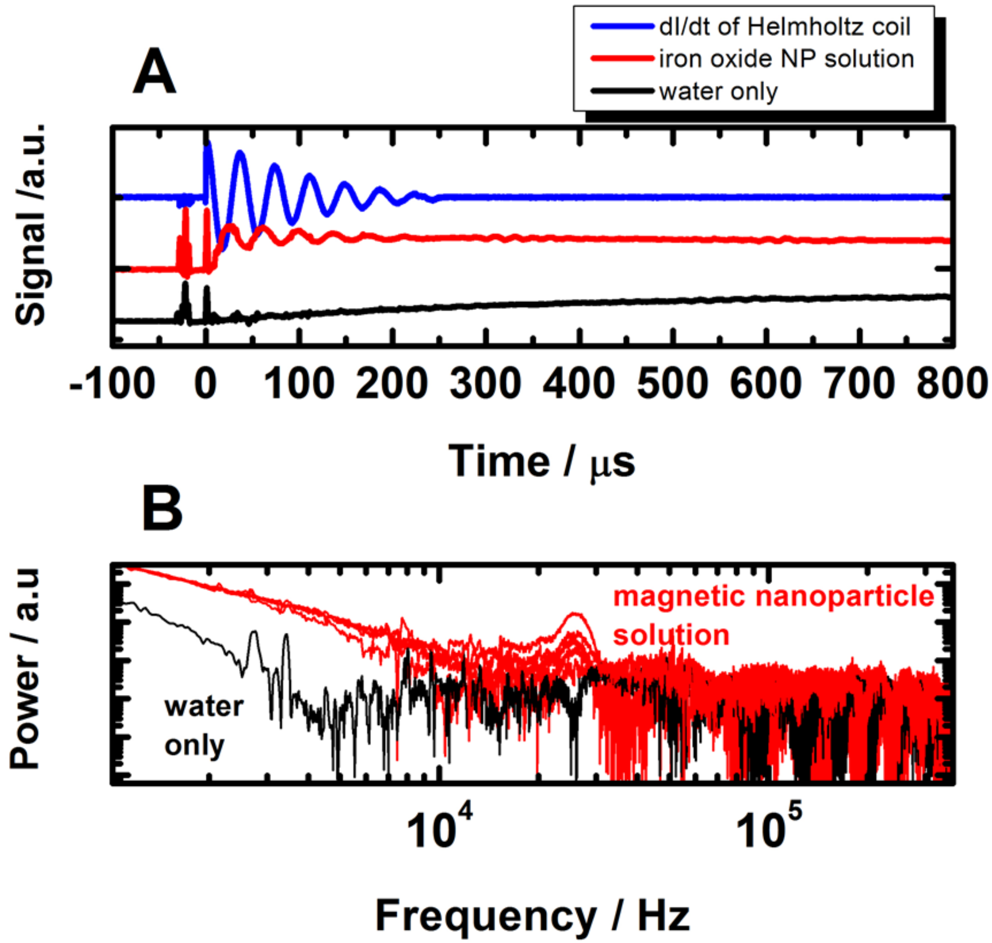
Podaru, G.; Ogden, S.; Baxter, A.; Shrestha, T.; Ren, S.; Thapa, P.; Dani, R. K.; Wang, H.; Basel, M. T.; Prakash, P.; Bossmann, S. H.; Chikan, V., Pulsed Magnetic Field Induced Fast Drug Release from Magneto Liposomes Via Ultrasound Generation. The Journal of Physical Chemistry B 2014, 118, 11715-11722.

Dr. George Podaru

Drug release mechanism: ultrasound from magnetic nanoparticles



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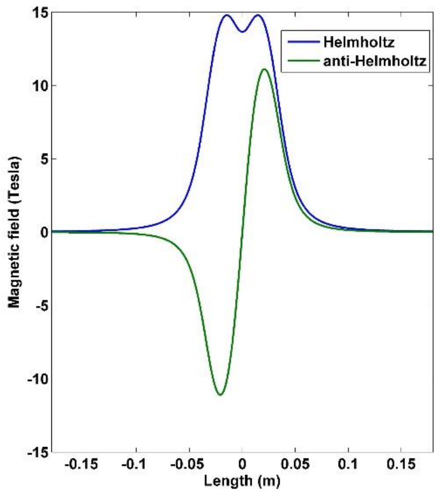
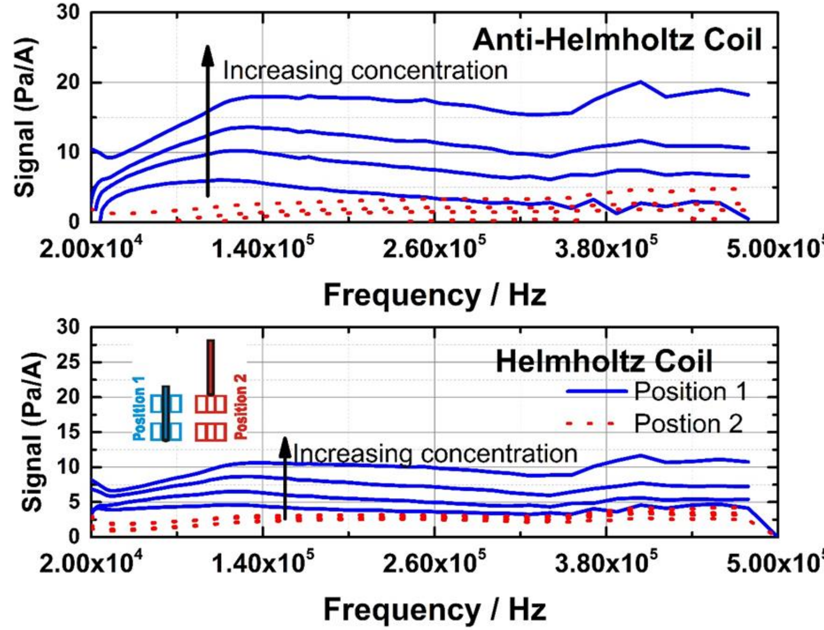
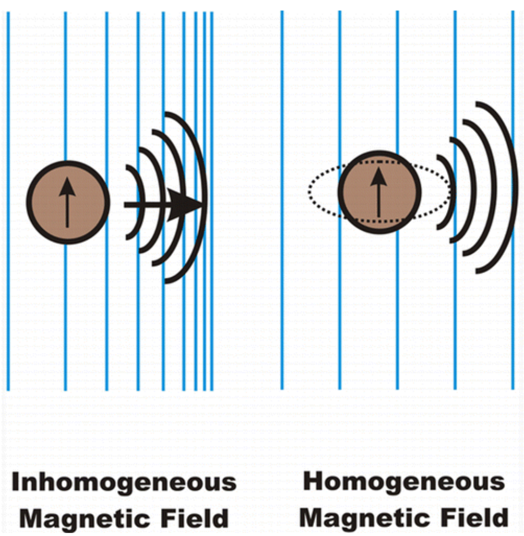
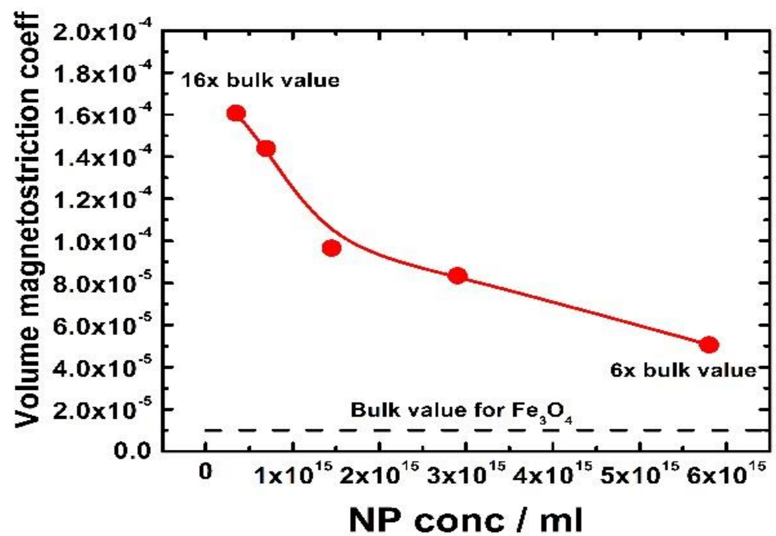
Podaru, G. V.; Chikan, V.; Prakash, P., Magnetic Field Induced Ultrasound from Colloidal Superparamagnetic Nanoparticles. The Journal of Physical Chemistry C 2016, 120, 2386-2391

Magnetostriction vs. particle movement









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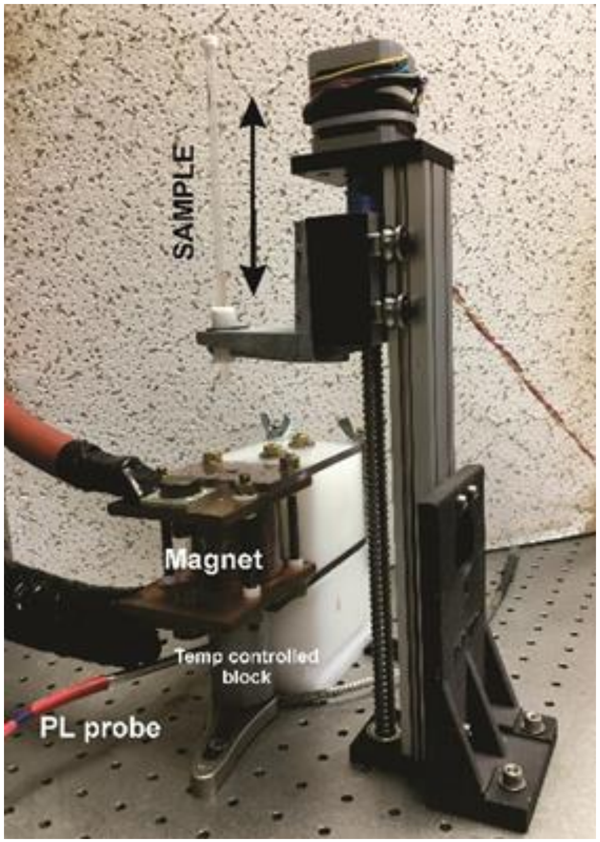
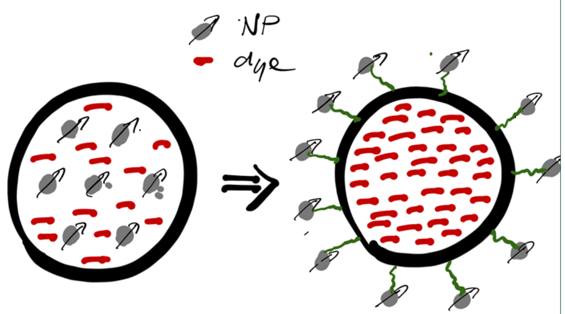
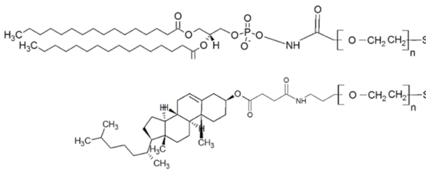
Moving forward: Manipulating structure of magneto liposomes

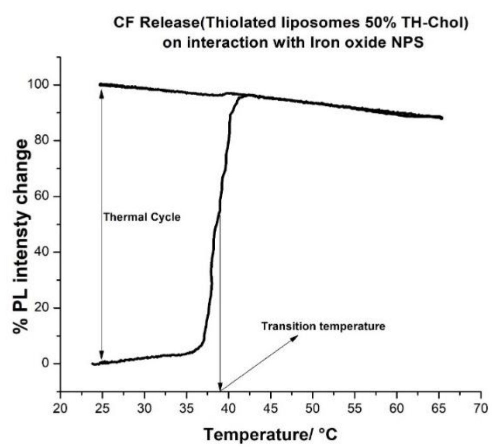
Basanta Acharya

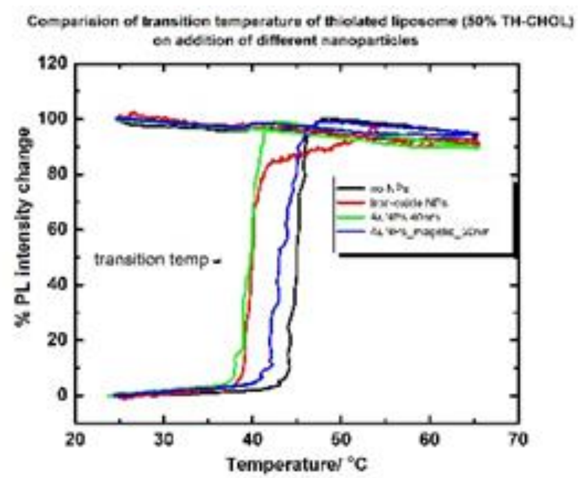






Commercial thiolated linkers





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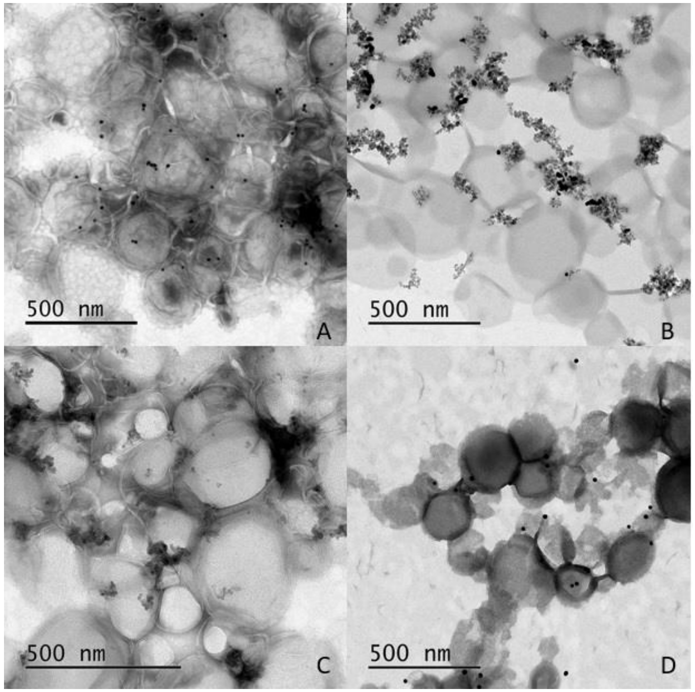

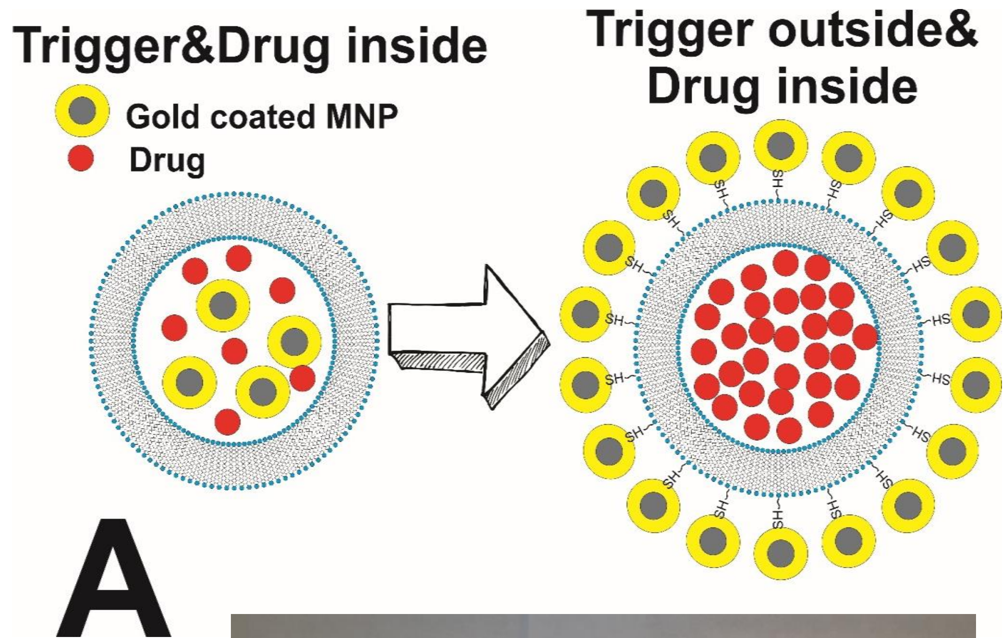

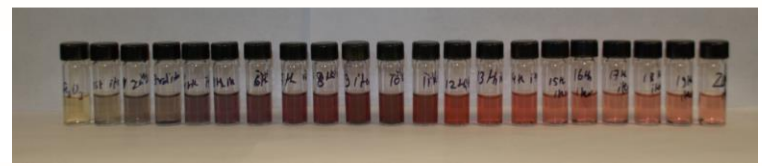

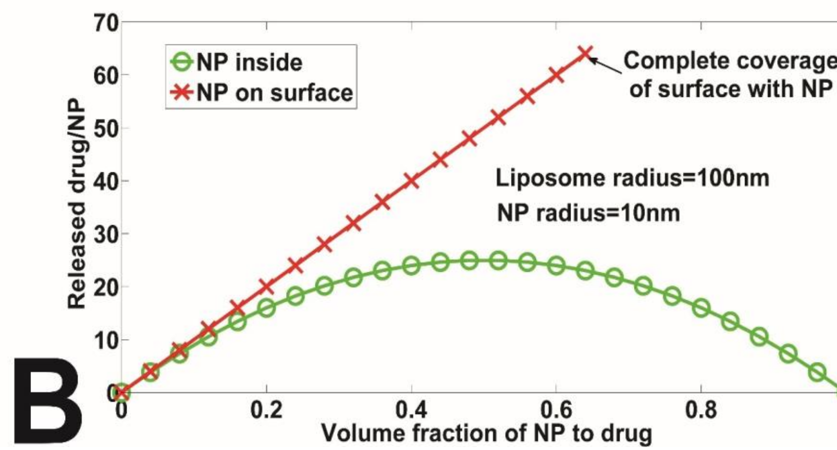

Volumes of NPs (µL)	Commercial Iron Oxide NPs	Gold coated Commercial IO NPs	Synthetic Iron Oxide	Gold Coated Synthetic IO NPs
0	4.8%	4.5%	4.7%	4.6%
2	5.0%	7.5%	10.5%	6.5%
4	3.6%	14.2%	6.6%	7.5%
6	9.5%	17.6%	7.5%	9.9%
8	3.9%	20.5%	5.6%	7.6%
10	3.8%	14.6%	7.4%	6.8%

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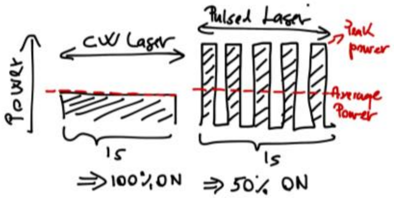

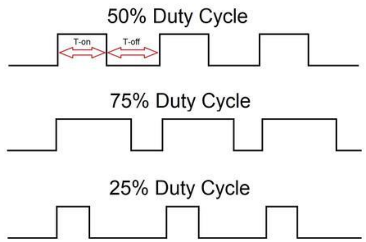

Magnetoliposomes and their efficiencies in drug delivery

Ref	Liposome/NP Formulation	Location of Trigger	Max Release (%)	Application Time (min)	Duty Cycle of Magnet (%)	Intensity of the Magnetic Field (mT)	Unit Time Release (% Release/s)
1	$PC/CoFe_2O_4$	Bilayer	90	50	100	330	0.03
2	DSPC/PEG/IONPs	Bilayer	180	30	100	-	0.1
3	MPPC/SPION	Bilayer	90	6	100	94.5	0.25
4	$HSPC/Fe_3O_4$	Core	20	180	9.77	1.5	0.00185
5	DPPC/FePt	Core	8.4	3.3×10^{-5}	0.001	3000	248,000

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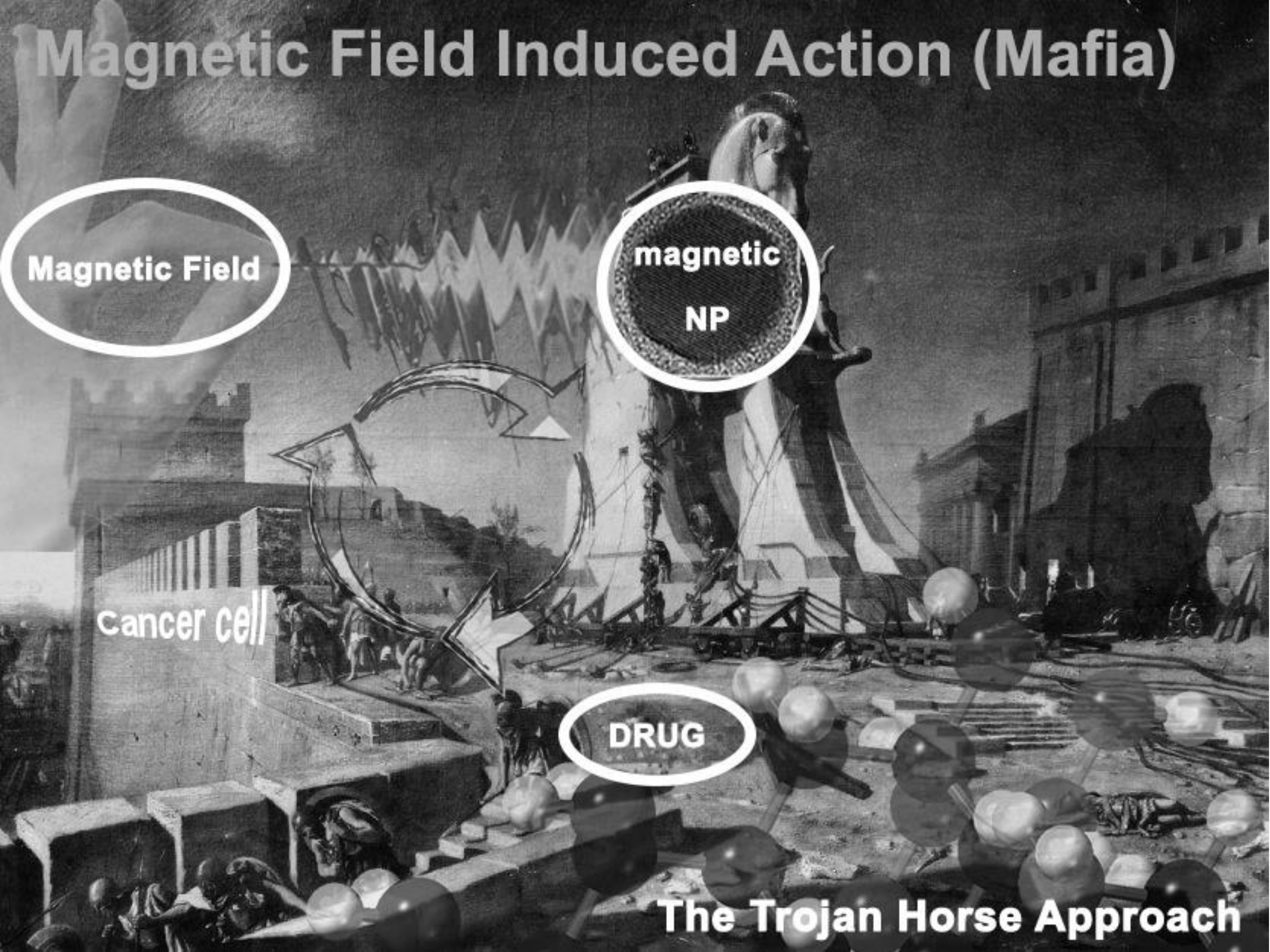
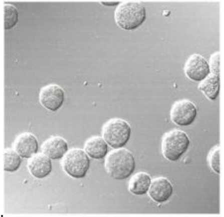

Magnetic Field Induced Action (Mafia)
Magnetic Field
magnetic
NP
Cancer cell
DRUG
The Trojan Horse Approach



Doxorubicin treatment of U-937 Cancer Cells

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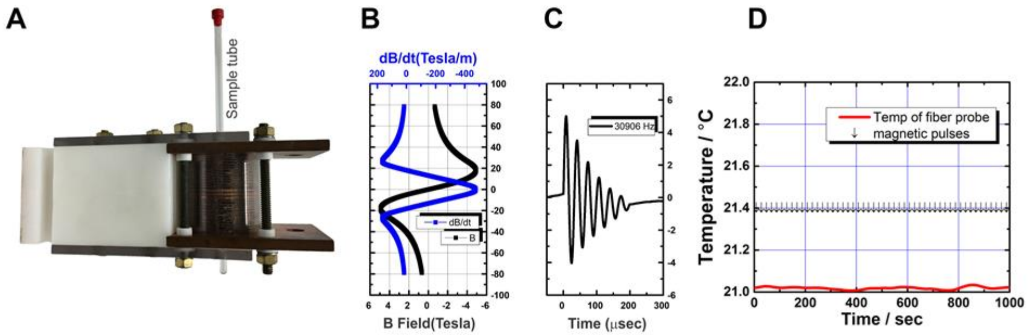
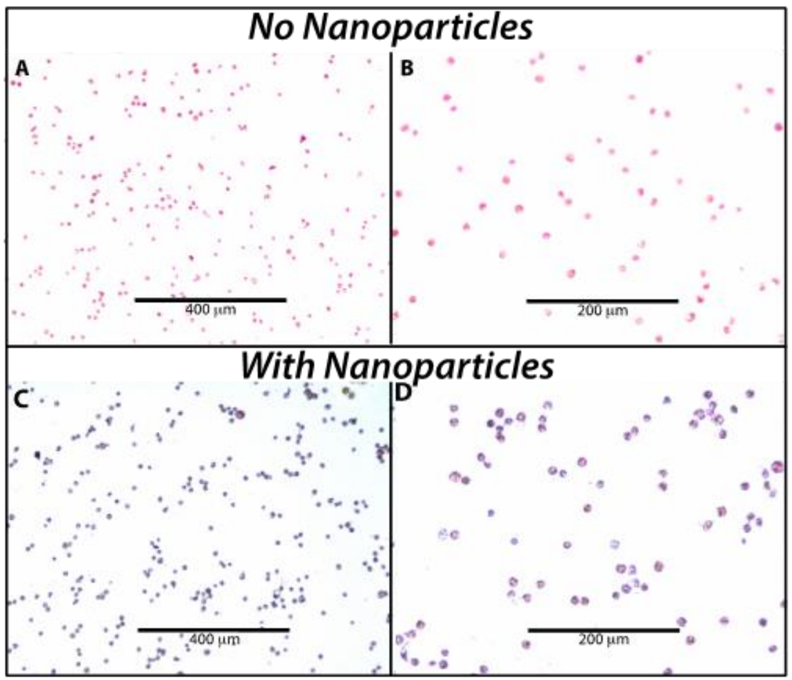
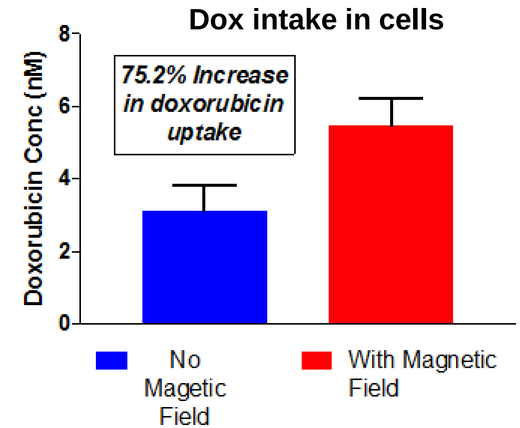
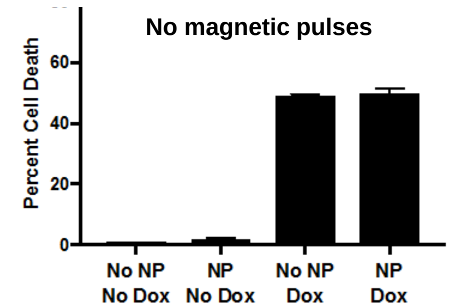
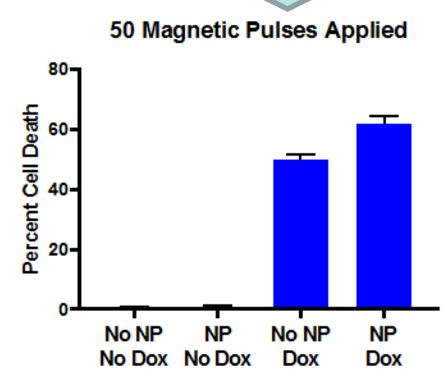
Basanta Acharya











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•Hulangamuwa, W.; Acharya, B.; Chikan, V.; Rafferty, R. J., Triggering Passive Molecular Transport into Cells with a Combination of Inhomogeneous Magnetic Fields and Magnetic Nanoparticles. ACS Applied Nano Materials **2020**, 3 (3), 2414-2420.