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Design of sensors for in-vivo detection of cancer related enzymes

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Design of sensors for in-vivo detection of cancer related enzymes

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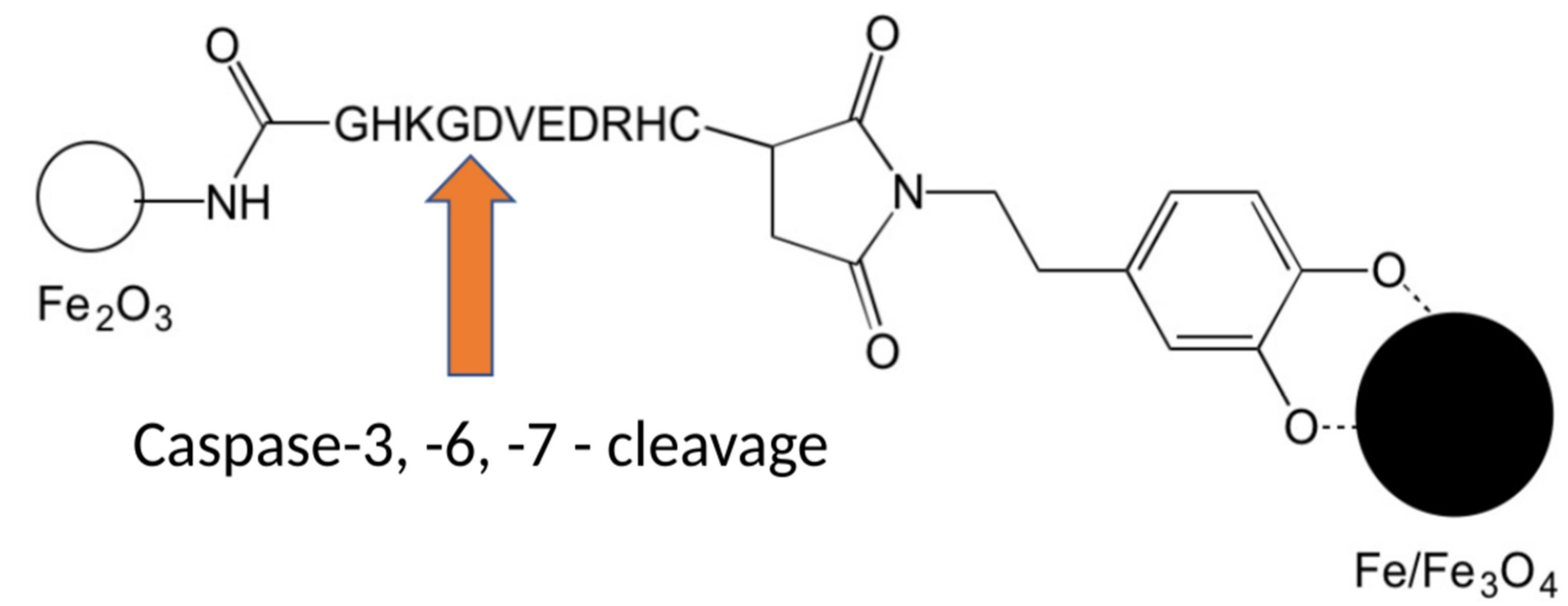
Background

- Cancer is among the leading causes of death in the world .
- In 2018, there were approximately 9.6 million cancer deaths.
- In the U.S. alone there were 1.7 million new cancer cases and 600,000 deaths.

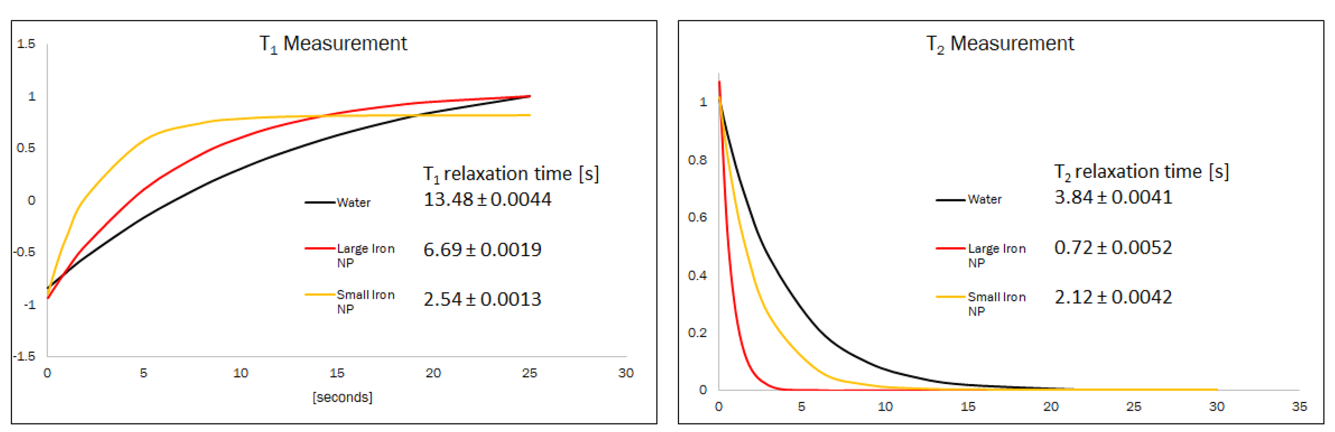
Objective

The goal of this project is to create a nanobiosensor, which would have T_1 and T_2 based imaging capabilities to measure enzymatic activity. This tool will be able to differentiate between benign and malignant tumors in-vivo and to quantify the effect of cancer treatments, such as chemotherapy and radiation therapy.



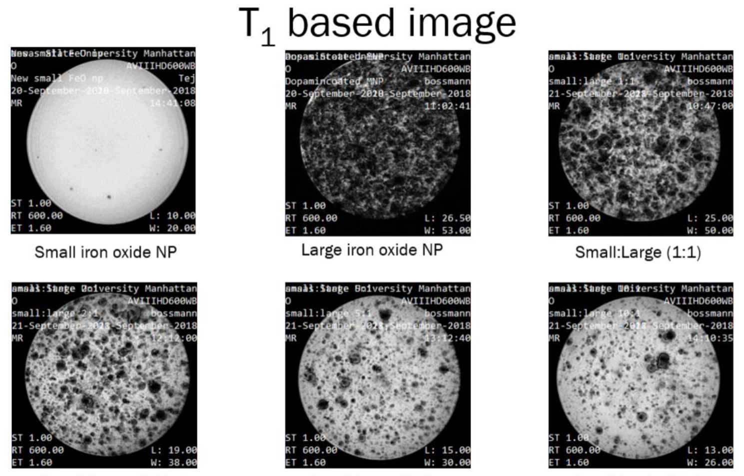
T_1 and T_2 Imaging

Water T_1 and T_2 measurements (600MHz)



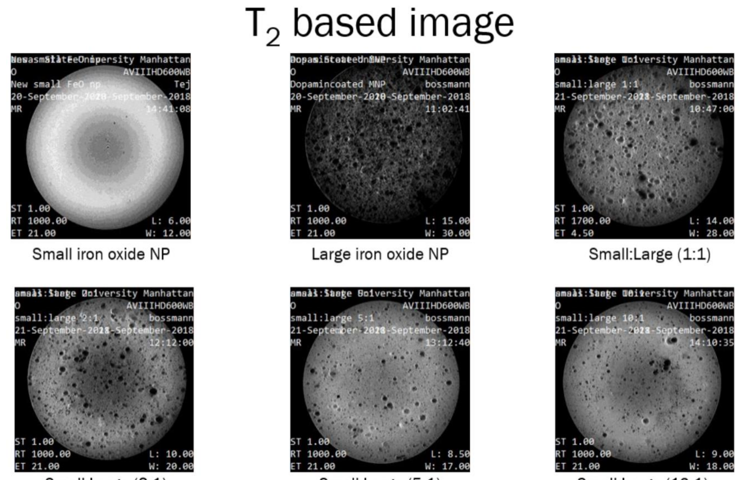
	T_1 (s)	T_2 (s)
D20/H20 (5%)	13.48 ± 0.0044	3.84 ± 0.0041
0.5 mg/mL Fe/Fe_3O_4 NPs (Large)	6.69 ± 0.0019	0.72 ± 0.0052
0.5 mg/mL Fe_2O_3 NPs (Small)	2.542 ± 0.0013	2.12 ± 0.0042

T_1 based image



Small Fe_2O_3 NPs are good T_1 contrast agents.

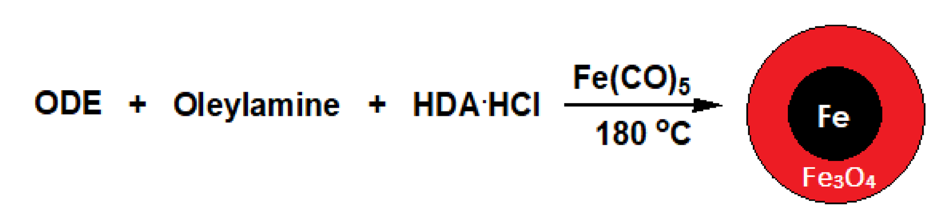
T_2 based image



Large Fe/Fe_3O_4 NPs are good T_2 contrast agents.

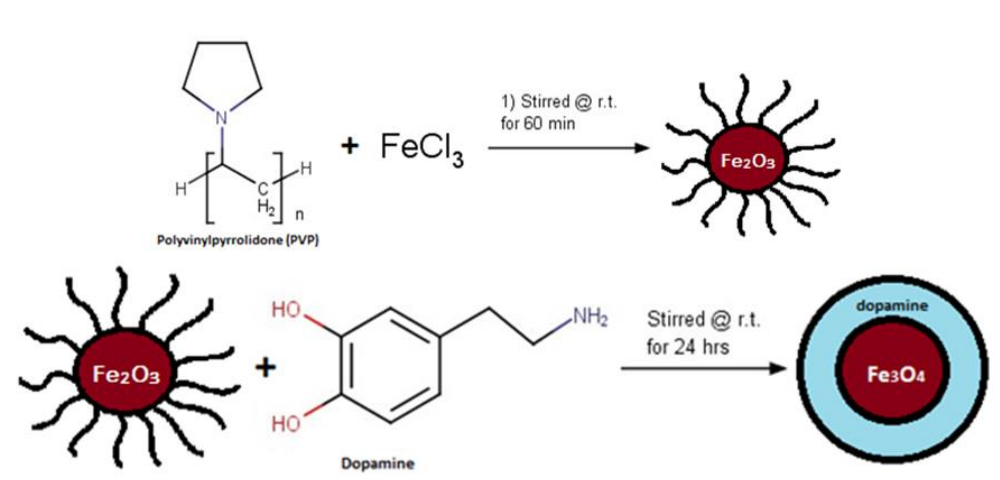
Methods

Synthesis of Large Magnetic Nanoparticles

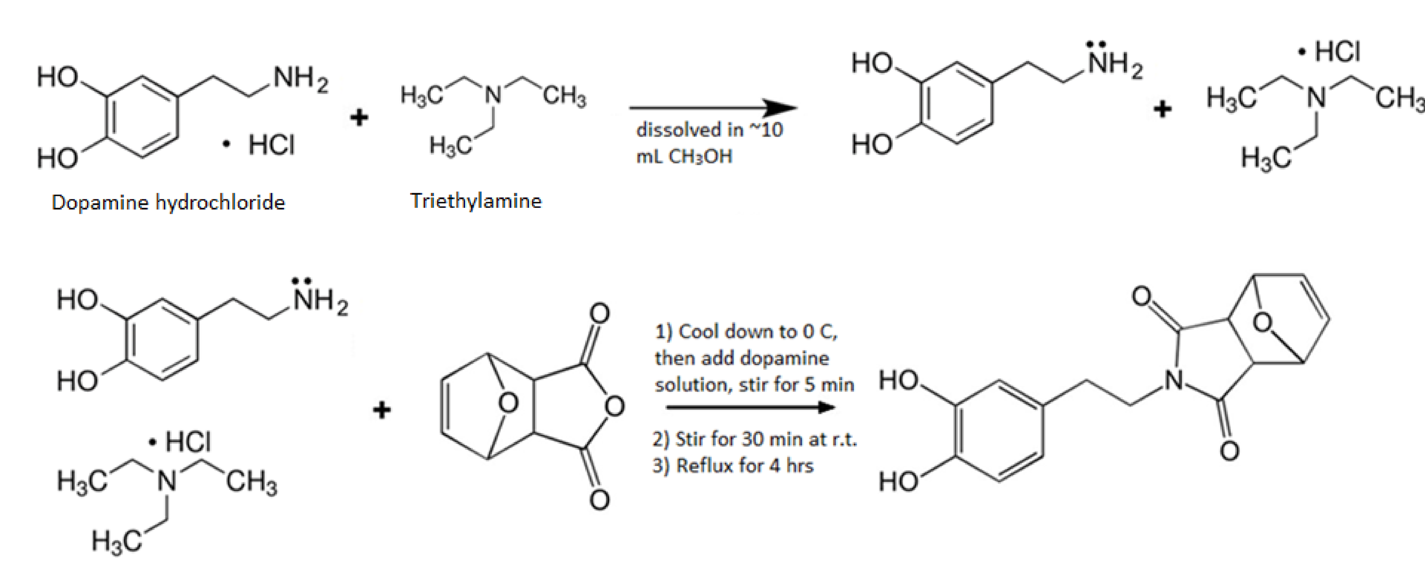


Dopamine Coating of Large MNP

Synthesis of Small Nanoparticles

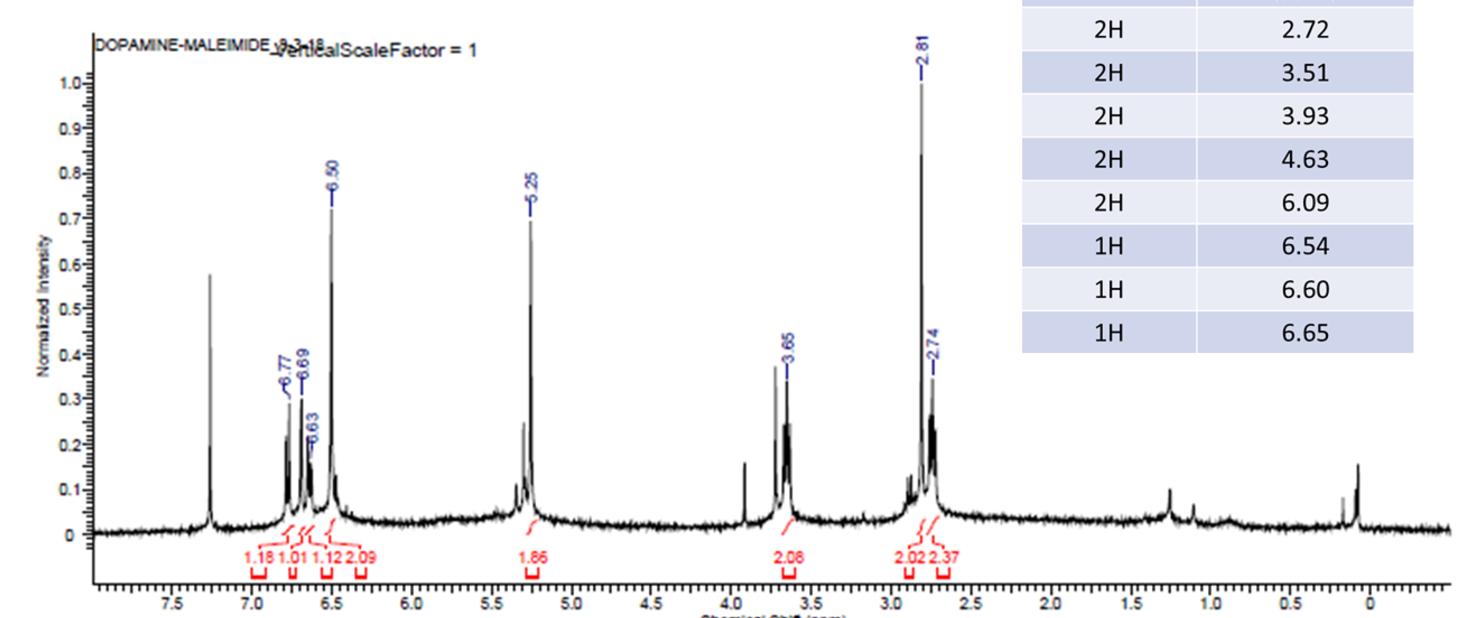


Synthesis of Protected Dopamine-Malemide Anchor



Proton ^1H NMR

Prediction 1H NMR	
Integration	Chemical Shift (ppm)
2H	2.72
2H	3.51
2H	3.93
2H	4.63
2H	6.09
1H	6.54
1H	6.60
1H	6.65



Results

- Dopamine-maleimide anchor was successfully synthesized.
- Results of the cysteine attachment were not very successful.
- Unfortunately, control had a higher sulfur content than sample.

Sulfur Analysis (ICP-OES)	
Sample ID	Sulfur Content (ppm)
Standard 1	5.00
Standard 2	8.00
Standard 3	10.00
Standard 4	30.00
Standard 5	50.00
Control (1mg/mL)	12.1808
Sample Strategy (1mg/mL)	7.3509

Future Work

- Try new methods to optimize the attachment of large NP to cysteine (peptide).
- Attach small NP to other end of peptide and assemble sensor together.
- Finally, move on to do in-vitro and in-vivo testing.

Acknowledgements

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