NRI: Mobile Microrobots for Precision Medicine

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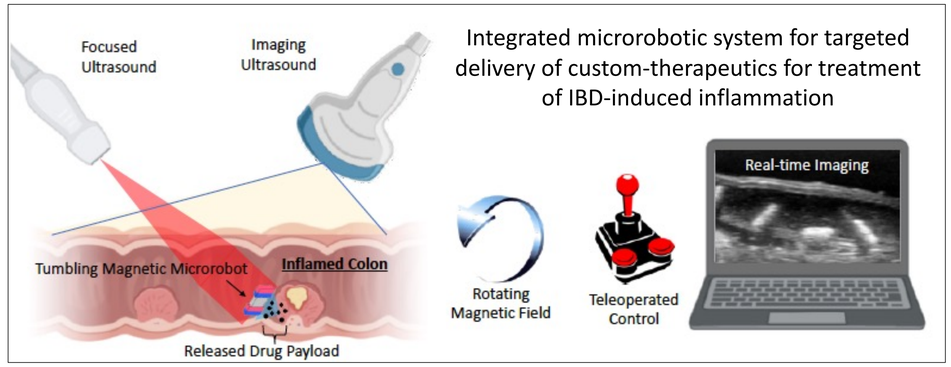
Motivation: Patients with inflammatory bowel disease (IBD) are at significantly increased risk of colorectal cancer (CRC), principally resulting from the effects of chronic intestinal inflammation. Current treatment of IBD is suboptimal despite the array of available pharmacotherapeutics. There is an unmet clinical need for more efficacious and less toxic therapies.

Hypothesis: A combined imaging/actuation system with high resolution, cross-compatibility, small footprint, and tissue penetration capabilities can be developed to actively guide, minimally invasive in vivo magnetic microrobots for the on-demand local delivery of compounds to treat IBD.

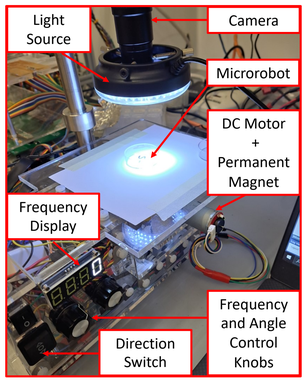
Research Approach: A tumbling magnetic microrobot, actuated with a rotating external magnetic field will be loaded with a thermally-responsive drug payload and controlled via teleoperation. Ultrasound will be used for real-time imaging of the microrobots in the colon. Once at a target location, a focused ultrasound system will be used to heat the microrobot and release the drug payload

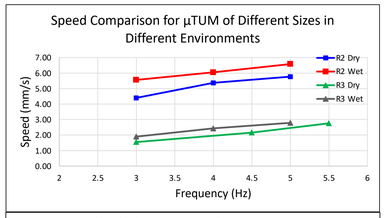


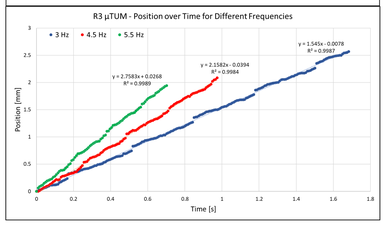
Specific Aims

Aim 1. Design a mobile microrobot system for *in vivo* locomotion within the GI tract of rats

- Fabrication and testing of control microrobot made from SU-8 and NdFeB magnetic particles
- Testing parameters: dimensions/aspect ratio (α), tumbling mode (ST, LT), frequency (1-5Hz), wet/dry conditions, inclination angle
- Performance metrics: forward velocity, accuracy, maximum inclination angle







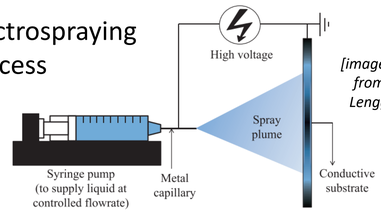
Microrobot	Maximum Incline Angle (Dry)	Maximum Incline Angle (Wet)
R1 LW	30°	60°
R1 SW	30°	60°
R2 LW	30°	60°
R2 SW	25°	60°
R3 LW	30°	60°
R3 SW	25°	60°

Frequency	Microrobot Speed	Trajectory Accuracy
3 Hz	1.55 mm/s	2.2 %
4.5 Hz	2.16 mm/s	4.8 %
5.5 Hz	2.76 mm/s	5.0 %

Aim 2. Design a release system capable of delivering a therapeutic payload from mobile microrobots

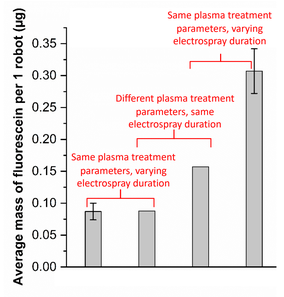
- Electrospraying process developed to coat microrobots with PLGA+ drug payload
- Drug loading onto the robots increases with increasing the total electrospraying time for as long as the PDMS surface remains hydrophilic (polarizable)
- Payload release profile is tunable via control of PLGA properties

Electrospraying process

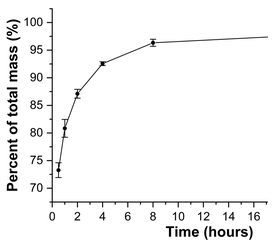


[image reproduced from Saallah & Lenggoro, 2018]

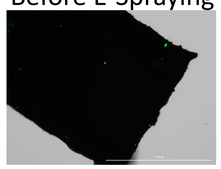
Drug Loading



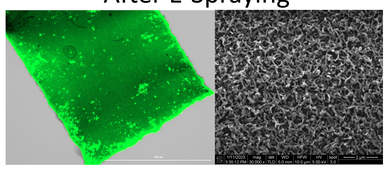
Payload Release Profile



Before E-Spraying

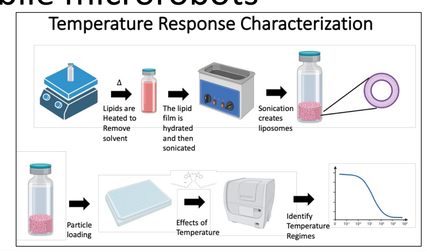


After E-Spraying



Aim 3. Design a focused ultrasound heating system for active *in vivo* targeting and delivery of a therapeutic payload from mobile microrobots

- Developed protocol for fabricating lipid nanoparticles (LNPs); evaluating response of LNPs to bulk heating
- Procured focused ultrasound system; characterizing system for use to stimulate release from thermally sensitive LNPs



Focused Ultrasound System

Broader Impacts: This project has great potential for impact in both the microrobotics and healthcare fields. Patients with IBD are at significantly increased risk of colorectal cancer. There is an unmet need for more efficacious and less toxic therapies, as proposed here. A systematic study of the optimal design features and operating modes for microscale robots in unstructured, complex terrains will enable exciting new applications in medicine and advanced manufacturing.

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