# Multifunctional Microbots for Therapeutics

## Thesis Abstract

Nature has perfected a fantastic inventory of tiny protein machines that inspired the scientists to design artificial small-scale machines. Artificial self-propellers for therapeutic delivery in the diseased body-parts have been considered to be one of the most emerging areas of nanoscale research. Unfortunately, the demanding *in vivo* therapeutic applications greatly precludes the development of such synthetic motors due to toxicity, immune rejection, low biocompatibility and expensive fabrication techniques.

Thus, my research was focused on fabrication of biocompatible micro/nanobots (MNMs) and their potential therapeutic applications. The objectives have been directed to implement - **(i)** simple, and low-cost fabrication processes **(ii)** use of plant-based materials in MNM design, **(iii)** fuel-free navigation of MNMs, and **(iv)** multi-functionality of MNMs, particularly drug loading and on-demand release before these artificial systems can be promoted for real-world biomedical applications. The objectives of the 5 chapters have been briefly discussed below:

**1.** Biocompatible and self-propelled micromotors were synthesized from the mesoporous button mushrooms with infused magnetic control on acid-alkali chemotaxis. The experiments show the potential of the iMushbots in retaining and transporting drugs in an alkaline medium such as human blood and releasing them in an acidic medium such as the cancerous tissues for cell apoptosis. The reported microbots can be thought of smart alternatives against the synthetic materials for targeted drug delivery applications in the pH-responsive systems.

**2.** Next, the feasibility of stimuli-responsive conditional movements of mushroom motor, namely a 'logibot' has been investigated for the construction of a host of optimized binary logic gates namely, AND, NAND, NOT, OR, NOR, and NIMPLY. The self-propelling logibot could rapidly sense the alkali-acid triggers, decide, and act on the basis of intensities of the pH triggers realized as potential outputs of the logic gates. This proved to be an eco-friendly alternative to the silicon-based computing operations for the development of intelligent pH-responsive drug delivery devices.

**3.** Further, an effective bacterial killing approach was explored using mushroom microbots (namely iButtonbots) that encourages the magnetic actuation to significantly improve water treatment strategies by enhance the mixing of *Escherichia coli*-laden water. The iButtonbots were immobilized with curcumin by electrostatic interactions, and superior bacterial killing was thus obtained using as compared to free CU due to the synergic effect. Introducing a swarm of such magnetically handled iButtonbots could be exploited for accelerated bacterial killing in contaminated areas.

**4.** Ultrasound-propelled ascorbic acid loaded nanomotors have been designed, namely Teabots, from *Camellia sinensis* that could offer efficient loading, localized transport, and release capabilities for anti-oxidative and anti-amyloidogenic responses. The motors show antioxidant properties at physiological pH range by scavenging intracellular ROS. Interestingly, the % release of ascorbic acid was significantly higher under the influence of ultrasound exposure, as compared to pH-dependent release. The motors were also efficient in the degradation of toxic amyloid fibrils preventing protein-aggregation derived diseases envisioned in treating neurodegenerative disorders.

**5.** We introduce a conceptual robotic platform from tea buds as a modality for magneto-robotic removal of biofilms of both Gram-positive and Gram-negative bacterial strains in a 'Kill-n-Clean' way. In the first platform, magnetically driven linear and spinning motions of microbots (T-Budbots) could efficiently kill and uproot the degraded biofilms, thus restoring the paths clogged by biofilm. Secondly, the microbots could ensure an efficient drug delivery system with a sustained pH dependent release of loaded drug at acidic microenvironment of biofilms resulting in bacterial killing.