CHARACTERIZATION OF MAGNETICALLY TRIGERABLE MILLIROBOTS FOR ON DEMAND DRUG DELIVERY USING A BRIGHTFIELD MICROSCOPY METROLOGY SYSTEM

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Abstract

Magnetic miniature robots are controllable devices that can access complex and narrow regions of the human body in a minimal invasive manner in cavities such as the gastrointestinal tract or vasculature, with the potential to perform targeted delivery of therapeutic substances. These devices, are capable of being actuated near the target position for releasing the carried substances [1]. To further improve drug delivery there is a need to design targeted drug delivery systems that allow precise actuation, modulation and release of substances for those diseases requiring variable release kinetics such as cancer diabetes etc.

We have developed a magnetically addressable low-cost robotic drug delivery system that has the ability perform on-demand drug administration via magnetic actuation [2, 3]. A key aspect to achieve precise control of drug release patterns is to characterize the robotic device response to external magnetic fields.

In this paper we present a non-contact metrology system to characterize the influence of discrete magnetic field strengths applied to the millirobots for on demand drug delivery. Our optical system is based on custom made bright field microscopy system (BFM) based on an Olympus PLN 4X WD~18.5mm, NA 0.1, a tube lens (f~180mm) and a DMK31BF03 CCD camera (The Imaging Source Europe GmbH, Germany) mounted on top of a custom made linear stage having a coarse resolution of ~ 3.3µm. The robotic devices tested were fixed vertically on a microscope cover glass which was then placed in between the magnetic actuator and the BMF system ensuring that the millirobot was kept perpendicular to the microscope optical axis. By focusing the microscope on the device without any magnetic field applied, a reference measurement was taken, then the magnetic actuator was then switched on provide discrete varying magnetic fields ranging from ~100-350 mT. By moving the linear stage to refocus on the device outer face its compression was accurately measured using the linear stage digital readout.

The BMF system allowed us obtaining the compression profiles for each magnetic field strength showing significant compliance with average volume reductions ranging from 6 to 40% under a range of 100 to 350 mT. Reversibility and damage happening from continuous use was assessed using both BMF and a scanning electron microscope (Zeiss Sigma FEG-SEM (Carl Zeiss, UK).

Finally, we explored the inhibition of HeLa cells by loading our devices to release 5-Fluorouracil in a concentration of ~ 25 mg/mL. Approximately 5x10^4 cells were plated on Petri dishes and incubated overnight, on the next day cell count increased to ~ 10x10^4. This was followed by magnetically release the drug using our device and returning the plates to the incubator for 3 days. By comparing the number of HeLa cells present on our test cultures before and four days after the drug release, we observed that cell count decreased to ~1x10^4.

The use of bright filed based metrology system has allowed us to characterize the effect of the applied magnetic field to measure the level of actuation in the developed millirobots. This is for selectively releasing a drug to a target region aiming to offer a more efficient drug delivery.

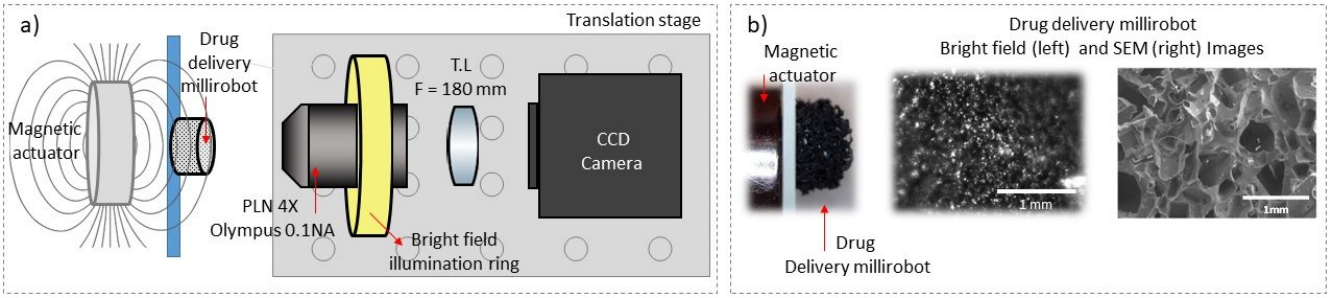

Fig 1. (a)Schematic representation of the experimental setup, (a) magnetically actuated drug delivery millirobot, from left to right, macro, brightfield microscopy and SEM images.

References

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