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TITLE: MODELING AND CONTROL OF MICROROBOTS USING ACOUSTIC PROPULSION FOR MEDICAL APPLICATIONS

KEYWORDS: Mathematical modeling, acoustic propulsion, flagellum dynamics, control of nonlinear systems, targeted therapy.

SUBJECT

1. Introduction:

This proposed thesis aims to lay a foundation for noninvasive and targeted medical treatments based on artificial microswimmers. We envision that the latter will carry various medical functionalities, navigate in biological ducts, and perform local treatments for lesions [1]. Recent experimental and theoretical studies demonstrate that microswimmers can be remotely propelled acoustically or magnetically, which is safe to the human body. In particular, acoustically propelled microswimmers can achieve excellent motility (~1 mm/s) under sound pressure in the accessible range of therapeutic ultrasound [2]. Diverse types of acoustic fields have been used to power microrobots. Focused ultrasound (FU) is capable of concentrating acoustic energy in a single zone, optimal for applications where high penetration or localized actuation is required. In addition, standing wave ultrasound (SWU) robots work on nodal planes, have demonstrated multiple advanced biomedical tasks, suitable for lab-on-a-chip applications. Finally, traveling wave ultrasound (TWU) employs tunable resonant elements responding to specific frequencies, holding great promise for in-vivo applications. Nevertheless, microswimmer-based therapy is still conceptual. It remains unclear how a microswimmer can be steered to move along a crooked fluidic channel—for example, the human intestine (Figure 1)—under acoustic or magneto-acoustic actuation. Modeling and control of magnetic-acoustic propulsion of flagellated microrobots is of key importance for in-vivo drug delivery applications [3].

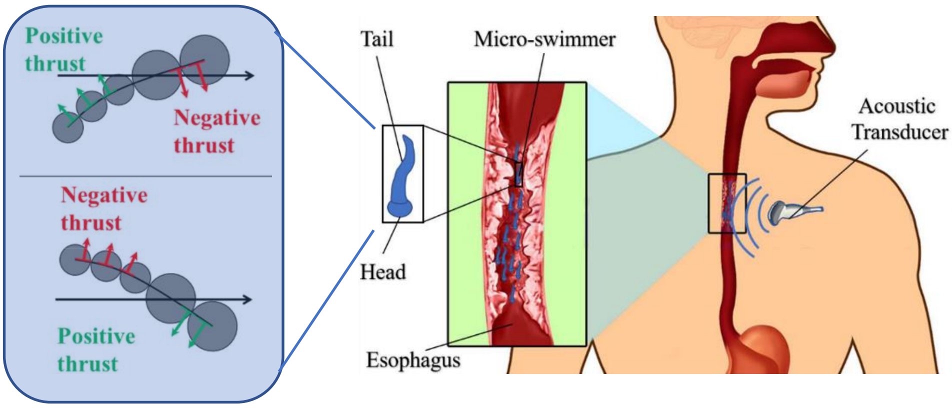

Figure 1: Schematic of microswimmer based treatment, where a therapeutic ultrasound is used to drive and image swimmers into the cancerous segment for targeted drug delivery.

2. State of the art:

Swimming at the microscale differs fundamentally from that at the macroscale owing to the different Reynolds number (Re), of which the order of magnitude is 10^6 for a human swimmer and 10^{-4} for a bacterium [4] in water. Based on the type of external stimulus, artificial microswimmers may be classified into those actuated magnetically or acoustically. Magnetic actuation may be more suitable for driving helical microswimmers. Under a rotating magnetic field generated by three-axis Helmholtz coils, a helical microswimmer rotates concomitantly, yielding a high motility (e.g., 320 µm/s [5]). In addition, steering a helical microswimmer is straightforward as its axis tends to align with the rotation axis of a magnetic field [6]. These advantages enabled some *in vivo* trials [7]. In addition, the rotating magnetic field cannot be focused on a local region containing microswimmers. In medical applications, the coils should have a diameter of several meters to accommodate the human body; however, they are only used to actuate some microswimmers, thereby resulting in significant energy wastage. Here, we are interested in investigating acoustic propulsion as sound can be focused.

Three types of acoustic microrobots are of interest: (i) Particles-based acoustic micro-swimmers can be moved by ultrasonic sound, a phenomenon known as acoustophoresis, because of non-zero averaged radiation forces over an acoustic period [7]. (ii) Acoustic flagellum propulsion (AFPs), shown in Fig.1, was much more efficient than acoustic streaming. Because acoustic energy can be easily focused (already used clinically, e.g., in ultrasonic lithotripsy), AFPs are expected to be easier to implement than magnetic ones. (iii) Finally, bubble-based acoustic microswimmers [8] are propelled by the oscillation of liquid–air interfaces induced by ultrasound. It has been demonstrated that acoustic bubble-based microswimmers can swim even faster than flagellum-based ones under the same sound pressure [9].

3. Research Objectives

For all three acoustically-based propulsion methods, theoretical modeling of steering mechanism are not well understood. Inspired by these observations, the candidate will established in this thesis theoretical mathematical models of acoustic propulsion for each type of acoustic propulsion to confirm that acoustic waves can control accurately the microswimmer steering in blood flow.

It will be attempted to make clear (i) how an acoustic wave actuates the motion and (ii) what is the optimum design of the microswimmer that achieves the largest swimming speed. In order to make the model more meaningful, the effects of inertia, viscous fluid, blood flow, material damping, and non-uniform body cross-section in the calculation. These effects are crucial because a realistic design of acoustic-based propulsion cannot avoid them. Based on the accurate modeling, state-space control of non-linear systems will be elaborated. This result motivates us to conduct experiments to verify this strategy of acoustic steering and to investigate other steering approaches by employing purely acoustic or magneto–acoustic forces. The key questions to be addressed in this thesis are as follows: (1) how to steer and control acoustic microswimmers efficiently; (2) can the predicted approaches of microswimmer steering be verified experimentally; and (3) what is the best implementable steering strategy.

The PhD work will focus mainly on the development of theoretical mathematical formulations related to modeling and control.

- Study existing references on acoustic microswimmers dynamics modeling.
- Mathematical models of acoustic propulsion methods: (i) particles-based acoustic propulsion, (ii) acoustic flagellum propulsion [10] and (iii) bubble-based acoustic propulsion [11] to confirm that acoustic waves can control accurately the microswimmer steering in blood flow.
- Numerical simulations: Quantitative simulations will be carried out to simulate the predicted motion for design optimization.
- Control of steering locomotion: Based on the state-space representation, nonlinear controllers for underactuated systems will be proposed for trajectory tracking along a reference path taking into account low Reynold's number media, pulsatile flow, vessel bifurcations, modeling errors and acoustic wave attenuation.
- Experimental validation: To confirm feasibility of the proposed acoustic steering strategies, verification experiments will be conducted. We shall first establish an experimental platform and then verify the proposed steering approaches and identify the one that is the easiest to implement.

4.3. Bibliography:

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