2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Acoustofluidic Based Wireless Micropump for Portable Drug Delivery Applications*

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Abstract— **In this study, an acoustofluidic based wireless micropump for drug delivery was proposed and fabricated. The key actuator of this micropump is a small gigahertz piezoelectric resonator, which could induce strong fluidic streaming at low applied power. This acoustofluidic micropump has stable and accurate dosage resolution (7.0 µL), and sufficient flow rate (1.34 mL/min). The miniaturized size and wireless controlled operation prove it as a portable drug delivery system.**

Clinical Relevance— **The acoustofluidic based micropump could apply for the drug administration in a safe, effective and stable form. It has potential to integrate with miniaturized sensors and electronic circuit to form portable drug delivery systems, realizing smart on-demand drug delivery.**

I. Introduction

With the advances in medical science, scientists not only focus on the therapeutic agents itself, but also strive to improve the approaches to administer therapeutic agents to biological systems, which is called drug delivery systems (DDS). Compared to traditional DDS, which normally controls the release time and the drug quantity, the modern integrated smart DDS is required to provide a precise control over the therapy. To achieve such goal, an ideal integrated DDS should consist of drug reservoirs, micropumps, valves, microsensors, communication and control terminals[1]. A recent trend for advanced DDS is to develop portable system for point of care applications[2]. As one of the executive components of the integrated DDS, micropump contains electromechanical units for precise liquid control, which is rather difficult for miniaturization. With the rapid development of micro-electro-mechanical systems (MEMS), the MEMs fabricated micropump has triggered a lot research interest, which features with small size light weight, low power consumption, wide flow rate range, low cost and the potential for integration with other microsensors and electronic circuits[3].

The existing micropumps (micropumps mentioned later refer to MEMS-based micropumps unless otherwise stated) can be generally classified as mechanical or non-mechanical micropumps, depending on whether containing moving parts (pumping diaphragms, check valves, etc.) or not. As a classical mechanical micropump, piezoelectric micropumps could achieve large flow rate (163.7 mL/min) and high back pressure (29.7 kPa) with the help of check valves at 400 V working voltage[4]. However, without the check valves, its pumping performance would decline heavily[5]. Another typical disadvantage of piezoelectric micropumps is high applied voltage (>100 V), which reduces their portability and operation safety. Other types of mechanical micropumps, such as the phase change micropump which normally reaches a flow rate of 49.1 µL/min and a generated pressure of ~0.7 psi powered by a biodegradable battery substitute[6], the shape-memory-alloy micropump powered by wireless charging[7], might have great portability but lack of precision control and sufficient flow rate.

Compared with the mechanical micropumps, non-mechanical micropumps can drive liquid continuously and smoothly. They have better stability and faster response time which is due to their compact structures. Reported micropump based on charge-injection electro-hydrodynamics can drive bidirectional flow with a flow rate of 6 mL/min and a backpressure of 14 kPa at 8 kV, which could be applied for wearable electronic applications[8]. Other types of non-mechanical micropumps include magnetohydrodynamic, electroosmotic, electrowetting, electrochemical, etc. In spite of the advantages as mentioned above, the non-mechanical micropumps normally require specific pumping mediums, and have rather little flow rate and low backpressure[9]–[11].

Here, we present an acoustofluidic based wireless miniaturized micropump for portable DDS applications (Fig. 1A). The key part of the micropump is a MEMS fabricated gigahertz (GHz) solid-mounted bulk acoustic resonator (SMR). It features with small size, low working voltage and power consumption, which make it very suitable for high-performance non-mechanical micropump. As shown in Fig. 1B, the acoustofluidic based wireless micropump is composed of a SMR, a micropump body, a printed circuit board (PCB), a conical capillary and an antenna. Once connected with the drug reservoir, it could drive the drug liquid to flow, delivering drug to targeted area on demand. In this work, we introduced the working principle of the acoustofluidic micropump, and discussed its feasibility for drug delivery applications.

II. Experimental

A. Principle and theory

Our group has been continuously working on high frequency acoustofluidic system for biological, chemical, and medical applications[12]–[14], where GHz acoustic wave is typically applied for cleaning, sensing, dispensing and so on. When propagating into fluid, acoustic wave decays along the wave propagation axis (set as *z*-axis), and the attenuation coefficient, β, is expressed as (1) [15]:

$$\beta = \frac{b\omega^2}{\rho c^3} \tag{1}$$

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where ω is the angular frequency of the acoustic wave, c is the sound velocity, ρ is the liquid density, and $b = 0.75\mu + \mu_B$, where μ and μ_B are the shear viscosity and bulk viscosity of the fluid, respectively. The attenuation coefficient is in proportion to the square of acoustic frequency, which means GHz acoustic wave has a very short attenuation length (β^{-1}) and a highly concentrated energy distribution. Thus, due to the nonlinear attenuation of the propagating acoustic wave, a rather large body force, F_b, could be generated by the acoustic wave, which is given by (2) [13]:

$$F_b(x,y,z) = \rho\beta\omega^2 a^2(x,y)e^{-2\beta z} \tag{2}$$

where a is the amplitude in (x,y) plane.

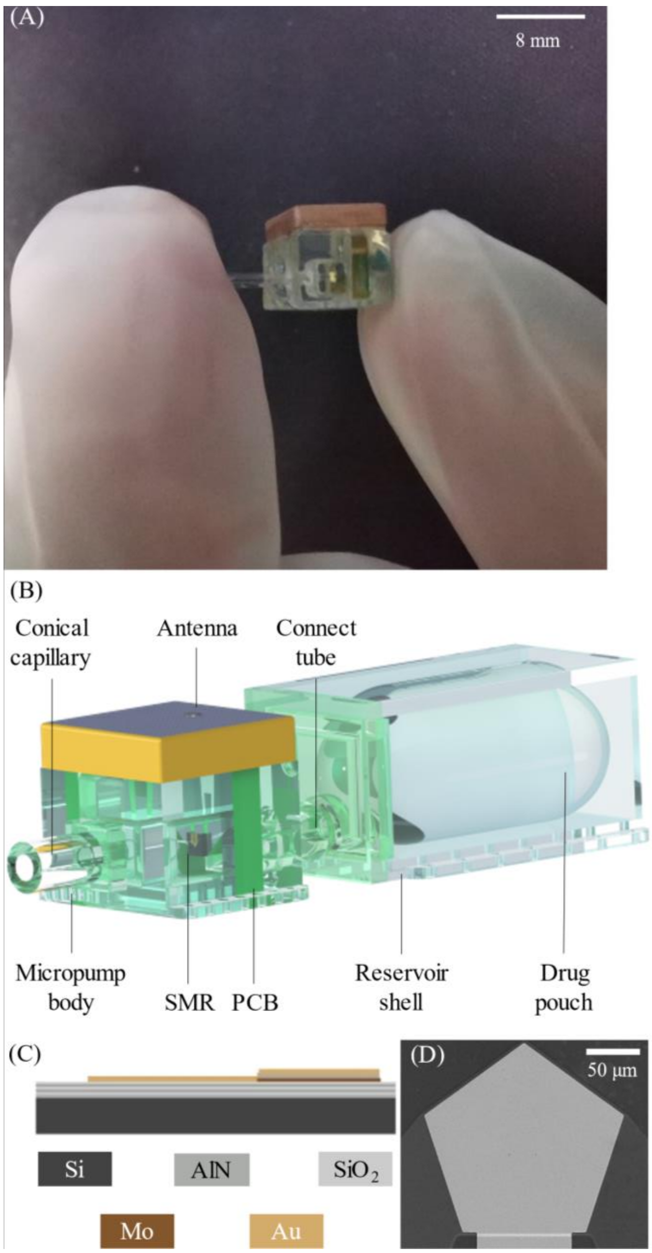

Figure 1. (A) Photograph of the wireless acoustofluidic micropump. (B) Schematic illustration of the acoustofluidic-based wireless micropump with a drug reservoir. (C) Sectional view of SMR. (D) SEM image of SMR surface.

The SMR used here has a resonate frequency of 1.565 GHz. Through inverse piezoelectric effect, the SMR generates acoustic waves in thickness-extension mode by applying voltage on the top and bottom electrodes. When contacting with liquid, the acoustic waves propagate from SMR into liquid and result a traveling acoustic wave, which has an attenuation length of 9.3 µm in water. A typical Eckart streaming could be observed above the SMR, where the jetting flow drives the liquid straight out from the device center. Due to the principle of mass conservation, the surrounded fluid recirculates in order to replace the forward jetting fluid. It continuously supplies to the device area, and then joins the jetting flow, thus generating stable acoustic streaming microvortex (Fig. 2A) [12].

As the micropump is designed by continuous flow pushed by the device in the direction of the acoustic propagation, the acoustic streaming microvortex should be restricted thus the jetting flow is maximized. To obtain stable unidirectional flow, a conical capillary was designed and inserted in the micropump body, which is vertically above the SMR surface (~100 µm). At this boundary situation, the rapid upward jet flow is confined in a narrow area and streams along the capillary, outflowing as droplets and driving the liquid to inflow, realizing unidirectional pumping (Fig. 2B).

B. Methods

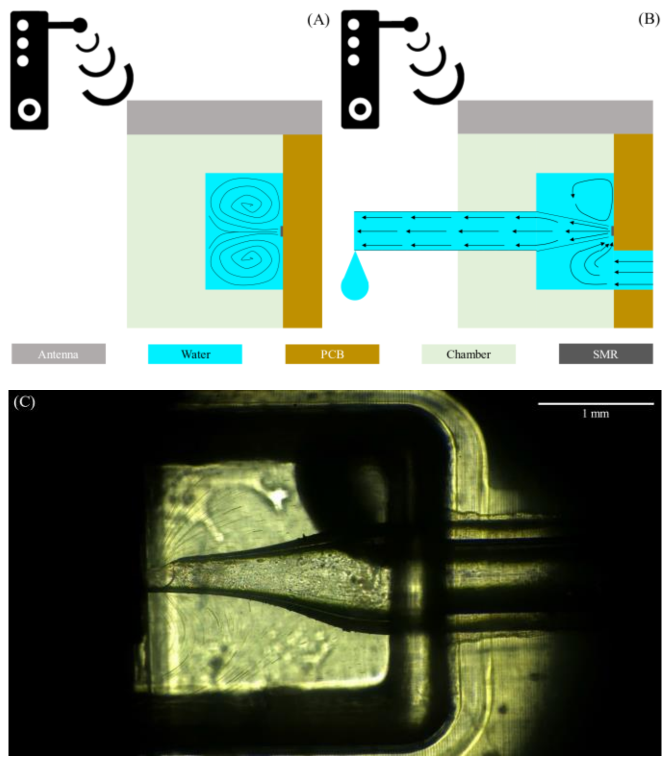

Figure 2. (A) Acoustic streaming vortexes actuated by SMR in a rectangular chamber. (B) Fluidic field of working acoustofluidic micropump. (C) Photograph of fluidic field (under 400 mW) in the micropump chamber taken by a high-speed camera.

The SMR is fabricated by typical MEMS approaches (Fig. 1C), and the detailed manufacturing process was reported in previous publication[13]. Figure 1D presents the diced SMR device which has a typical pentagon structure with the sides of

114 μm. The micropump body was fabricated using a 3D-printer (Form 2™, Formlabs Inc., 35 Medford St. Suite 201, Somerville, MA 02143, USA) out of the photopolymer clear resin (FLGPCL04®, Formlabs Inc., 35 Medford St. Suite 201, Somerville, MA 02143, USA). The conical capillary was placed perpendicularly above the surface of the SMR with the distance of ~100 μm. A commercial antenna (GPS+BD ceramic antenna, 1561/1575.42 MHz, Boan Tong Xun, China) was connected with the SMR through a simple PCB to achieve the wireless charging. The overall assembly of the acoustofluidic micropump-based DDS is shown in Fig. 1B.

To illustrate the flow field in the micropump chamber, the tracking microspheres with diameter of 9-13 μm (110P8, Lavision GmbH, Germany) and a high-speed camera were used. Through overlapping frames of the video (2000 fps) taken by the high-speed camera, the tracks of microspheres were recorded, which represents the flow field.

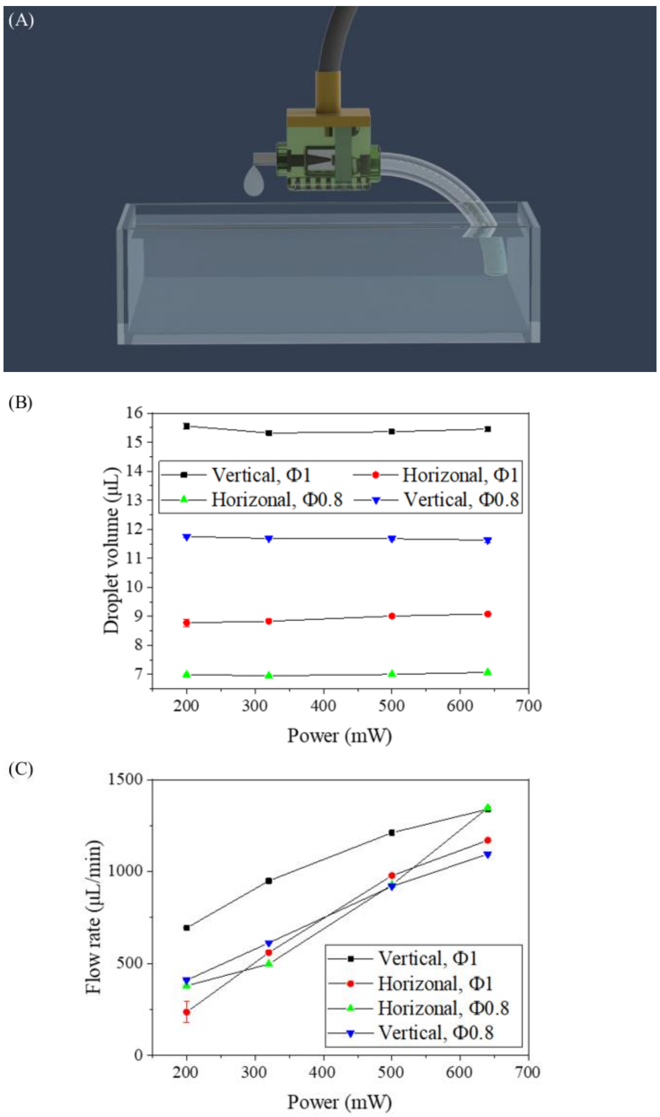

Figure 3. (A) The illustration of the setup for recording the droplets formation. The volumes of droplets (n = 5) (B) and the flow rates of the micropump (C) through tubes with outer diameters of 0.8 and 1 mm at different postures (vertical and horizontal) under different applied powers (200, 320, 500 and 640 mW).

To assess the stability and accuracy of the pumping droplets generated by the micropump under different applied powers, the high-speed camera was focused at the end port of the tube connected with the capillary, recording the continuous generation of the droplets under different powers. The experimental setup was illustrated in Fig. 3A. Assuming the droplets were rotational symmetric at the last moment before drop, the volume of each droplet could be estimated according to its outline from frame image. Combining the generation time, the flow rates in open environment could be got as well. We assessed the performances under situations of two outlet tubes with different outer diameters of 0.8 mm and 1 mm, respectively.

To prove the feasibility of the acoustofluidic micropump to deliver drug drops by wireless radio frequency (RF) signal, we recorded the pumping processes with a camera (at 30 fps). The commercial GPS antenna (glue stick antenna, 1575.42 MHz, Boan Tong Xun, China) was chosen as transmission antenna, emitting a RF signal of 1.565 GHz at 8 W. It was placed above the micropump with a distance of ~5 mm.

III. Results and Discussion

As shown in Fig. 1A, the fabricated micropump has a typical dimension with ~9×9×9 mm^3, which is smaller than a thumb. It can be connected with different drug reservoirs through a soft silicon tube to meet different therapeutic requirements, which is illustrated in Fig. 1B.

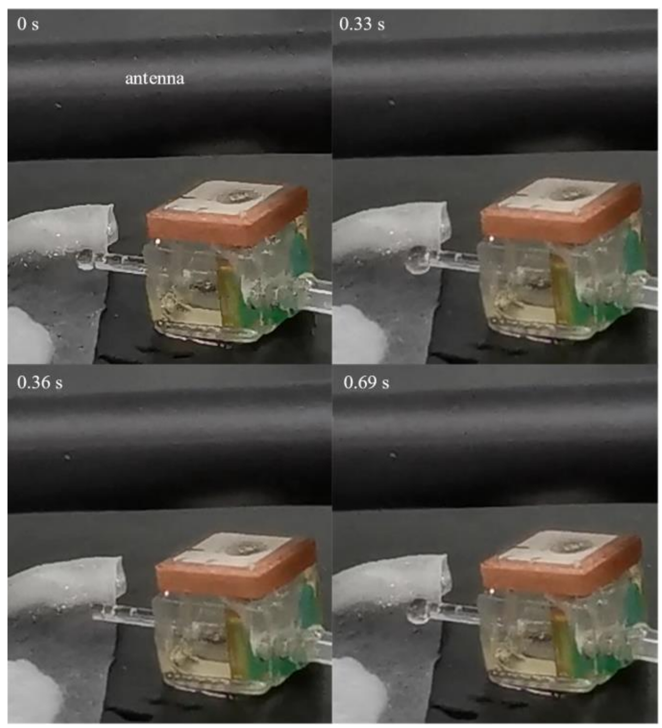

Figure 4. The processes of droplets produced by the acoustofluidic micropump powered by wireless charging.

To monitor the flow, we used microspheres and high-speed camera to study the flow behavior during the pumping. Figure 2C shows that the fluid above the SMR surface is pushed by the body force and moves upward when SMR turned on. Once entering the capillary, the jetting flow is separated from other fluids in the chamber and moves along the capillary tube. The

SMR gives fluid the kinetic energy, and the boundary situation guides fluid to move. Thus, the pumping performance of this acoustofluidic pump could be tuned by changing the guide tube, meeting different therapies.

Here, we evaluated the performance of the GHz micropump as a droplet infusion pump (Fig. 3A), which mainly considered the drop resolution, stability, and the flow rate[16]. Through recording the generated droplets, the volume and time of each droplet can be calculated. As shown in Fig. 3B, C, the volume of the pumped droplets can be tuned from ~7.0 μL to ~15.5 μL depending on the inside diameter of the tube which proves the high-resolution dispensing. We then verified the applied power to the SMR from 200 to 640 mW, the droplet volumes remained the same. This indicates the pumping has a rather good stability which is actually very important to be used as a wireless micropump. Figure 3C demonstrates a wide range of adjustable infusion pumping rates ranging from 1.34 mL/min in Φ0.8 mm tube at 640 mW to 0.23 mL/min in Φ1 mm tube at 200 mW. This could satisfy most of the therapeutic requirements.

Comparing with other MEMS micropump, the GHz acoustofluidic micropump has a low and safe applied voltage (<10 V) and a large flow rate/size ratio (1.8 kL/(min·m^3)). Besides, the micropump can efficiently pumping droplets from wireless charging. The formation time of each droplet is less than 0.69 s at 8 W with a distance of 5 mm, indicating a flow rate of ~0.21 mL/min. All these results, especially the wireless charging function demonstrates the big advantage of the GHz acoustic pump as a portable system.

IV. Conclusion

In summary, an acoustofluidic-based wireless-charging micropump has been developed for safe, precise and efficient drug delivery applications. We illustrated the working principle of the acoustofluidic micropump, the design and construction of the miniaturized drug delivery system. As a droplet infusion pump, it could produce droplets with different volumes tuned by the boundary situation of the outlet. A pumping resolution of 7.0 μL and a maximum flow rate of 1.34 mL/min were reached. This acoustofluidic based wireless micropump will be furtherly investigated as an integrated smart DDS for personalized medicine applications, for improving therapeutic effects and saving medical resource.

Acknowledgment

The authors gratefully acknowledge financial support from the National Natural Science Foundation of China (NSFC No. 21861132001), National Key R&D Program of China (2018YFE0118700), Tianjin Applied Basic Research and Advanced Technology (17JCJQJC43600), the 111 Project (B07014), and the Foundation for TALENT SCIENTISTS OF NANCHANG INSTITUTE FOR MICRO-TECHNOLOGY OF TIANJIN UNIVERSITY.

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