

LOW-POWER THERMOMECHANICAL MODULE FOR TARGETED INGESTIBLE DEVICE BIOPSY

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ABSTRACT

We demonstrate a **novel low-power thermomechanical biopsy module enabling closed-loop sampling** of gastrointestinal (GI) mucosal tissue from an ingestible capsule device. The actuation module utilizes a 3D-printed cam and follower mechanism triggered by a microfabricated thin film heater to drive a 3D-printed biopsy punch into the GI wall for tissue collection. The module can be triggered using 50 mA of instantaneous current draw and a power of 150 mW, while producing 2.4 ± 0.058 N of force, collecting samples of 4.7 ± 2.1 mm³. This biopsy module is the first to be capable of operating with a single ingestible sized battery and without the use of external stimulus, providing a realistic path toward minimally invasive clinical capsular biopsy.

KEYWORDS

Biopsy, Ingestible Device, Actuation, GI tract.

INTRODUCTION

Ingestible capsule devices offer a promising minimally-invasive alternative to traditional means of performing gastrointestinal (GI) health monitoring and intervention in regions that are difficult to access through traditional means (i.e. the small intestine) [1]. Often tissue samples must be collected, or biopsied, for evaluation by a pathologist to reach a definitive diagnosis of GI diseases. However, no commercially available ingestible capsule devices have the capability of tissue sampling. Biopsy capsule prototypes have failed to translate due to the lack of depth targeting, reliance on external operation, or high-power requirements not attainable by the available ingestible sized batteries [1], [2], [3]. Thus, these capsules are incapable of closed-loop sampling of GI mucosa without operation by medical professional.

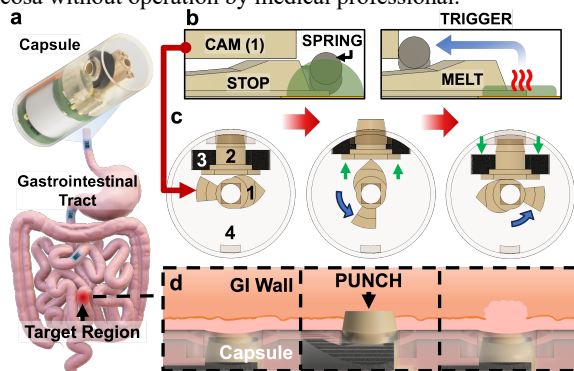


Figure 1: (a) The biopsy module, integrated with an ingestible device, travels to the target region in the small intestine (SI), where the onboard electronics trigger cam and follower mechanism (CnF). (b) The adhesive holding a preloaded spring is melted allowing it to jump over the stop and drive the cam. (c) The CnF is comprised of: (1) cam, (2) biopsy punch (follower), (3) foam spring, and (4) capsule housing. The spring drives the CnF, turning the cam counterclockwise. At $\sim 90^\circ$ of rotation, the biopsy punch is forced up out of the capsule housing. At $\sim 180^\circ$ the biopsy punch is forced back into the capsule by the foam spring. (d) The punch is actuated into the GI wall, collecting a sample of the mucosa.

In this work, we present a novel **low power, biopsy module** for sampling **intestinal mucosa** enabling **closed-loop** operation from a **battery powered** ingestible capsule device (Figure 1a-d). We demonstrate the integration of the module with an ingestible battery and evaluate key electrical properties of the system as well as its output force. The module's ability to capture suitable biopsy samples was evaluated on agarose tissue analogues.

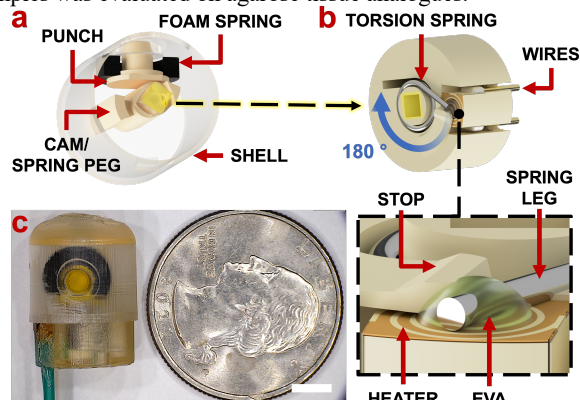


Figure 2: CAD rendering of the biopsy module depicting (a) the CnF body aligned via a center pin, and (b) the trigger body featuring the microheater and torsion spring. The mechanical stop and ethyl vinyl acetate (EVA) immobilize the loaded spring until triggering. (c) An image of the fully assembled capsule (Scale bar: 5mm).

MATERIALS AND METHODS

The biopsy module is composed of two main bodies: (Figure 2a) housing shell containing the cam and follower (CnF), and (Figure 2b) a trigger body which features a preloaded torsion spring and microheater. When deployed, the torsion spring lead drives the rotation of the cam, prompting actuation of the follower punch for tissue biopsy. The biopsy module was fabricated by 3D-printing the CnF components, capsule shell, and spring trigger modules with the Phrozen Sonic Mini 8K Resin 3D Printer (Phrozen Tech Co., Ltd.) using biocompatible resin (Formlabs Inc.) (Figure 2c). Polyethylene foam sheets (McMaster-Carr) were cut into 2 mm thick, 5 mm diameter rings with a 3 mm diameter center hole and fixed atop the skirt of the 3D-printed punch. A microfabricated thin film gold heater (Figure 2), previously published by our group [4], was fixed atop a 3D-printed holder with ethyl cyanoacrylate adhesive (Newell Brands) and connected with wires via silver conductive epoxy adhesive (MG Chemicals). This holder was inserted in a slot in the triggering body. A corrosion-resistant 302 stainless-steel torsion spring (McMaster-Carr) was loaded by immobilizing one end in a slot in the 3D-printed housing, then rotating the free leg of the spring 180° counterclockwise from its starting position and fixing it to the $\sim 50 \Omega$ resistive heater with ethylene-vinyl acetate (EVA) adhesive (The Gorilla Glue Company). The CnF and triggering bodies of the capsule are press fit together, aligned by the 3D-printed center axle.

COMSOL Multiphysics 5.4 (COMSOL AB) was utilized to model a simplified cam and follower mechanism to characterize follower displacement from cam rotation over time. The mechanical force output of the module was measured using an Instron 5942

universal testing system (Instron). Modules were fixed in a custom 3D-printed holders and immobilized in EVA, then deployed into the stationary load cell.

A DC power supply (Agilent), limiting peak voltage and current to 3.3 V and 60 mA, respectively was used to initially demonstrate module actuation (Figure 5a). To evaluate current draw, power and triggering time, biopsy modules were deployed using both a 3 V ingestible sized battery (Energizer). Modules were deployed into 0.2 % w/v agarose phantoms, simulating intestinal mucosa. The collected sample volume was calculated from mass difference of the punch after deployment.

RESULTS AND DISCUSSION

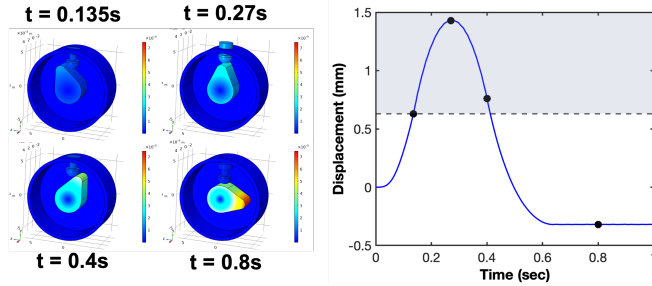


Figure 3: COMSOL simulations depict the rotation of the cam and resulting follower translations at 0.135 s, 0.27 s, 0.4 s, and 0.8 s (left). The vertical displacement of the follower over time (right). The gray region represents the GI wall and indicates anticipated depth of biopsy.

The COMSOL simulations resulted in an estimated displacement of 0.8 mm for the follower out of capsule shell (Figure 3). This should be sufficient to penetrate and collect the mucosal tissue without risk of perforation, as the thickness of the SI mucosa and wall are 0.4-1 mm and ~1.5 mm respectively [5].

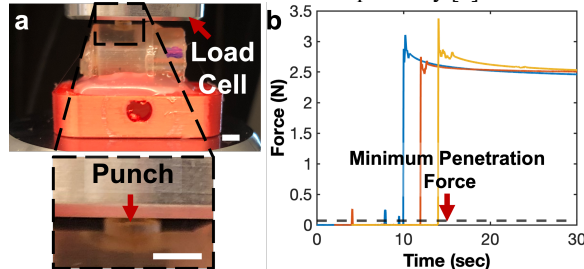


Figure 4: (a) Image of the experiment where modules are triggered against a load cell. (b) Results of the experiment showing the force output of the load over time for 3 modules. (scale bar: 3 mm; $n = 3$)

The average force output of the system was shown to be 2.4 ± 0.058 N with an impulse force (peak) of 3.07 ± 0.31 N (Figure 4a-b). The resulting force is 24x greater than the force necessary to penetrate intestinal mucosa for the cross sectional area (2.5 mm^2) of the punch rim, given the yield stress of intestinal tissue (0.58 MPa [5]), confirming the module's ability to penetrate tissue.

The average triggering time of the module with the 3 V battery was 24 ± 13 s, ranging from 9-36 s ($n=4$). Variation in deployment times was due to inconsistent application of EVA to immobilize the spring leg on the microheater. Higher volumes of EVA resulted in longer deployment times. Process variations of microheater resulted in resistance variation between 50-60 Ω . Thus, modules were triggered using current values between 50-60 mA and a power output of 150-180 mW, which is far less than values reported in literature [2][3].

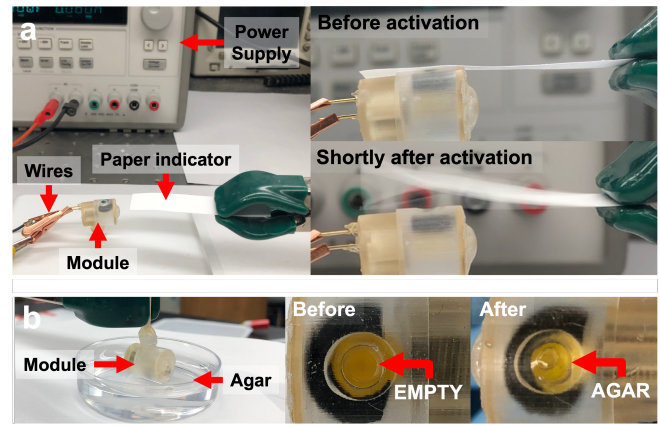


Figure 5: (a) Capsule being triggered via a power supply with a paper indicator for marking the sub-second actuation. (b) Collection experiments showing agar collected in the punch. ($n = 3$)

The biopsy module was evaluated on agar tissue phantoms to quantify collected sample volume. Agar samples collected by the module ranged from 3-7 mm^3 with an average of $4.7 \pm 2.1 \text{ mm}^3$. These results fall in the range of samples suitable for biopsy evaluation by a pathologist (Figure 5b) [3].

CONCLUSION

This work demonstrates the first biopsy module capable of on command tissue sampling from a battery powered ingestible capsule device. The module is capable of 2.4 N force output, collection of 4.7 mm^3 of sample while only requiring a power output of less than 180 mW. Future work will include optimizing the low melt adhesive polymer application for faster triggering as well as the development of sealing and preservation components of the device. The module will also be integrated with a full ingestible device featuring sensors for localization and remote triggering. Further development of this technology will enable autonomously operated capsule devices that could help reduce the burden of GI healthcare screening.

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