NFCapsule: An Ingestible Sensor Pill for Eosinophilic Esophagitis Detection Based on Near-field Coupling

Junbo Zhang
junboz2@andrew.cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

Gaurav Balakrishnan
gbalakr1@andrew.cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

Sruti Srinidhi
ssrinidh@andrew.cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

Arnav Bhat
abhat@andrew.cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

Swarun Kumar
swarun@cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

Christopher Bettinger
cbetting@andrew.cmu.edu
Carnegie Mellon University
Pittsburgh, PA, USA

ABSTRACT

This paper presents NFCapsule, a light-weight, battery-free, and ingestible biomedical sensor that can potentially enable non-invasive detection of active eosinophilic esophagitis (EoE). EoE is an allergen-induced inflammatory condition of the esophagus; its diagnosis generally involves invasive, wired, and time-consuming endoscopy. In contrast, NFCapsule aims to wirelessly detect active EoE by tracking tissue impedance through an ingestible pill that the patient swallows. Specifically, recent biomedical research has shown that active EoE induces observable changes in the electrochemical impedance of the esophagus tissue due to an increase in its intercellular spacing. We design the NFCapsule pill based on RLC resonant circuits and model the target tissue as an impedance component that changes the resonant properties of the pill circuit. Further, the NFCapsule reader identifies the resonant properties of the pill by consistently monitoring the amount of energy transferred to the pill as it goes through the esophagus, and converts this information to estimates of bio-impedance. We implement NFCapsule pill prototypes with flexible polyimide PCBs and gelatin capsules (27 mm in height and 10 mm in diameter) and evaluated NFCapsule with both ionic agarose hydrogel models and ex vivo porcine esophageal tissues (no human patients involved). We show that NFCapsule maintains high classification accuracy under various practical scenarios (e.g., blockage, bending, movement, etc.) and achieves 85% average accuracy between healthy and unhealthy tissue samples.

CCS CONCEPTS

• **Human-centered computing** → Ubiquitous and mobile computing systems and tools.

KEYWORDS

near-field, inductive coupling, resonant circuit, ingestible electronics, wireless systems

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1 INTRODUCTION

Eosinophilic esophagitis (EoE) is an allergen-induced inflammatory condition of the esophagus that currently affects close to 200,000 patients in the United States today and has a growing prevalence [22]. Patients suffering from this condition can experience a range of symptoms such as chest or gastric pain, inability to swallow, and gastrointestinal blockages. Current diagnostic protocols are cumbersome and inconvenient, typically involving periodic retrieval of tissue biopsies via endoscopy [23]. This can be painful to the patient and also considerably time-consuming.

Imagine a future where the invasiveness of endoscopic measurements and tissue biopsies can be replaced with a single capsule. Instead of setting up an appointment with a doctor when a patient experiences inflammatory symptoms and losing valuable time to perform diagnostic tests, the patient wears a peripheral reader device around their neck and simply swallows an EoE sensor capsule at home. The tissue health data is then automatically recorded by the reader as the capsule goes down the esophagus and ready to be sent over to the patient's smartphone. This paper seeks to build a system that takes a step forward towards this vision. We present NFCapsule (Fig. 1), a light-weight, battery-free, and ingestible biomedical sensor that can potentially be used for EoE detection. NFCapsule is built upon near-field coupling to effectively sense the tissue health and wirelessly send the data over to the NFCapsule reader. Our prototype is evaluated with both hydrogel-based tissue phantom models and ex vivo porcine esophageal tissues to emulate various tissue health conditions; no human patients were involved. Our results show 85% average end-to-end classification accuracy.

NFCapsule's underlying sensing principle is bio-impedance measurement. According to recent research [67], the bio-impedance of the esophageal epithelial tissue can serve as a quantitative measure for EoE diagnosis. Just like other human body tissues (e.g., skin), the esophagus tissues, which mainly consist of cells and extracellular fluids, can be modeled as equivalent circuits with complex

impedance values. This is because both the intra-cell fluid (cytoplasm) and the inter-cell fluid (extracellular fluid) are ion-rich and conductive; this conductivity can be modeled in a resistance term. Meanwhile, the boundaries of cells (cell membranes), though relatively non-conductive, can have charges accumulated on both sides during various metabolic activities, emulating a capacitance term. Therefore, bio-impedance is closely related to cellular activities and serves as a good indicator of important physical parameters of the tissue, which can exhibit observable changes when a certain disease develops. For example, active EoE induces a notable increase in intercellular spacing in the esophageal epithelial tissue compared to healthy tissue. As a result, electrochemical impedance can be leveraged to detect active EoE [23, 36, 59].

While bio-impedance measurements are promising as they yield accurate and early diagnostic capabilities, current methods of measuring the esophagus impedance in a patient usually involve endoscopes or catheters. This is not only invasive and wired, but also required to be administered in a clinic by a healthcare provider, resulting in a comparable time and labor investment as traditional EoE endoscopy. Therefore, we design the NFCapsule pill as an ingestible sensor to explore the feasibility of wirelessly examining the health condition of the esophagus tissue. In fact, there is a growing interest in designing ingestible electronics as replacements for endoscopies for a variety of gastrointestinal (GI) conditions as a result of their non-invasiveness and improved patient experience. For example, we see capsule cameras [60] that record video clips as they go down the GI tract and send the videos back wirelessly to a peripheral receiver outside of the human body. Compared to these sensors that integrate multiple power-hungry modules with batteries, NFCapsule further features a light-weight, battery-free design where we limit our design space to only simple circuit layouts (e.g., capacitors, resistors, and metal traces) and rely on near-field coupling to power the NFCapsule pill. This unlocks its potential to be made digestible in the future (Sec. 9).

The secret sauce of NFCapsule originates from electrical resonators – adding a complex impedance to a perfectly tuned resistor-inductor-capacitor (RLC) resonance circuit detunes it. Since NFCapsule is built on near-field coupling, it naturally requires a coil antenna (R and L) to receive energy and communicate, as well as a corresponding capacitor (C) to tune the circuit to the desired resonant frequency. If we plug the esophageal tissue into this coil circuit, generally speaking, the higher the tissue impedance (both the real and imaginary components), the more severe the circuit detunes. In other words, if we could quantify how much the RLC circuit detunes, then we could estimate the tissue impedance. Therefore, we design coils with probing pads for the NFCapsule pill to effectively embrace esophagus tissues as part of its circuit. This design choice turns measuring the impedance value into quantifying the resonance detuning, thus eliminating the requirement for complex calibrated high-end instruments. We show in our evaluation that NFCapsule can effectively distinguish between healthy and unhealthy tissues.

However, realizing such a method involves multiple challenges in practice. First, after the user swallows the NFCapsule pill, the reader will no longer have physical access to it. Hence, we need some form of indirect feedback. NFCapsule leverages a simple but important intuition: the peripheral reader is essentially delivering energy to the coil on the NFCapsule pill as it generates the electromagnetic field to read the pill. Therefore, the more resonant the coil is, the more energy would be delivered to the coil. In other words, the reader can indirectly measure the coil resonance by monitoring the amount of energy it transfers to the coil. Our NFCapsule reader follows such a design and continuously monitors the change in energy level as the NFCapsule pill goes down the esophagus.

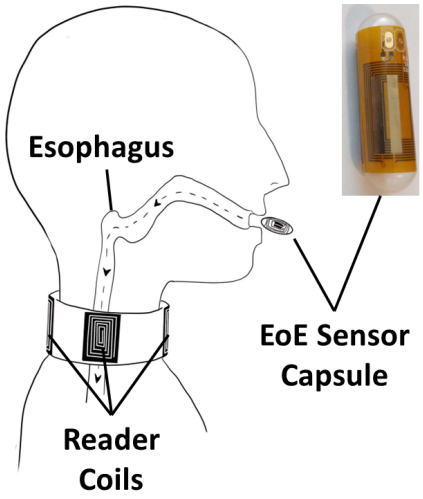

Figure 1: NFCapsule includes a reader device worn at the user's neck with multiple coil antennas (to be integrated into a flexible choker in the future) and an EoE sensor capsule that interacts with the user's esophagus tissue.

Next, NFCapsule must map the amount of transferred energy (i.e., its reading) to a certain target impedance value. The main challenge here is the non-linear relationship between these two quantities: in general, even a small change in the coil impedance, when it is close to the optimal resonant value, can lead to a large variation in the amount of energy the coil can absorb from the reader. Meanwhile, the same amount of change in the coil impedance when it is far from the optimal value may have little or no impact. Said differently, if working out of its "comfort zone" (i.e. away from resonance), NFCapsule would give less and less accurate results as the coil becomes less resonant, because the relationship between the reader's reading and the target impedance becomes flat. To deal with this problem, NFCapsule adopts a dual-coil design. Specifically, one of the coils is designed at 13.56 MHz and the other at 27.12 MHz. Further, they are designed sensitive to different ranges of impedance values (i.e., non-overlapping "comfort zones"). The NFCapsule reader then operates at both frequencies to monitor the amount of transferred energy from the reader itself to the NFCapsule pill. In this way, NFCapsule ensures that at least one of the coils can work within its "comfort zone". We show NFCapsule's performance with this dual-coil design in Sec. 8.

Finally, in practice, the reader's measurement can fluctuate between different swallowing trials because many factors can affect the reading. For example, the way a user wears the peripheral reader can easily influence the distance between the coil and the reader, and hence the reading. While this can be mitigated by a one-time calibration each time the user wears the reader, the fluctuation of NFCapsule pill's orientation inside the esophagus is completely

out of control. Specifically, as we show in Sec. 6.2, although the degree of freedom a NFCapsule pill can have inside the esophagus is limited, it can still rotate along a certain axis, making the reading fluctuate. To deal with this, NFCapsule adopts a straightforward solution with multiple reader antennas around the user's neck, where each of them attempts to access the NFCapsule pill from a different angle. We use an RF switch to multiplex these antennas – at a given time, only one antenna will be active, and this effectively emulates multiple readers simultaneously collecting data from different directions. We show NFCapsule's performance in an end-to-end deployment in Sec. 8.5.

We implemented NFCapsule pill prototypes (27 mm height and 10 mm diameter) using flexible polyimide PCBs and 000-size gelatin capsules. We did not involve clinical studies with human patients and chose not to induce EoE in live animals due to ethical considerations. Instead, we evaluated NFCapsule's classification accuracy with both agarose hydrogel-based tissue phantom models, which are shown (Sec. 7) to effectively emulate real tissues, as well as ex vivo porcine esophageal tissue samples, with which we follow an established processing method [83]. NFCapsule performs well under various practical scenarios with different reading ranges, blockage materials, radii of curvature, and moving speeds, and achieves 85% average accuracy in an end-to-end test with varying pill orientations.

Contributions: This paper contributes the following:

- A novel design of an ingestible pill sensor that can potentially be used to detect active EoE through a significantly less invasive process.
- The design of an RF frontend on flexible PCBs to estimate tissue bio-impedance within a capsule's small form factor.
- A detailed system implementation and evaluation on agarose hydrogel models and ex vivo porcine esophageal tissues.

2 A PRIMER ON EOSINOPHILIC ESOPHAGITIS

Eosinophilic esophagitis is an inflammatory condition of the esophagus, the upper section of the gastrointestinal (GI) tract that connects the mouth to the stomach. It is classified as an allergen-induced condition, with patients demonstrating sensitivity to a highly subjective and varying range of food groups. As the disease progresses in severity, symptoms can range from mild local inflammation and discomfort while swallowing to experience complete esophageal blockages, severe pain while swallowing, and chest pain. EoE affects between 40-60 people for every 10,000 in the US population, with an increasing rate of incidence in adults and children [22, 79]. With no universal treatment option for EoE, early diagnosis and allergen identification is key to managing the condition.

A major challenge in optimizing EoE diagnostic protocols is it presents similar symptoms to some other GI conditions such as gastroesophageal reflux disease (GERD). As a result, the current standard of care starts by examining and treating patients for GERD to eliminate it as the diagnosis. If symptoms persist, the GI doctor usually performs an endoscopic procedure to examine the tissue and looks for markers of EoE: (1). presence of eosinophilic white blood cells; (2). dilation of intercellular spaces. These markers are challenging to find and might be confused with other conditions at early stages of the disease. Even if they are found, it still remains a challenge to identify the specific allergen. Patients will typically start a food elimination diet where they introduce one food group at a time to observe the reaction. However, with these responses starting out in a mild manner and a likely delay between experiencing symptoms and visiting the clinic for examination, efficient and early diagnosis remains a big hurdle.

Recent research on leveraging bio-impedance for GI tract condition diagnosis opens up new opportunities, where bio-impedance is shown capable of identifying certain GI tract diseases and even distinguishing between GERD and EoE [3] since they induce different changes in tissue impedance values. Inspired by these observations, we present NFCapsule based on bio-impedance sensing and near-field coupling as a first-step towards exploring the feasibility of a remote and at-home detection of EoE (we do not consider GERD in this paper). Our work can potentially unlock the ability for patients to consume a NFCapsule pill in close conjunction with their food elimination diets for quick and real-time monitoring of tissue-level response to the food groups, thus facilitating the diagnosis and treatment of EoE in the future.

3 DESIGN DECISIONS

Since NFCapsule aims to solve the invasiveness and inconvenience of traditional endoscopy and esophagus impedance measurement, it is naturally expected to be wireless and ingestible. Given the rich design space and literature in ingestible devices, NFCapsule made several unique design choices.

Why battery-free: An integrated battery in ingestible devices can greatly improve their capability of sensing and communication. In fact, most FDA-approved ingestible devices (e.g., pill cameras) do have integrated batteries, which make it possible to send video clips with acceptable frame rates. They generally adopt silver oxide batteries instead of traditional Li-ion ones because the latter would raise potential toxicity and self-ignition risks. However, the battery remains the major factor that determines the size of ingestible devices – as an example, the commercial product PillCam COLON 2 [60] measures 32.3 + 0.5 mm in length and 11.6 mm in diameter, primarily owing to battery size. Large capsules can be uncomfortable for patients to swallow and may create a heightened risk of capsules getting stuck in the GI tract. This can lead to blockage or perforation, both of which could need surgical intervention. This has actively motivated recent research in new battery technologies [10, 43] with potential biocompatibility and small form-factor. However, these remain experimental and are currently not commercially available.

Why chipless: In general, wireless sensors for human sensing applications take two broad design approaches. The more common design approach is modular – dedicated sensors are integrated with several independent units including a communication module, in which a chip sends digital data back for analysis [55, 68, 82, 89, 97]. Most commercial ingestible devices follow this design as well, which in principle provides accurate and stable measurements. However, when it comes to bio-impedance, an active measurement process generally involves applying a certain source voltage/current to the target and then analyzing the response signal. This can be highly power-hungry. As an example, in our initial feasibility study, a commercial impedance measurement module [24] can make only

4 complete measurement attempts before a 0.2 F supercapacitor depletes; further, the latter needs 2 minutes to be fully charged with commercial NFC development kits [38].

In the other design approach, the sensor itself is a communication module. This usually leads to a chipless design, where analysis is carried out with physical-layer signals instead of digital data bits. This approach trades off some accuracy and stability, but has a great potential to decrease the cost, form-factor, and design complexity. It can be battery-free as well with NFC/RFID technologies. One way to design such a chipless sensor is by modeling the target human body part as a conductor and connecting it with an antenna (i.e., the communication unit). If the antenna circuit was incomplete (i.e., open circuit), it now becomes complete (closed) and its response (i.e., physical-layer signals) changes along with any variations in the target human body part. If the antenna was already complete, the target can still affect its response particularly in the near-field where the dielectric properties of the human body part influence the electromagnetic signals. Prior work around *complete antenna* developed mainly around LC-resonator circuits [15, 21, 34]. Further, the *incomplete antenna* approach has also been explored, primarily in the far-field, to build systems for user interfaces (UI) [29, 50, 51, 69, 85] and medical applications [30, 33]. NFCapsule naturally chose to follow the incomplete antenna approach given the task of bio-impedance measurement, and to our knowledge, is the first to use this approach for sensing EoE.

Why near-field coupling: Technologies for power and communication in human sensing generally fall into far-field solutions and near-field solutions. The former builds on far-field radiations while the latter usually leverages inductive (magnetic) coupling (e.g., [17, 18]). In general, a desired feature of near-field inductive technology over its far-field counterpart is that it can better penetrate human tissues and reach deeper inside our human body, while far-field radiations mainly get absorbed or reflected because our human body is primarily composed of water. This makes near-field technology preferable for NFCapsule, where the communication happens between a peripheral reader and an in-body sensor in the esophagus. Therefore, NFCapsule adopts near-field coupling for its power and communication, and we further choose ISM bands (e.g., 13.56 MHz and 27.12 MHz) based on three considerations. First, the ISM bands are dedicated for research purposes and at the same time enjoy a variety of commercial off-the-shelf devices, which has greatly facilitated NFCapsule's initial feasibility study. Second, these bands have well-defined regulations regarding safety to refer to. According to FCC part 15, NFCapsule must meet a maximum field strength of around 100 dB μV/m at 3 m (around 4.77 dBm EIRP), while the NFCapsule reader has a maximum output power of around -1.5 dBm. This ensures that NFCapsule's transmission remains FCC compliant. Third, since near-field technologies have been well adopted in smartphones, we have a future expectation that NFCapsule's reader can be integrated into smartphones as well, although this is not our current focus.

4 NFCAPSULE'S ARCHITECTURE

In this section, we briefly describe NFCapsule's high-level design and outline the rest of the paper. At a high level, NFCapsule is a self-contained battery-free ingestible pill that patients swallow to sense

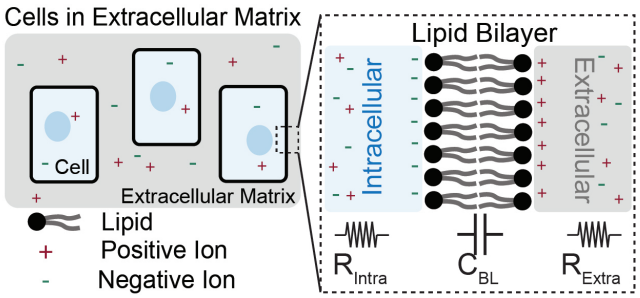

Figure 2: The bio-impedance of tissues is a complex number that consists of a resistance (real) part contributed by the aqueous ions inside and outside cells, as well as a capacitance (imaginary) part contributed by the lipid membrane barriers.

EoE. The pill contains RF front-end components to communicate with an externally worn reader. Prior to swallowing the pill, patients wear a reader "collar" (Fig. 1) that contains multiple coils around the neck. The patient is then instructed to remove metallic jewelry (if any) and swallow the pill along with water. Once the pill is swallowed, it is scanned by the external reader as it passes down the esophagus momentarily (a pill is in the reader's range for typically around 0.5 seconds, which is sufficient to obtain a measurement). It is designed to be ingestible and will eventually pass through. The reader's signal measurements are then collected for analysis and potentially sent to medical providers.

Paper Outline: For the rest of this paper, we first describe the basic sensing principle of NFCapsule– how it estimates tissue impedance (Sec. 5); then, we describe its hardware and system design challenges (Sec. 6); finally, we conclude with a detailed system implementation and evaluation (Sec. 7-8).

5 NFCAPSULE'S SENSING APPROACH

To work in the near-field and be able to receive energy from the reader, the NFCapsule pill naturally requires a resistor-inductor-capacitor (RLC) circuit. At a high level, the NFCapsule pill embraces the target tissue as part of its circuit that changes its resonance properties; this information is extracted by the NFCapsule reader as it tries to power the NFCapsule pill. In this section, we first briefly introduce the formulation of bio-impedance (Sec. 5.1), then describe the underlying physics of NFCapsule – RLC resonant circuits and near-field energy transfer through magnetic coupling (Sec. 5.2).

5.1 Bio-impedance formulation

Biological tissues can be formulated as complex soft composite materials with lipid membraned cells dispersed in an extracellular matrix (Fig. 2). The interior and exterior of the cells contain freely flowing aqueous ions, while the bilayer lipid membranes serve as barriers to ionic flow. Here, the former contributes mainly to a resistance component, while the latter to a capacitive component. This effect can be captured by a complex impedance value, with its real part corresponding to the resistance and its imaginary part to the capacitance. Formally, this parameter is called the tissue's electrochemical impedance, or bio-impedance. It is a parameter of the tissue that can be measured to gain important insights into the

tissue properties. The most prominent and relevant parameter indicated by bio-impedance is cellular density within a tissue. At lower cellular densities, the ions in the extracellular matrix are subject to fewer obstructions, leading to lower impedance values. Therefore, bio-impedance has been used to diagnose and monitor a variety of medical conditions that impair tissue barrier integrity [57, 72]. In the case of gastrointestinal conditions, prior research has shown that EoE induces a lower cellular density in the esophageal epithelium, leading to a decrease in tissue impedance [3]. This makes bio-impedance measurements an emerging detection mechanism for diagnostic purposes [23, 36, 59].

5.2 RLC Circuits and Near-field Coupling

RLC circuits and resonant frequency: The *source device* circuit in Fig. 3 shows a typical RLC circuit where a (real) resistor R, an inductor L, and a capacitor C are connected in series. With an AC excitation V at a certain frequency f, we have:

$$V = I(j\omega L + \frac{1}{j\omega C} + R). \quad (1)$$

Here, $\omega = 2\pi f$. The resonant frequency f^* of such an RLC circuit is given by $f^* = 1/2\pi\sqrt{LC}$ – when the excitation frequency $f = f^*$, the terms from L and C in Eqn. 1 cancel out, and the current $I = V/R$ can be maximized (called "resonance"). We note two important takeaways. First, when $f = f^*$, the maximized current is reversely proportional to R. Hence, a large R leads to a small current. Formally, this is captured in the quality factor $Q = \frac{1}{R}\sqrt{\frac{L}{C}}$, which indicates how well an RLC circuit resonates. Second, when f becomes off f^*, the current I is generally smaller than that at f^*.

Near-field coupling and energy transfer: Fig. 3 shows a typical energy transfer setting built on RLC circuits, where the *source device* and the *receiver device* are both tuned to the resonant frequency ($f_s = f_r = f^*$). According to basic electromagnetic theory, the AC current flowing through the source inductor will generate a time-varying magnetic field in its surroundings, which can induce an AC current in the receiver coil if the receiver device is nearby. This is referred to as magnetic coupling, inductive coupling, or near-field coupling since it happens in the close proximity of these two devices. Mathematically, we can model this as:

$$V_s = I_s(j\omega L_s + \frac{1}{j\omega C_s} + R_s) - j\omega^* M I_r = I_s R_s - j\omega^* M I_r, \quad (2)$$

$$j\omega^* M I_s = I_r(j\omega L_r + \frac{1}{j\omega C_r} + R_r) = I_r R_r. \quad (3)$$

Here, we use subscript s for the source and r for the receiver, and M denotes the mutual inductance between the source coil and the receiver coil. From Eqn. 2 and 3, we can further calculate V_s as:

$$V_s = I_s R_s - j\omega^* M \frac{j\omega^* M}{R_r} I_s = I_s R_s + I_s \frac{\omega^{*2} M^2}{R_r} = V_0 + V_t. \quad (4)$$

Here, V_0 is the voltage we can observe on the transmitter antenna (source coil) and V_t is the voltage "transferred" to the receiver. We note two important takeaways from the above formulation: (1). the presence of a receiver device leads to a decrease in V_0, which can be consistently monitored at the source; (2). a stronger coupling effect leads to a larger V_t, hence a greater decrease in V_0.

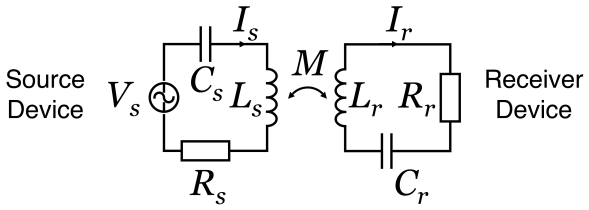

Figure 3: A basic energy transfer setup between a source device and a receiver device based on near-field coupling.

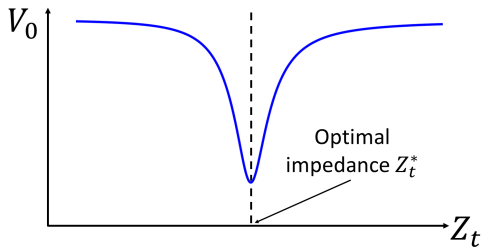

Figure 4: Illustratively showing the qualitative relationship between observed voltage V_0 and target impedance Z_t.

NFCapsule's observation: The NFCapsule reader and pill devices are effectively the source and receiver devices in Fig. 3, respectively. In this case, the source is perfectly tuned. The receiver, however, has the target bio-impedance as a circuit component, which is unknown and subject to change. As introduced in Sec. 5.1, tissue impedance generally contains both real and imaginary parts, thus a change in its value affects both the resonant frequency and the quality factor of the NFCapsule pill circuit. This leads to a variation in the strength of magnetic coupling between the pill and the reader, which is reflected by a change in V_0, the voltage we observe on the reader antenna. As an example, if a pill was tuned such that it could resonate well with a piece of healthy tissue as part of its circuit, and the reader measured $V_{0,h}$, then replacing the healthy tissue with an unhealthy one would detune the pill circuit, resulting in a new reading $V_{0,u}$ that is much likely larger than $V_{0,h}$.

Fig. 4 shows a qualitative relationship between V_0 and the target impedance Z_t. If the receiver circuit is tuned to resonate best with Z_t^*, then when Z_t is off Z_t^*, we observe an increase in V_0 in general. Of course, the target impedance Z_t is a complex number that comes in both real and imaginary parts; NFCapsule has to take into account both of their influences. In addition, V_0 is a complex voltage as well, so in practice, NFCapsule leverages both the amplitude and phase of V_0 to estimate the target bio-impedance.

While the mapping between V_0 and tissue health in principle appears straightforward, in practice various design challenges emerge. This includes changes in pill orientation and calibration errors that could impact system performance. Further, NFCapsule's RF front-end and operating frequency must be designed to maximize system accuracy. Next, we deal with these system design issues.

6 NFCAPSULE'S DESIGN CHALLENGES

Realizing such a sensing modality (Sec. 5) in a wireless system involves multiple practical system design challenges. In this section,

we describe how NFCapsule is designed to address several issues that are likely to appear in practice.

6.1 Coil Design

The NFCapsule pill device has a stringent form-factor requirement. Ideally, we would like our pill devices to be less than 30 mm in length and less than 12 mm in diameter, since this is roughly the size of a well-designed commercial product [60]. Meanwhile, NFCapsule adopts a metal trace loop coil design for the NFCapsule pills, which generally comes flat. This leads to two potential ways to integrate the coil with the capsule (Fig. 5): (a). embedding a flat coil inside the capsule, where the maximum width of the coil depends on the diameter of the capsule; (b). wrapping a bent coil outside the capsule, where the perimeter of the capsule determines the maximum width of the coil. While the latter solution allows a larger coil in principle, the performance of a coil antenna generally degrades when it is bent – for example, the more it is bent, the smaller its $|S_{11}|$ value becomes (Fig. 5 (c)). This leads to weaker resonance at the center (operating) frequency and hence degraded performance. Which solution shall we take? NFCapsule did a comprehensive simulation study in ANSYS Electromagnetics.

We start with fixing several design variables. First, we adopt a rectangular shape for our coils because it has intuitive and easy-to-control parameters. Specifically, this includes coil width, coil height, trace height, trace width, number of loops, and distance between traces. They are all considered as potential design variables in our simulation study. Second, we fix our trace height to be either 17.4 µm or 34.7 µm, corresponding to 0.5 oz and 1 oz of copper at PCB online manufacturers. This greatly facilitates prototyping NFCapsule coil designs. Next, followed by this practicality consideration, the trace width and distance between traces are naturally limited within a design space that online PCB manufacturers can offer. With all these considerations, the coil height is limited within around 28 mm (corresponding to the height of the NFCapsule pill), and the coil width has a maximum possible value of around 37.7 mm (corresponding to the circumference of the NFCapsule pill). In addition to these coil parameters, we also include radius of curvature parameters (a small radius leads to a large bending angle, hence relatively severe bending) in our simulation study.

We then carried out a series of systematic simulations and got a number of valuable insights that helped finalize our coil design. First, we quickly ruled out wrapping a whole coil (360°) around a capsule mold because the coil would no longer be an efficient resonator. In fact, if we choose to bend the coil, the bending angle (with respect to the center of a cylinder model) should ideally stay within 0°-150°; exceeding this limit introduces extremely severe performance degradation. This narrows down the maximum possible value of the coil width to be around 18.8 mm if we follow design (b) in Fig. 5. Meanwhile, the maximum coil width would be around 11 mm for design (a). Hence, the question of choosing between these two designs translates to whether a large bent coil could potentially outperform a small flat coil. NFCapsule decided to adopt design (b) based on the results of our simulations.

Specifically, we observed that under all the above design constraints (especially the trace height and width, which determine the overall amount of metal a coil has), spreading out the metal traces within a limited surface area is extremely important – if not, the coil quickly degrades to a piece of metal resistor and loses its resonance. This translates to having larger coil height, coil width, and distance between traces, i.e., a larger coil is preferred for a NFCapsule pill device. We followed this route and carefully studied the resonance properties of coils with a variety of coil parameters and bending parameters, which led us to our final decision to follow solution (b) and design a coil as large as possible with optimal efficiency (i.e., resonance properties). We show towards the end of this design section a photo of our coils as well as their schematic layout.

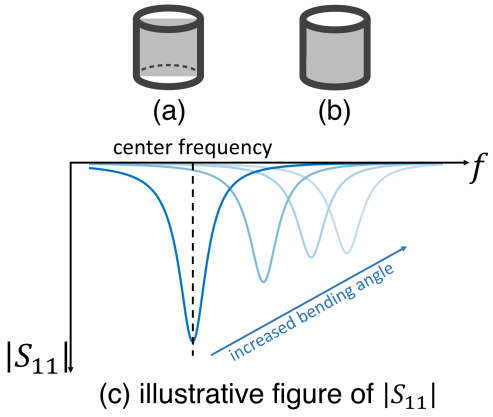

Figure 5: Instead of design (a), NFCapsule adopts design (b) to wrap a bent coil around the capsule to obtain a larger coil area, although this may sacrifice some coil performance (c).

6.2 Pill Device Orientation

NFCapsule leverages the amount of energy transferred from the reader to the pill to extract information of the target bio-impedance. However, the target bio-impedance is not the only factor that influences the energy measurement – in fact, the orientation of the pill can also have a large impact. We know from basic electromagnetic theory that in the energy transfer process introduced in Sec. 5.2, if the source coil and the receiver coil are not aligned (e.g., the worst case is that two coils are perpendicular to each other), then part of the magnetic flux from the source coil will fail to reach the receiver coil, resulting in weaker coupling. In other words, if every time the NFCapsule pill enters the esophagus with a random orientation, then this will also cause a random and undesirable error to the NFCapsule reader's readings. Given that the pill orientation can have three degrees of freedom, this can be quite challenging.

Luckily, NFCapsule does not have to deal with all three degrees of freedom, but only one. Consider a small piece of esophagus tissue with a capsule inside (Fig. 6). We can model it as a cylindrical tube and denote its central axis as the Z-axis. Then, the rotation along the Z-axis is the only variable that NFCapsule has to model. The reason for this originates from the biological characteristics of the esophagus. The esophagus in vivo performs peristaltic contraction to squeeze food towards stomach; hence, its effective diameter is smaller compared to the measured value when it is extended after anatomy. Meanwhile, our proposed NFCapsule pill's height (i.e., length) is much larger than its diameter. Because of these, an

ingestible device inside an in vivo esophagus with a similar profile as the NFCapsule pill is very likely to always orient as shown in Fig. 6; this has been verified in multiple studies around ingestible electronics [7, 8]. In a simple sentence, our esophagus will compress a long capsule so that it orients along its central axis. This fact greatly helps eliminate the potential requirement to estimate the 3D orientation of NFCapsule pills in real-time.

However, NFCapsule still has to address the rotation along the Z-axis, which turns out to be completely out of its control – the user has no way to precisely control the orientation of the pill when they swallow it with liquids. To deal with this, NFCapsule adopts a simple strategy – it uses multiple coil antennas at the NFCapsule reader that surround the user's neck (as previously shown in Fig. 1). Our current prototype of the NFCapsule reader implements four coil antennas equally spaced around the target region, and we use an SP4T RF switch to multiplex them. In other words, the reader periodically switches between four potential reader coils to effectively emulate four independent readers simultaneously collecting data around the target region (but with roughly 1/4 sampling rate). Given the high sampling rate of our reader device (more than 0.2 Msps) as well as the high switching speed of RF switches (tens of nanoseconds at the fastest), the NFCapsule reader can be seen simultaneously collecting data from four directions in effect, generating four "separate" data streams. This solution is simple and straightforward, but helps eliminate the need to know the orientation of the NFCapsule pill device *a priori*. With four data streams, our current classification protocol exploits the one with maximum amplitude and phase variation, and we use a simple thresholding method to distinguish between healthy and unhealthy models; yet, we note that it is in principle feasible to estimate the pill orientation given data from four directions as well as integrating advanced classification models (e.g., machine-learning based algorithms), and this is left as future work.

6.3 Impact of the Human Body

System Range: While in medical applications near-field technologies may be able to penetrate more than 20 cm into the human body [74], in practical human sensing applications one should expect around 10 cm at most penetration range under RF regulations. The average neck size (radius) of adults falls into 5-7 cm, while technically NFCapsule should target a very high accuracy at 2-4 cm, because the esophagus lies behind the trachea and the trachea is about 2.5-3 cm [61]. Therefore, it would be ideal if NFCapsule could achieve high performance within 4 cm while maintaining a reasonable accuracy at 5-6 cm.

Multipath and Attenuation: Since NFCapsule targets a short range, the impact of signal multipath is limited because the strength of electromagnetic field in the near-field fades rapidly. Our experiments also demonstrate this. Instead, the signal attenuation from human neck tissues is a more significant challenge and may deteriorate system accuracy. The precise impact on accuracy depends on the width of neck tissue between the esophagus and the reader coil, which varies for different users. In Sec. 8.2, we evaluate NFCapsule and show its accuracy under blockage.

Avoiding Other Sources of Error: We note a few other common sources of error that could be avoided by advising users on best practices prior to consuming the NFCapsule pill. First, the probing pads on the pill can be sensitive to ion-rich fluids like acidic beverages (e.g., orange juice). Therefore, the user is expected to use the pill only with water. Second, conductors near the neck region can cause measurement error at the NFCapsule reader because they also interact with the reader's electromagnetic field. Therefore, the user is expected to remove objects such as jewelry during tests.

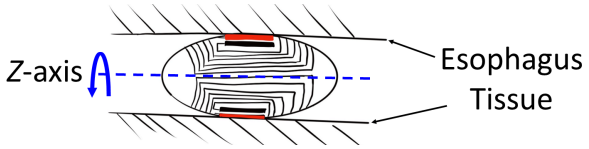

Figure 6: The NFCapsule pill device has a limited degree of freedom inside the esophagus; we only have to take into account the rotation along the Z-axis.

6.4 NFCapsule's Dual Coil Design

In this section, we describe our solution to a key challenge in impedance measurement using near-field circuits. Specifically, it is quite easy to quickly detect a near-field system moving from a resonant state to a non-resonant state (or vice-versa), since resonance results in substantial voltage changes at the reader. However, distinguishing between two non-resonant states is much more prone to noise, since voltage differences are much less significant.

Mathematically, we have shown in Fig. 4 the relationship between V_0 and Z_t. However, the non-linear nature of this relationship poses a challenge for NFCapsule – when Z_t is near Z_t^*, a small change in Z_t is enough to produce a noticeable variation in V_0; yet, when Z_t is far from Z_t^*, even a large change in Z_t might still lead to the same V_0 reading. Said differently, if a coil encounters a Z_t value that is out of its "comfort zone" near Z_t^* (i.e. near resonance), then it might give a poor impedance resolution in Z_t, leading to wrong classifications. To make things even worse, as the distance between the NFCapsule pill and the NFCapsule reader increases, the "comfort zone" also shrinks, and the variation in V_0 becomes less observable. NFCapsule has to address this to ensure consistent performance across a wide range of Z_t values under various scenarios (e.g., varying reading range).

A natural solution one can come up with is to use multiple coils, for example, two. We can tune these coils *a priori* such that they have different Z_t^* values, for instance, one with healthy tissues and the other with unhealthy tissues. In this case, as shown in Fig. 7, the "comfort zones" of these two coils are around Z_h and Z_u, respectively, and effectively cover a wider range of possible Z_t values together. Now, no matter what impedance value Z_t between Z_h and Z_u, NFCapsule should be able to give a reasonable estimate. In practice, this can be done with a straightforward impedance transformation – if another complex impedance is connected in shunt with the target tissue, it will effectively map the target impedance to a new value. Further, if we change the value of this shunt impedance, then Z_t^* will also change accordingly. In this way, we can produce coils that are sensitive to different ranges of target impedance values. We can then use the collective information from multiple coils to make a classification decision.

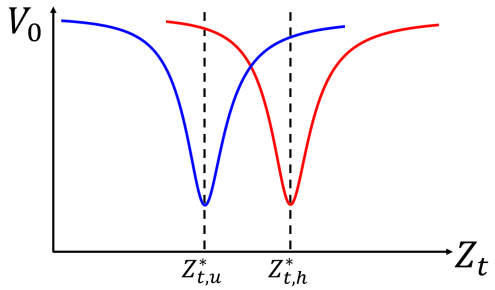

Figure 7: Illustrative curves showing the qualitative relationship between V_0 and Z_t with two coils tuned to different optimal impedance values.

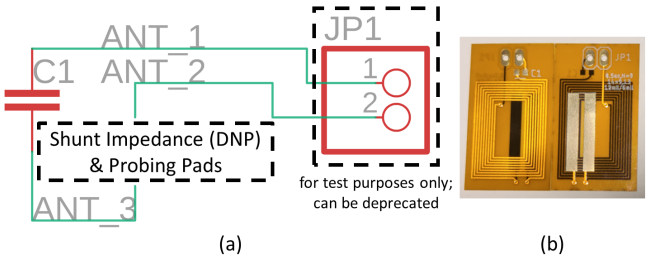

Figure 8: The coils on a NFCapsule pill device has a simple circuit layout. The shunt impedance can be connected in parallel with the target tissue during actual tests. Meanwhile, the jumper is designed solely for test purposes.

However, such a solution assumes that we can distinguish these coils, which, under NFCapsule's chipless design, is infeasible. Without chip information, these coils will look identical at the reader, which only tries to seek potential resonators blindly. In this case, the reader only observes a single V_0 value – it cannot tell the respective amount of energy absorbed by different coils.

To identify different coils without chips, NFCapsule leverages different frequency bands. Specifically, in addition to tuning two coils with different Z_t^* values, NFCapsule further lets them operate at two different frequencies, namely the 13.56 MHz ISM band and the 27.12 MHz ISM band. The NFCapsule reader works at two frequencies simultaneously and records the respective V_0 readings for each of them. In this way, NFCapsule can easily relate a V_0 reading to a specific Z_t^* value. We further ensure that our coils will not interfere with each other – a coil tuned at 13.56 MHz would have significantly degraded performance at 27.12 MHz and its response would become negligible. Said differently, these two coils work independently in effect – the NFCapsule reader does not need to distinguish between them; only one coil will effectively respond to its electromagnetic field at a certain operating frequency.

To this end, we present the schematic layout of our coils for NFCapsule pill devices. We see in Fig. 8 (a) that the circuit diagram of our coils is quite simple: the shunt impedance (not populated during manufacture) can be connected between our probing pads; meanwhile, the jumper is designed for test purposes only. In practice, we short connect them, so this can definitely be deprecated to further save space. Fig. 8 (b) shows the 13.56 MHz coil. These designs for both frequencies were sent out to online PCB manufacturers. We then populated them with desired circuit components.

6.5 Calibration

NFCapsule requires a one-time system calibration before actual usage with a single NFCapsule pill, and this calibration process is established upon the following three assumptions.

The user swallows the calibration pill when healthy: The NFCapsule pills need to be tuned with Z_h and Z_u values, as mentioned in Sec. 6.4. In practice, this can be done with statistical values among populations so that NFCapsule works for most people. Additionally, as introduced in Sec. 2, early EoE diagnosis protocols involve food elimination diets. In this case, we can calibrate Z_h values prior to the introduction of each potential allergen. However, we do acknowledge that NFCapsule might require further development to account for Z_h and Z_u variations among large populations. We further elaborate on this in Sec. 9.

The user's neck can be modeled straight: Imagine using NFCapsule on a daily basis in real life – it is inevitable that the user takes off the reader antennas after a trial and wears it again later when needed. Therefore, the height of the reader antennas is subject to random fluctuation. NFCapsule assumes that the user's neck can be modeled as a straight cylinder, so that even if the height changes, the relative distance between the reader antennas and the esophagus inside the user's body remains roughly the same.

The reader antennas have a relatively fixed orientation towards the user's neck: As in Sec. 6.2, NFCapsule adopts a multi-coil reader design. The reader antennas will be integrated like a collar where the distance between different antennas is fixed. For a certain coil on a NFCapsule pill that operates at either frequency, four reader antennas will surround the user's neck, for example, at the front (1), on the left (2), at the back (3), and on the right (4), respectively. We cannot assume that the esophagus is precisely on the central axis of the user's neck, even if we modeled the user's neck as a straight cylinder above. Therefore, the distance to the esophagus is different for these antennas. NFCapsule requires the user to wear the antennas according to their numbers at a relatively fixed position, for example, antenna 1 always at the front. Given the collar design, the only fluctuation between trials would be some slight rotation of the belt. This is equivalent to the case where the positions of the reader antennas are perfectly fixed, while the NFCapsule pill goes through the esophagus with a random rotation on its Z-axis. This is expected to be addressed in Sec. 6.2.

7 IMPLEMENTATION

7.1 NFCapsule System Setup

Reader Setup: The NFCapsule reader is implemented with USRP N210 software-defined radios (SDR) carrying BasicTx and BasicRx daughterboards and synchronized via an external clock. They are connected to the reader antennas via RF splitters to emulate a full-duplex reader. The reader antennas are rigid, custom-design PCB coil antennas; we envision making them flexible and integrated into a collar reader in the future. The reader antennas are further

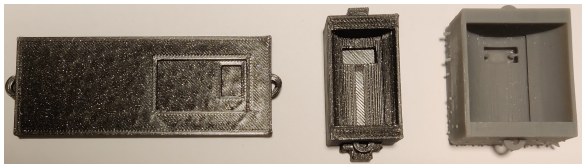

Figure 9: We use a variety of custom 3D-printed molds as coil holders for planar (left) and bent (middle and right) tests.

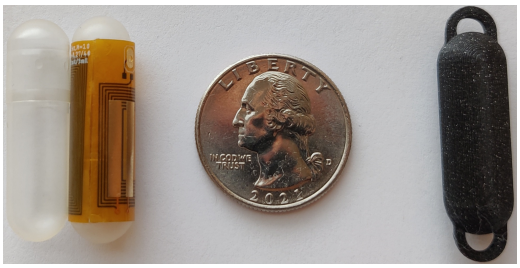

Figure 10: NFCapsule pill device prototype with a gelatin capsule (27 mm height and 10 mm diameter) and a 3D-printed capsule mold for movement tests.

multiplexed with an SP4T RF switch [25]. The NFCapsule reader is controlled by an ASUS 8G RAM 64-bit laptop running Ubuntu 20.04 via a NETGEAR Gigabit Ethernet switch and an Arduino Uno [2]. We use C/C++ scripts to control the reader's transmission and reception, and we process our collected data offline in MATLAB.

Pill Device Setup: The NFCapsule pill prototype is implemented with 2-layer polyimide flexible PCB coil antennas. These PCBs are flexible enough to be wrapped around or embedded into our custom 3D-printed molds (Fig. 9). A capsule prototype composed of gelatin is shown in Fig. 10. The original capsule measures 22 mm in height and 10 mm in diameter. To fit our current coils completely in, our final prototype (with a slightly elongated capsule) measures 27 mm in height. Note that the current jumper connections (designed to test the coils individually for convenience) can be deprecated, which can make the NFCapsule pill device even smaller.

For convenience, we 3D-print a capsule with two hooking rings using a biocompatible poly-(lactic acid) (PLA) filament. This facilitates experiments involving linear translation of the capsule to simulate swallowing.

7.2 Bio-impedance Model Setup

This paper does not involve any clinical studies with humans. Due to ethical reasons we also do not consider inducing EoE in live animals. Instead, we consider two kinds of bio-impedance models.

Ionic Agarose Gel Model: Agarose hydrogels have been utilized for a variety of biomedical applications as tissue phantom models due to their close mechanical and structural properties to the tissue extracellular matrix. Adding varying concentrations of sodium chloride (NaCl) to agarose gels leads to different properties. To make them, low-temperature gelling agarose from Sigma Aldrich [78] was heated to 65 °C in varying concentrations of NaCl solutions to produce final agarose concentrations of 15 mg/mL. Once fully

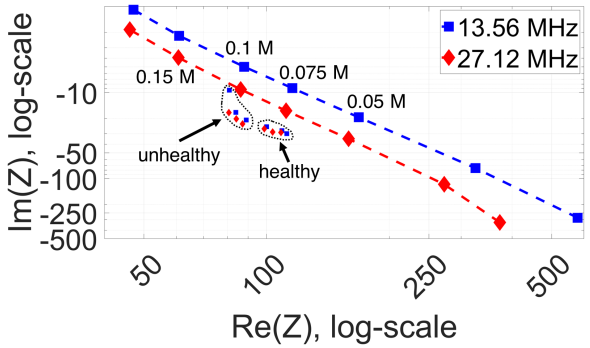

Figure 11: Ground truth impedance values of gel models with different NaCl concentrations show the practicability of using gel models to emulate real tissue samples.

dissolved, the solutions were cast on the desired surface using a pipette and allowed to gel at room temperature for approximately 30 minutes. Throughout all experiments with gel models, we control the volume to be 100 µL.

Ex Vivo Porcine Esophageal Tissue: We follow an established procedure to process our esophagus tissue samples [83]. Fresh porcine esophageal explants were obtained from Animal Biotech [9]. The tissue was stored at 4 °C and experiments were performed on the day of arrival. An existing protocol was followed to damage the esophageal epithelium ex vivo and create a "disease" group (i.e., damaged). Depending on the experiment, either planar sections of the tissue were cut (for VNA measurements) or the esophagus was left intact (for Sec. 8.5). The tissue was then washed with 1x phosphate buffered saline (PBS). The disease group was treated in 0.1 M hydrochloric acid and followed by washing in 1x PBS. We then evaluate NFCapsule (in Sec. 8.5) using both healthy and damaged tissues.

Emulating Real Tissues with Gel Models: A significant advantage of using gel models to emulate real tissue samples is their high controllability – for example, we can keep the volume of gel models precisely the same, and we can ensure a consistent contact area between the "tissue" and the probing pads on a NFCapsule pill. Therefore, for systematic quantitative experiments, we use gel models instead of planar pig esophageal tissue samples.

Previous research points out that the ionic concentration of biological tissue extracellular matrix is near 0.1 moles/liter (0.1 M), i.e., the effective ionic concentration in tissues with low cellular densities approaches 0.1 M. That is to say, empirically, unhealthy tissues should exhibit similar properties to those of 0.1 M gel models in bioimpedance measurements. To see the case for NFCapsule, we produced gel models with varying NaCl concentrations from 0.00625 M to 0.2 M. We then design custom PCB interfaces with similar probing pads as on the NFCapsule pill coils to connect these gel models to a Keysight N9916A Microwave Analyzer [46] and obtain their ground truth impedance values at NFCapsule's operating frequencies. Meanwhile, we also measured the bioimpedance of both healthy and damaged pig esophagus tissues (approximately 2 cm × 2 cm, multiple pieces for each group) with the same measurement setting at NFCapsule's operating frequencies.

Fig. 11 shows the measurements. The data points on each curve correspond to decreasing concentrations (0.2 M, 0.15 M, 0.1 M, 0.075 M, 0.05 M, 0.025 M, 0.0125 M). Both axes are in log scale. The small scattered points show the VNA readings with planar pig esophagus tissue samples. We see that both the gel models and the tissue samples exhibit a negative imaginary part in their impedance values, indicating a capacitive behavior. In addition, as the NaCl concentration decreases, the impedance value increases; this is consistent at both frequencies and for both real and imaginary parts. The gel models capture the real part behavior of tissue samples pretty well, although there is generally an offset in the imaginary part. In practice, when we tune the individual NFCapsule pill coils with shunt impedance, this can be taken into account and corrected.

8 EVALUATION

Several system variables can potentially influence NFCapsule's performance. We design a series of experiments where we introduce one of them at a time and study their individual impact.

First, we examine the impact of reading range, blockage material, radius of curvature, and moving speed (Sec. 8.1 - Sec. 8.4). We use 3D-printed molds (Fig. 9) as coil holders and test 13.56 MHz and 27.12 MHz coils separately. We use gel models with different NaCl concentrations to emulate tissues. According to Fig. 11, we divide gel models into an "unhealthy group" (NaCl concentration $\geq$ 0.1 M) and a "healthy group" (NaCl concentration $\leq$ 0.075 M). We mainly use 0.05 M to 0.15 M because of their close emulation on tissue impedance. We report the mean and standard deviation values of NFCapsule's classification accuracy as our evaluation metric.

Next, we examine NFCapsule's end-to-end performance (Sec. 8.5) with ex vivo pig esophagus tissues and a complete NFCapsule pill prototype, with a specific focus on the pill orientation (i.e., the angle of rotation along the Z-axis upon the pill entering the esophagus tissue sample, as mentioned in Sec. 6.2). We report NFCapsule's classification accuracy between healthy and damaged tissue samples when operating at (a). 13.56 MHz only and (b). both frequencies.

8.1 Reading Range

Method: In this section, we examine the influence of reading range – the distance between a NFCapsule coil and a single reader antenna. The NFCapsule coil is kept flat in a 3D-printed holder, with only air in between the holder and the reader antenna. We evaluate 13.56 MHz and 27.12 MHz coils separately; we report the accuracy when both are used as well. Gel models are used in this experiment.

Result: Fig. 12 shows the accuracy of NFCapsule when the reading range varies. When the NFCapsule coil is close to the reader antenna, it can perfectly distinguish gel models belonging to different groups; as the range increases, the accuracy experiences a slight drop. We note that our 13.56 MHz coils and 27.12 MHz coils achieve similar performance in this experiment; therefore, we include mainly 13.56 MHz coils in our following tests in Sec. 8.3 and Sec. 8.4. Meanwhile, when both coils are used (tuned differently according to Sec. 6.4), the accuracy is slightly improved. This is because some of the false negative samples (i.e., unhealthy samples classified as healthy) can be corrected with the readings from both coils. We evaluated NFCapsule with up to 5.5 cm reading range, at which NFCapsule achieves 91.7% classification accuracy with both coils. It meets the expectation in Sec. 6.3 given that the esophagus lies behind the 2.5-3 cm thick trachea.

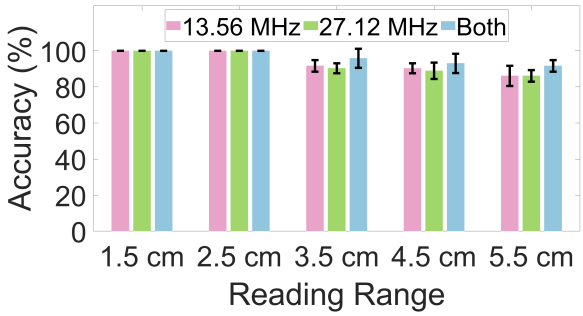

Figure 12: NFCapsule's classification accuracy on gel models with both kinds of coils. The result is grouped by reading range on the X-axis. Overall, combining the collective information from both coils helps improve the accuracy.

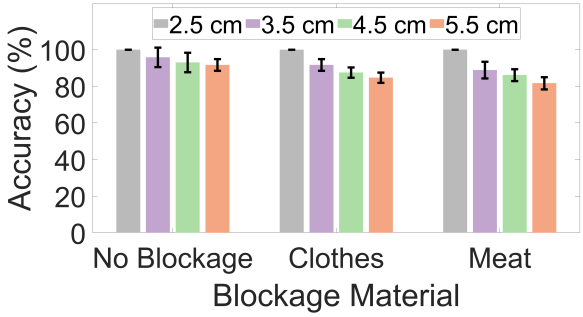

Figure 13: NFCapsule's classification accuracy on gel models with blockage. The result is grouped by material on the X-axis; each group contains four accuracy values of different reading ranges. We see clothes and meat induce similar performance drop to NFCapsule.

8.2 Blockage Material

Method: In this section, we examine the influence of blockage. Similar to Sec. 8.1, the coil is kept flat in a holder. We consider two kinds of blockage that NFCapsule is likely to encounter in practice: (1). clothes – we use a piece of folded cloth (56% polyester, 24% rayon, and 20% cotton) that measures 2 cm in height; (2). meat – we use a piece of raw steak (2 -2.5 cm) stored in a plastic food bag. To see their individual influence, we introduce them separately and compare with "no blockage". We use both coils and only report the collective classification result. Gel models are used in this experiment.

Result: Fig. 13 shows the evaluation result. We consider four reading ranges: 2.5, 3.5, 4.5, and 5.5 cm. We see that meat has a slightly larger impact. At a mild range (3.5 cm), NFCapsule achieves 91.7% and 88.9% for clothes and meat, respectively; at the most challenging range (5.5 cm), this drops to 84.7% and 81.7%. Given this result,

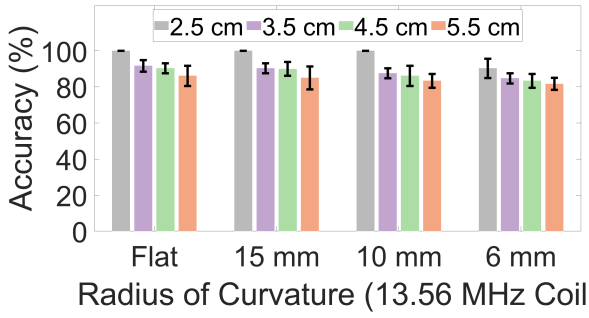

Figure 14: NFCapsule's classification accuracy on gel models with varying radius of curvature. The result is grouped by radius on the X-axis; each group contains 4 accuracy values of different reading ranges. A smaller radius causes more performance drop; 6 mm is close to our capsule's actual size.

a potential user is recommended to wear the NFCapsule reader directly around the neck without clothing.

8.3 Radius of Curvature

Method: In this section, we examine the influence of radius of curvature – the bending parameter when we wrap a NFCapsule coil around a cylinder mold. We choose 15 mm, 10 mm, and 6 mm in our tests. Given the length of our coils, they translate roughly to 50°, 75°, and 125° if we calculate the bending angle with respect to the center of the cylinder mold. We use custom 3D-printed molds to hold our coils at a specific bending angle, with only air in between the holder and a single reader antenna. We evaluate only 13.56 MHz NFCapsule coils. Gel models are used in this experiment.

Result: Fig. 14 shows NFCapsule's classification accuracy with different radii of curvature. The baseline is the flat case with 86.1% accuracy at 5.5 cm. As expected, NFCapsule experiences a performance drop as the radius of curvature becomes smaller; when the radius is 6 mm, NFCapsule achieves 90.3% and 84.7% at 2.5 cm and 3.5 cm, respectively. The radius of our capsule mold is 5 mm, so this accuracy should suffice in practice. At 5.5 cm range with severe bending, NFCapsule maintains 81.7% classification accuracy. Therefore, we went on to integrate the NFCapsule coils with our capsule molds and perform an end-to-end test in Sec. 8.5.

8.4 Moving Speed

Method: In this section, we examine the influence of moving speed. Specifically, we fix the position of our reader coil, and drag the coil horizontally over it at different speeds. The coil is placed in a flat coil holder with hanging rings on both ends. We then connect our custom 3D-printed "rod" with a digital mixer [19] to use it as a rotation motor and wind thin copper wires, which are tied at the hanging rings on the coil holder. Fig. 15 shows the setup, where we consider only horizontal translations as mentioned in Sec. 6.2.

Given that human esophagus measures around 25 cm in average and food travels through it in 2 to 3 seconds (corresponding to 12.5 cm/s and 8.3 cm/s, respectively), we consider 4 moving speeds

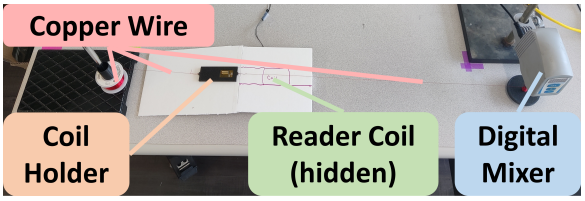

Figure 15: NFCapsule's translation experiment setup. A digital mixer is used to wind the copper wire. The coil holder moves over the reader coil with a controlled and consistent speed to emulate the movement in a swallowing behavior.

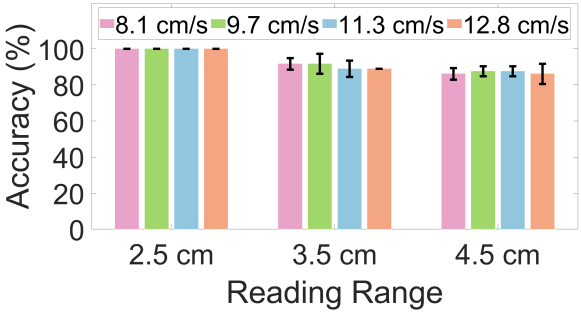

Figure 16: NFCapsule's classification accuracy on gel models with different moving speeds. The result is grouped by reading range on the X-axis. Overall, a moving coil does not introduce much performance fluctuation.

– 8.1, 9.7, 11.3, and 12.8 cm/s. They translate to 245, 215, 185, and 155 rpm for our digital mixer. We involve three reading ranges (2.5, 3.5, and 4.5 cm) with a single reader antenna. We evaluate only 13.56 MHz NFCapsule pill coils. Gel models are used in this experiment.

Result: Fig. 16 shows our evaluation result. We do not see much variance across different moving speeds. At first glance, this might be surprising; however, given the speed of electromagnetic wave propagation as well as the sampling rate of the NFCapsule reader (0.2 Msps to 2 Msps in our experiments), there is enough time for the reader and pill to interact with each other and for this interaction to be captured by the reader. Therefore, we conclude that a moving capsule will not pose a significant challenge for NFCapsule as long as the speed remains within the empirical range.

8.5 Pill Orientation

Method: In this section, we examine the end-to-end performance with a complete NFCapsule pill prototype – a capsule with two flexible coils wrapping around, operating at 13.56 MHz and 27.12 MHz, respectively, as described in Sec. 7. We use the same translation platform in Sec. 8.4 with our capsule mold (Fig. 10). The NFCapsule pill device is dragged through (i.e., inside) a piece of ex vivo pig esophagus tissue from the beginning to the end with a constant speed, while the reader antennas are positioned outside of the tissue. Fig. 17 shows the experiment setup; we unplugged unnecessary wires in the photo for aesthetic considerations.

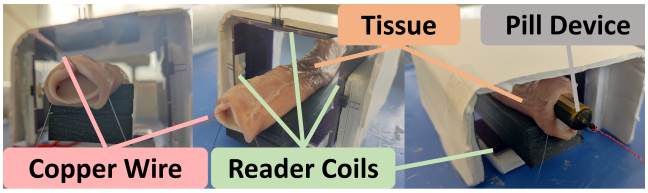

Figure 17: NFCapsule's end-to-end setup with a complete NFCapsule pill prototype and a damaged pig esophagus tissue. The test in the photos only involves the 13.56 MHz coil.

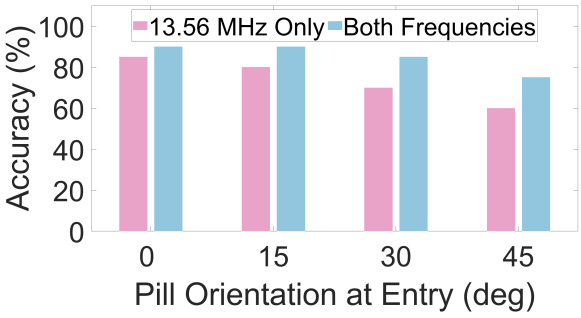

Figure 18: NFCapsule's end-to-end performance with different pill orientations at entry. The result is grouped by pill orientation. We see that operating at both frequencies help NFCapsule better distinguish between healthy and damaged tissues; yet, a misalignment between the reader antennas and the coils on the pill introduces a performance drop.

In this experiment, both healthy and damaged tissues are used, and we repeat the experiment twice – one set with only 13.56 MHz active and the other with both frequencies. Further, given the symmetric reader antenna placement, we control the entry angle of the pill to be 0°, 15°, 30°, and 45° to effectively sample the possible orientation along the Z-axis. Note that it is possible for the pill to change its orientation slightly as it travels, which is likely to happen in practice as well; we do not deliberately control this in our experiment.

Result: Fig. 18 shows NFCapsule's classification accuracy. First, NFCapsule performs better when both coils are active – as explained in Sec. 8.1, the accuracy is mainly influenced by false negatives; introducing two differently tuned coils help correct some of them. Second, while at 0° entry angle NFCapsule achieves good accuracy, as the entry angle becomes less and less ideal, the system performance degrades. Overall, NFCapsule shows 85% classification accuracy across all entry angles when operating at both frequencies; yet, we do note that a misalignment between the pill and the reader antennas poses a great challenge for NFCapsule.

9 DISCUSSION

NFCapsule Pill Orientation: Sec. 8.5 shows that NFCapsule will experience a drop in performance if the pill and reader antennas are not perfectly aligned. In fact, coil misalignment is a major challenge in general for magnetic coupling systems (e.g., wireless power transfer). A potential solution to mitigate its influence for NFCapsule might be adopting a single ring-shape antenna around the user's neck and accordingly design the pill coils to induce a signal change when it passes through the reader antenna. While a whole new set of experiments are required to test the effectiveness of such a solution, we leave it as one of our future directions.

Calibration: NFCapsule uses a simple thresholding technique to distinguish between healthy and unhealthy tissues, and thus requires calibration (Sec. 6.5). In practice, for a large population, we can expect NFCapsule to be calibrated to the statistical average. However, it is possible that NFCapsule falls short on certain users whose tissue impedance values diverge from the empirical value, which can be one of NFCapsule's limitations.

Human Patients: Our current evaluation on NFCapsule's performance does not involve human patients. However, human patients can pose potential new challenges. For example, the human neck contains complex tissue structures including airways and arteries, which might affect the communication; human patients can also have relatively mild EoE conditions at local areas on the esophagus tissue rather than a global one. Prior research on wired impedance measurement [44] showed around 90% sensitivity on human patients, which sets a practical target for improving NFCapsule in a step towards clinical usage. We do believe that extensive clinical study with human patients would greatly help to further optimize and improve NFCapsule's design in the future.

From Ingestible to Digestible: There is a rich history and literature on the design of ingestible devices [8]; we also see plenty of them receiving FDA approval and being used in the clinic. Although many of them are made of rigid, non-degradable, and potentially toxic components (e.g., IC chips and PCBs), they are encapsulated in miniaturized form factors to pass through the digestive tract intact. The current NFCapsule pill prototype contains non-degradable components (polyimide substrates, metallic traces, and capacitors); they are wrapped around a structural core that can be designed with a controlled degradation rate to allow the non-degradable components to eventually pass through. We expect the NFCapsule pill to have a lower risk profile compared to the aforementioned non-degradable devices.

In the future, we envision digestible NFCapsule pills that can eliminate any risk of GI tract obstruction. Our design process for NFCapsule has been committing to only simple circuit layouts (regular capacitors and metal traces), excluding complex sensing modules. The next step includes making NFCapsule pills with edible metals and gelatin hydrogel-based structural elements that are fully digestible, while using non-toxic thin-film electronics to manufacture our circuit elements [4]. We have planned on this as our future work in collaboration with material scientists..

Future Optimization Directions: As a general design bottleneck in ingestible devices, the pill size has also been a constraint in NFCapsule's design process. The current NFCapsule pill has an acceptably small form-factor, which is mainly determined by the efficiency requirement of our coils, but might still be too large for patients with severe difficulties to swallow. Exploring ways to make NFCapsule digestible may open up the opportunity to design even

smaller pills: (1). choosing a suitable edible metal material may lead to more efficient coil designs; (2). improved fabrication of the metal traces could enable longer ranges and more compact coil design parameters (e.g., trace height). Meanwhile, the NFCapsule reader may also be optimized: (1). since its function is relatively simple – blindly seeking potential resonators and monitoring signal changes, it is possible to make it battery-powered or smartphone-powered, leading to a portable design; (2). while our current reader antennas are rigid PCBs, it is possible to integrate soft, flexible coil antennas and design a wearable collar reader. We will explore these potential optimizations in the future.

10 RELATED WORK

Gastrointestinal sensors and ingestible electronics: There is an extensive interest in designing gastrointestinal sensors for a variety of diagnostic and monitoring applications [7, 80]. For instance, there have been multiple proposed designs for ingestible capsules to measure internal body temperature [13, 63, 64], pH [16, 32], gastrointestinal pressures [6, 20, 54, 65], and gas and biomolecular sensing [42, 62, 96]. There have also been successful implementations of pill-sized cameras to perform capsule endoscopies [26] such as the PillCam from Medtronic [28]. These implementations are composed of conventional IC electronics with miniaturized form factors. While the devices should pass safely through the gastrointestinal system intact, there is a risk of obstruction and tissue damage if they get stuck [73]. As a result, there is a vision to transition the design of ingestible electronics capsules to be constructed with edible and biodegradable materials [77]. This has included structural and insulating materials [37, 75, 93], conductive materials [14, 45], and battery materials [47, 48, 56]. Although NFCapsule is composed of ingestible but not fully-digestible materials, the prior work cited here will serve as foundations to construct the next iteration made from fully digestible materials.

Bio-impedance measurement: Bio-impedance has been a popular sensing modality to enable various human sensing applications [35, 68, 81, 94]. Among bio-impedance related research, electrochemical impedance spectroscopy (EIS) has been one of the most prevalent technologies. It has been leveraged extensively for a wide range of diagnostic and monitoring applications. These include evaluating cellular density in cell culture [11, 92], monitoring chronic wound healing [31, 53, 81, 84], diagnosing skin cancers [1, 12], and detecting edemas [27, 70]. These demonstrations, while robust, are typically wired and entail bulky and expensive backend instrumentation such as potentiostats and network analyzers. NFCapsule is inspired by relevant EIS research on EoE, and aims to extend similar underlying principles to a wireless and low-profile design.

The impedance-based diagnosis of EoE utilizes the increased intercellular spacing of the esophageal epithelium of a diseased patient [71]. Proof-of-concept studies measured the transepithelial electrical impedance of biopsied tissue to show that the value of individuals with EoE was significantly lower than that of healthy patients [88]. This work was extended to measuring the esophageal impedance in patients by modifying the head of an endoscope [3, 5, 44]. These studies showed that the impedance of a patient's esophagus could be measured non-destructively to accurately diagnose EoE. These techniques involving endoscopes remain invasive and wired, therefore motivating capsule-based wireless sensors.

Wireless Body Sensing: There is a rich literature in using wireless signals for human sensing applications, where human bodies interact with wireless signals and change their properties. Traditional far-field solutions leverage far-field radiations, for example, using Wi-Fi [39, 52, 58, 90, 91, 95] and RFID [40, 41, 66, 76, 86]. Near-field solutions, on the other hand, build on inductive (magnetic) coupling [15, 18, 21, 49, 87]. NFCapsule follows the latter and builds the NFCapsule pill as a wireless sensor for human sensing applications. Instead of integrating multiple independent modules including a chip [55, 97], NFCapsule adopts a chipless design building on prior work [29, 30, 33, 50, 51, 69, 85] on incomplete antennas. NFCapsule models the target tissue as part of its circuit to infer the properties of the target tissue uniquely in the EoE context.

11 CONCLUSION

This paper presents NFCapsule, a sensory system that can potentially enable non-invasive detection of active eosinophilic esophagitis (EoE). We design ingestible NFCapsule pills that are light-weight and battery-free based on RLC resonant circuits with only circuit components as simple as basic capacitors and metal traces. We model the target esophagus tissue as a circuit component that induces changes in the NFCapsule pill circuit, and design our NFCapsule reader to detect the pill's response by consistently monitoring the amount of energy transferred from the reader itself to the NFCapsule pill. We further adopt a dual-coil design for the NFCapsule pill to ensure robustness. A detailed evaluation shows that NFCapsule achieves high classification accuracy under practical scenarios including blockage, bending, and movement, and has 85% average classification accuracy between healthy and damaged porcine esophageal tissue samples. While the current study of the NFCapsule prototype did not involve any human patients, we plan an extensive clinical study as our future work. Bio-impedance is a pivotal metric for varied on-body and in-body conditions. We believe NFCapsule is the first step towards a broader exploration of wireless platforms to sense bio-impedance that pose a minimal burden on patients.

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