Capsule-Based Bioimpedance Sensing for Inflammatory Biomarker Detection in Gastrointestinal Tract

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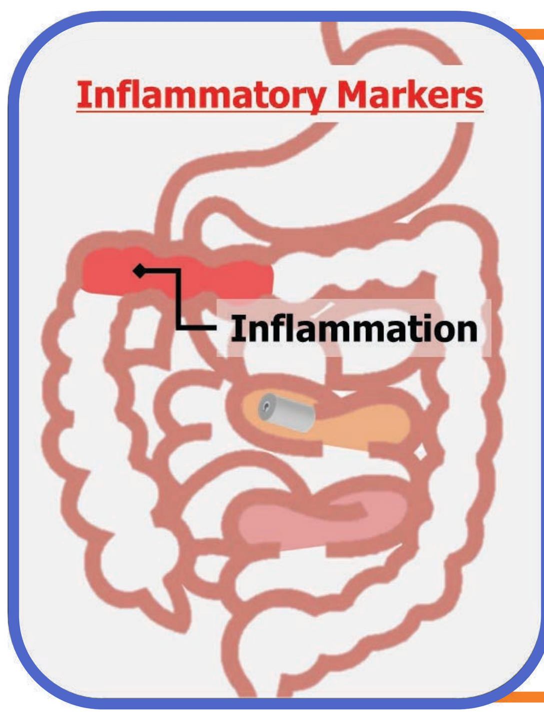
Motivation & Significance



- Inflammatory Bowel Disease (IBD), comprising Crohn's Disease (CD) and Ulcerative Colitis (UC), is a chronic **inflammatory condition** in the GI tract suspected to be caused by an **unknown** combination of genetic, microbiome, immune, and environmental factors[1]
- Pro-inflammatory cytokines IFN-γ and TNF-α **inhibit** intestinal **ion transport channels**, leading to an osmotic pressure imbalance and **leakage** of water and electrolytes through **epithelial tissue**[2]
- Inflammation linked to an **increase** in **conductive ions** and basal **permeability** of tissue surface

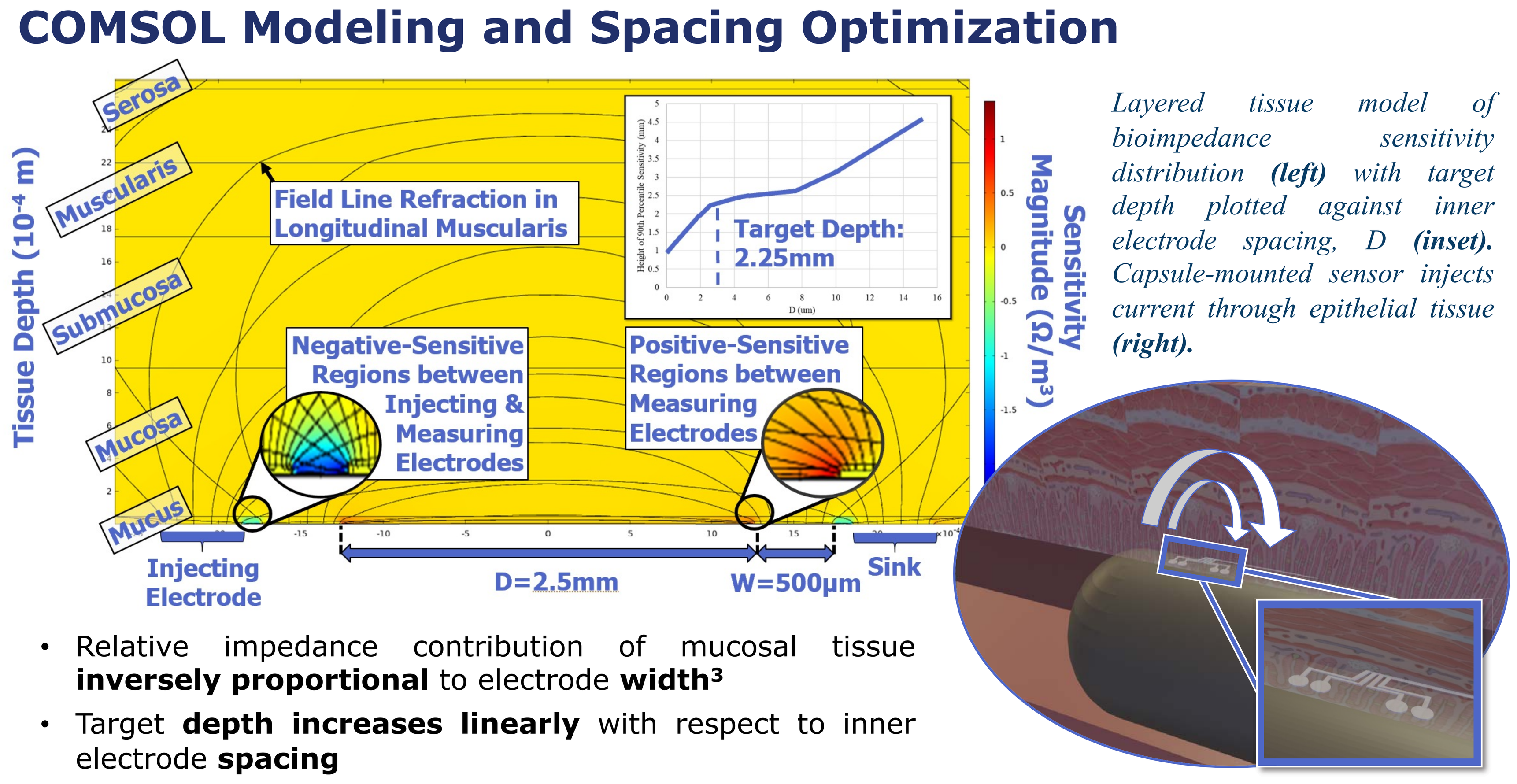
- Few **non-invasive** sensing platforms exist to address **localized tissue inflammation** within **inaccessible** areas of GI tract, such as the small intestine
- Flexible, capsule-mounted sensors to monitor epithelial conductivity **integrate** well with other biomarker sensors for **studying** the **underlying mechanisms** of inflammation

Innovation

- Mounting **bioimpedance sensors** onto **ingestible capsule platforms** enables monitoring of tissue integrity with targeted signal penetration depth
- **Breach in mucosal integrity** causes a **decrease** in measured impedance of tissue affected by **inflammation**
- **Testing** apparatus to **characterize** bioimpedance sensors traveling along tissue phantom at rate of **peristalsis**

Bioimpedance Sensor Design

COMSOL Modeling and Spacing Optimization

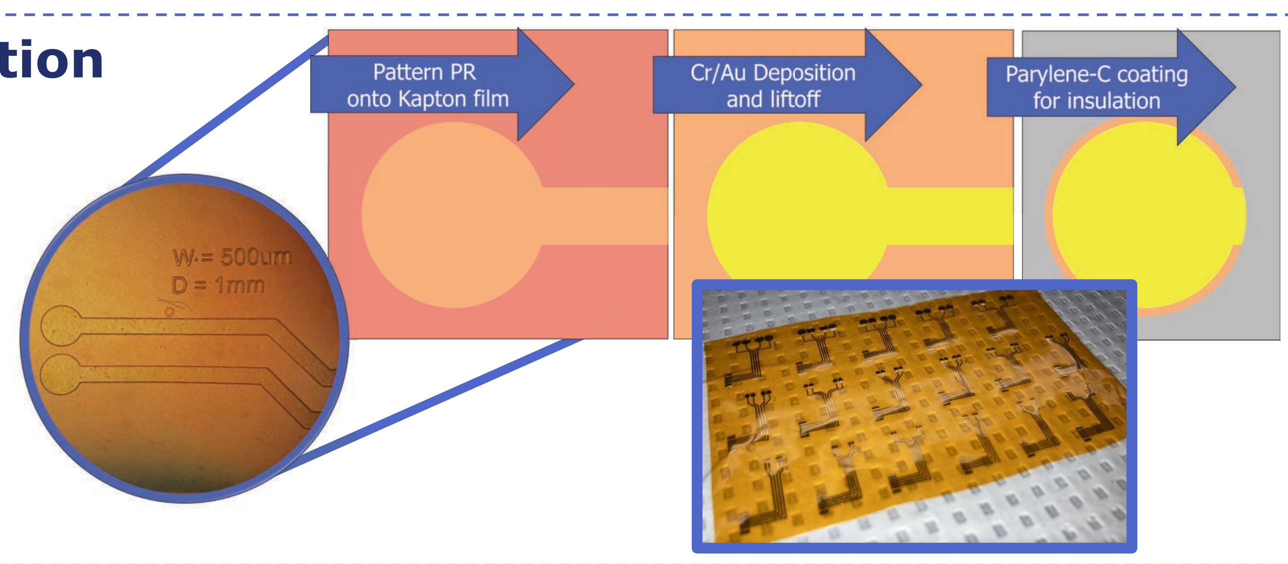


Layered tissue model of bioimpedance sensitivity distribution ***(left)*** *with target depth plotted against inner electrode spacing, D* ***(inset).*** *Capsule-mounted sensor injects current through epithelial tissue* ***(right).***

- Relative impedance contribution of mucosal tissue **inversely proportional** to electrode **width**[3]
- Target **depth increases linearly** with respect to inner electrode **spacing**

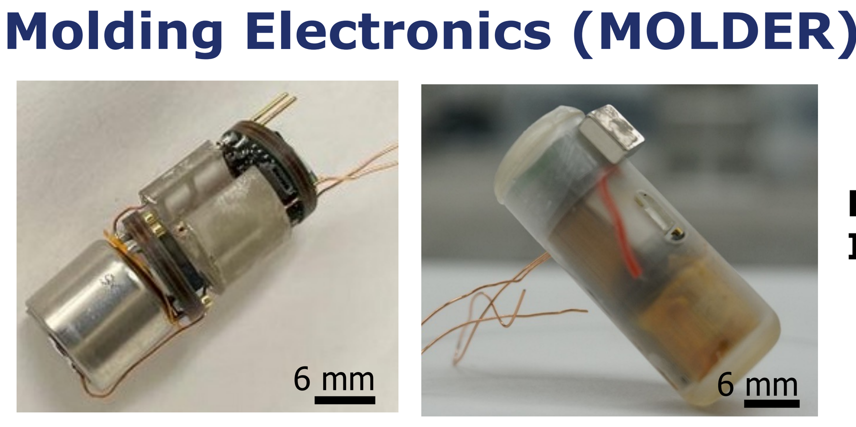
Sensor Fabrication

- Use **photomask** to pattern sensors and deposit **Cr/Au** using electron-beam evaporator
- **Parylene-C** will serve as an **insulation layer** to protect traces from shorting

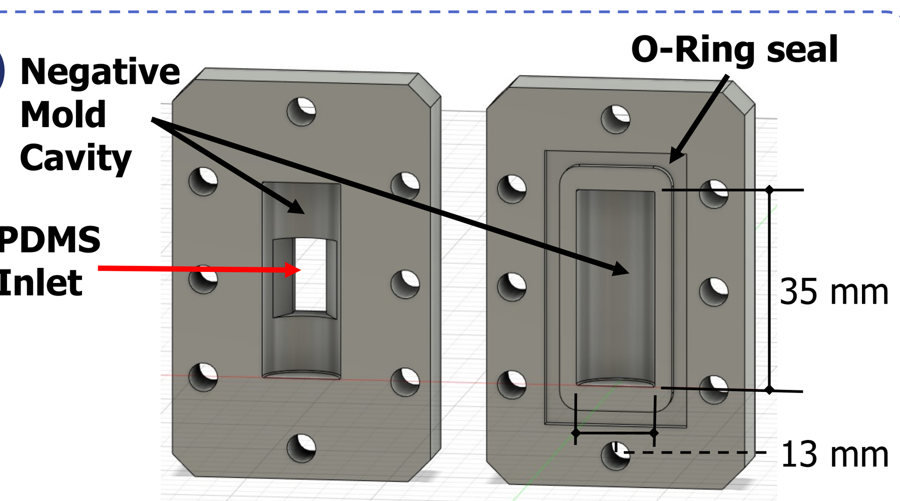


Packaging

Molding Electronics (MOLDER)

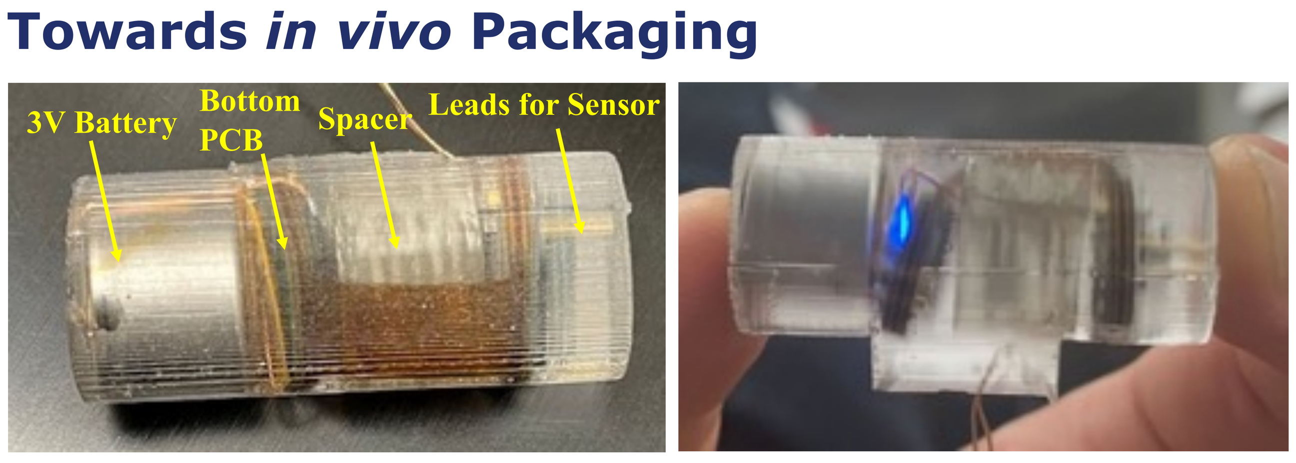


Photograph of PCB, 3D-printed spacer, and battery connected ***(left)*** *with 30-gauge wires[4]. Electronics are* ***encapsulated in a protective hard shell*** *(right). Scale bar: 6mm.*



Negative molds for ***encapsulating capsule electronics*** *in* ***PDMS*** *were* ***3D printed*** *using* ***Fused Filament Fabrication (FFF).***

Towards *in vivo* Packaging

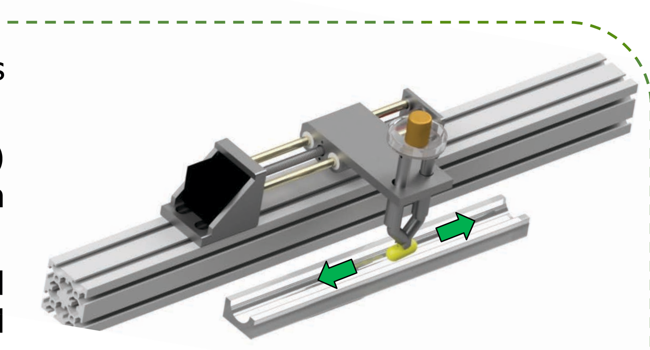


- Revision of PDMS mold would allow the **impedance sensor strip** to **fold across the side wall of capsule.**

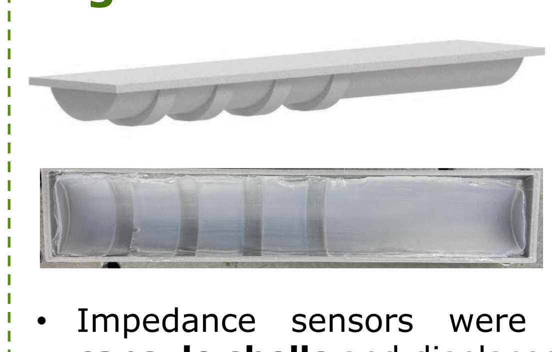
Photograph of PCB, 3D-printed spacer, and battery in a ***PROTOTYPE*** *mold of cured PDMS* ***(left).*** *The blue LED indicates the hardware continues to operate even after the molding process* ***(right).*** *During packaging, the battery is* ***disconnected using an external magnet.***

GI Simulation Setup

- Arduino-powered motor moves capsule holder laterally across tissue at a rate of **1.4 cm/min** modeling **peristaltic speeds**[5]
- **Sliding member** allows application of **70 gram-force (gf)** force directly on the capsule to model forces experienced in the GI tract[6]
- Allows **testing of drug delivery system,** actuation, and impedance sensor response to various simulated environments

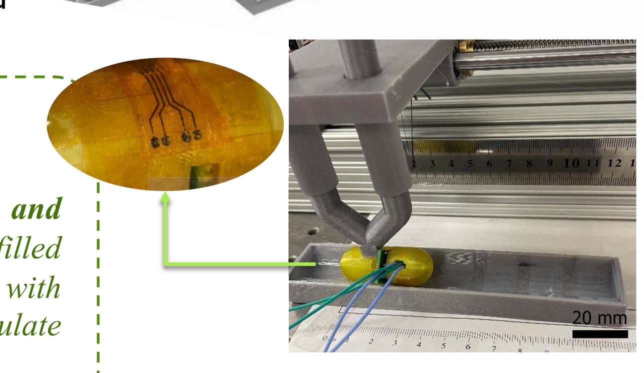


Agar Environment Molding



CAD rendering of agar mold (top) and photograph (left) of *agar (3% w/v) filled channel with 6-mm gap segments filled with phosphate-buffered saline (PBS) to simulate partial or "no contact" regions.*

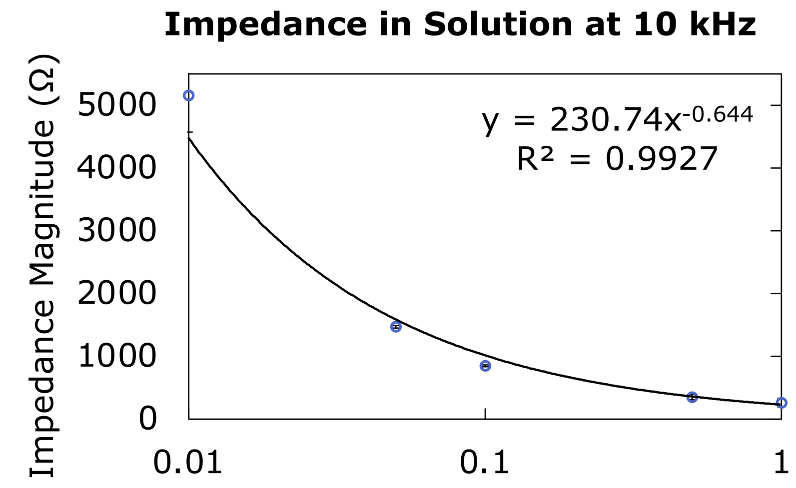
- Impedance sensors were attached to **3D-printed** dummy **capsule shells** and displaced using the testing apparatus

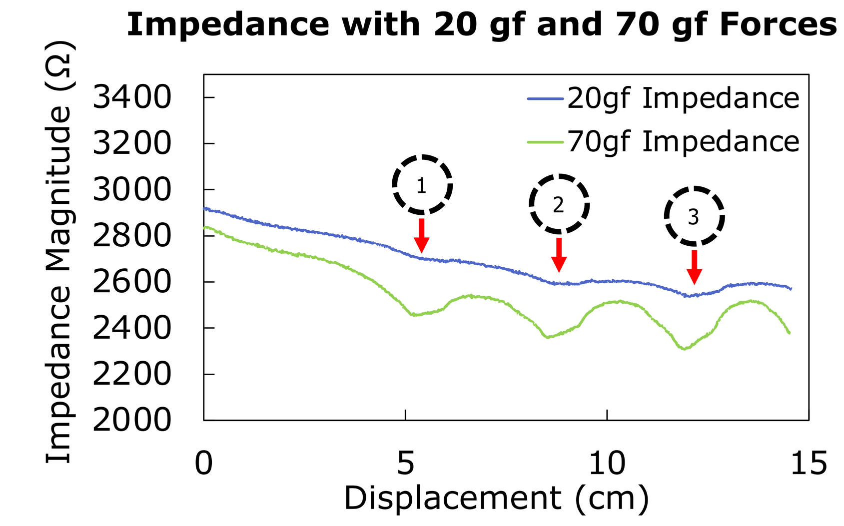


Test setup ***CAD rendering (top),*** *close-up of* ***capsule impedance sensor (left), test setup (right)***

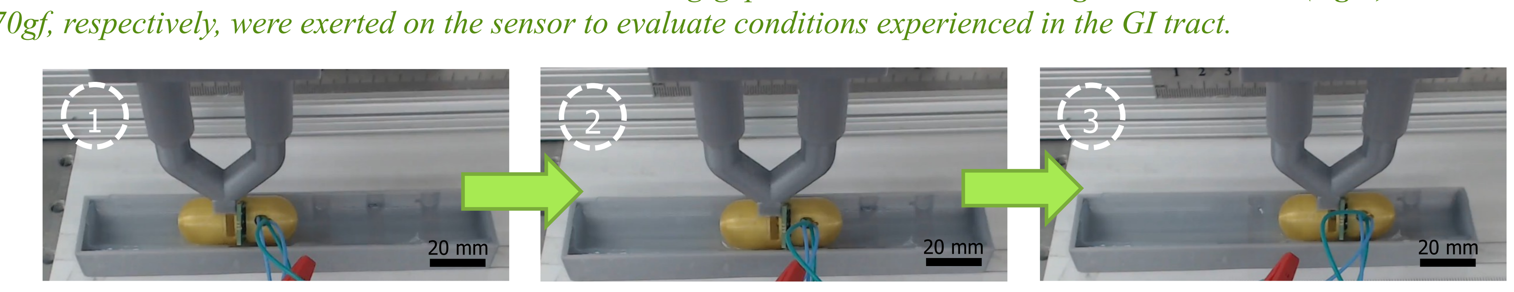
Results

Impedance Sensing Along an Agar Track





Bioimpedance electrodes were characterized (10 kHz) using a Biologic VSP-300 potentiostat at several KCl concentrations ***(0.01-1 M) (N =3, left).*** *The sensor was* ***attached to a capsule shell and actuated across an agar track*** *filled with 1x pH7 PBS.* ***Impedance measurements*** *were recorded while traversing gaps in the mold* ***simulating "non-contact" (right).*** *Forces of 20gf and 70gf, respectively, were exerted on the sensor to evaluate conditions experienced in the GI tract.*



Capsule crossing ***first (left), second (middle), and third (right)*** *agar gaps.* ***Fourth gap not pictured***

Significance:

- Quantify **impedance sensor response** to **no contact** with agar **in presence** and **absence of liquid** and **varying applied forces**
- Evaluate impedance sensor **measurement drift** over time
- Assess **impedance sensor response** in various **ion concentrations** to **simulate electrolyte loss** through **inflamed mucosal tissue**

Future Work

- **Quantify target depth** with respect to electrode width and spacing to validate FEM model
- Use sensors to **characterize permeability** of porcine intestinal **tissue**
- Further investigate the effects of small bowel environmental conditions, such as **contact pressure** and **intestinal viscosity,** on *in vitro* motion artifacts
- Consider effect of **speed** or **acceleration** on impedance sensor results

References

1. C. Abraham *et al.*, "Inflammatory Bowel Disease," *N. Engl. J. Med.*, 2009; **2.** D. Magalhaes, J. Cabral, P. Soares-da-Silva, F. Magro, "Role of epithelial ion transports in inflammatory bowel disease," *Am. J. Gastrointest. Liver Physiol.*, 2016; **3.** P. Kassanos, *et al.*, "A tetrapolar bio-impedance sensing system for gastrointestinal tract monitoring," 2015 IEEE 12th International Conference on Wearable and Implantable Body Sensor Networks (BSN), 2015; **4.** J.M. Stine et al., "Miniaturized capsule system for hydrogen sulfide detection in the gastrointestinal tract", Hilton Head Workshop 2022: A Solid-State Sensors, Actuators, and Microsystems Workshop 2022; **5.** M.A. Straker et al., "Region-targeted bilayer coating technology for ingestible devices and systems", Hilton Head Workshop 2022: A Solid-State Sensors, Actuators, and Microsystems Workshop 2022; **6.** L. Barducci *et al.*, "Fundamentals of the gut for capsule engineers," *Prog. Biomed. Eng.*, 2020.

Acknowledgements

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