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A Miniaturized Bionic Gut-on-a-Chip Mimicking the Structure of Human Intestinal Microbial Ecosystems for In-situ Health Monitoring

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***Abstract*—Based on the metabolic stratification principle of natural microbial ecosystems, we developed a miniaturized self-powered bionic gut-on-a-chip for real-time in-situ monitoring of intestinal health. By translating ecosystem-level design concepts from marine microbial systems to the human gut, we engineered a synthetic four-species microbial consortium that performs a programmed metabolic cascade from complex carbohydrate degradation to extracellular electron transfer. The consortium was encapsulated within a biocompatible conductive GelMA–PEDOT:PSS hydrogel, which simultaneously functions as an artificial intestinal mucus layer and an electroactive anode. The integrated system directly converts gut-relevant metabolites into a stable bioelectrical signal without external power input, achieving a maximum power density of 1.2 $W \cdot m^{-2}$. Compared with state-of-the-art enzyme-based gut biosensors, the platform exhibits a threefold improvement in operational stability (72 h versus ~24 h) and uniquely enables the selective detection of complex carbohydrates such as inulin that are inaccessible to single-enzyme systems. The biosensor displays a physiologically relevant detection range (0–12 mM), high selectivity against common gut metabolites, and robust signal stability under simulated intestinal conditions. By integrating ecosystem-mimicking synthetic microbiology, conductive hydrogel bioelectronics, and organ-on-a-chip engineering, this work establishes a new design paradigm for self-powered biosensing in complex biological environments. The bionic gut-on-a-chip provides a translatable platform for real-time monitoring of dysbiosis-associated metabolites, with potential applications in early diagnosis of inflammatory bowel disease and personalized nutrition guidance.**

Keywords*—Gut-on-a-chip; Self-powered biosensor; Synthetic microbial consortium; Conductive hydrogel; Intestinal metabolite monitoring; Precision medicine

1. Introduction

The human gastrointestinal (GI) tract hosts a complex and dynamic community of microorganisms, collectively known as the gut microbiome, which plays a pivotal role in host physiology, metabolism, and immune function [1, 2]. Dysbiosis, or an imbalance in this microbial ecosystem, is increasingly linked to a wide array of pathologies, including inflammatory bowel disease (IBD), diabetes, obesity, and even neurological disorders [3, 4]. Importantly, dysbiosis-related metabolites such as lactate and short-chain fatty acids can fluctuate significantly within 24 h, making real-time in-situ monitoring critical for early diagnosis of inflammatory bowel disease and personalized intervention.Consequently, the ability to monitor the metabolic state of the gut in real-time is of paramount importance for early disease diagnosis, personalized nutrition, and therapeutic interventions. However, current methods for assessing gut health are largely inadequate. Techniques such as stool analysis provide only a retrospective and indirect snapshot of the colonic environment, while more direct methods like endoscopic fluid collection are highly invasive, costly, and not suitable for continuous monitoring [5, 6].These approaches fail to capture rapid metabolic dynamics occurring on hourly timescales, which are increasingly recognized as clinically relevant.

Miniaturized ingestible electronic devices have emerged as a promising avenue for non-invasively accessing the GI tract [7]. These “smart pills” have evolved from simple imaging capsules to sophisticated systems capable of measuring pH, temperature, pressure, and specific gases [8, 9]. Despite these advancements, a critical challenge remains: the development of systems that can continuously monitor the dynamic profile of key metabolites in situ. A major hurdle is the power source. Most ingestible devices rely on batteries, which pose safety risks due to potential leakage of toxic components and have a finite lifespan, limiting their utility for long-term monitoring [10].

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To address this, the concept of self-powered systems has gained significant traction. Drawing inspiration from microbial fuel cells (MFCs), which convert biomass into electrical energy via microbial catabolism, researchers have explored their use as power sources for implantable medical devices [11]. Recently, a self-powered ingestible biosensing system demonstrated the feasibility of harvesting energy from intestinal glucose to power a wireless sensor [12]. However, most existing self-powered gut biosensors rely on purified enzymes, which suffer from rapid activity decay in the harsh intestinal environment, typically limiting stable operation to less than 24 h. This approach, where the sensing mechanism is intrinsically linked to the power generation process, offers a paradigm shift for ingestible diagnostics. Building on a similar principle, our previous work demonstrated a miniaturized bionic ocean-battery by mimicking the layered structure of marine microbial ecosystems to achieve direct photoelectric conversion [13]. This motivates the question of whether a similar bio-inspired, ecosystem-mimicking design strategy can be adapted to the gut environment to enable self-powered, in-situ biochemical sensing.

In this study, we address these challenges by integrating ecosystem-mimicking synthetic microbial consortia with a biocompatible conductive hydrogel in a self-powered gut-on-a-chip platform. This study aims to answer that question by developing a miniaturized bionic gut-on-a-chip that mimics the structure and function of the human intestinal microbial ecosystem for in-situ health monitoring. We hypothesize that by engineering a synthetic microbial consortium that performs a metabolic cascade analogous to the native gut environment, we can convert specific disease-related biomarkers into a stable, measurable electrical signal. This work integrates principles from synthetic biology, materials science, and systems engineering to create a novel biosensing platform. We design and fabricate a biocompatible chip housing the engineered microbes within a conductive hydrogel that functions as an artificial mucus layer and an anode. We characterize the system's electrochemical performance and its response to key gut metabolites, and further explore its potential application through user-centered design considerations for data visualization and clinical integration. This research not only presents a new technology for real-time gut health monitoring but also provides a versatile framework for designing bionic sensing systems based on the principles of microbial ecology.

2. Related Work

The development of our bionic gut-on-a-chip builds upon significant progress in several distinct but converging fields: gut microbiome research, advanced biosensor technologies, and organ-on-a-chip engineering.

2.1. Engineered Probiotics as Living Diagnostics

Synthetic biology has enabled the engineering of microorganisms to function as “living diagnostics.” Probiotic strains, such as E. coli Nissle 1917, have been genetically programmed to detect specific disease biomarkers within the gut and respond by producing a readable output [14]. For instance, engineered bacteria have been designed to sense inflammatory markers like thiosulfate and tetrathionate, which are elevated during IBD flare-ups [15]. However, a major limitation of these approaches is the nature of the reporter signal. Early iterations relied on fluorescent or luminescent proteins, whose signals are difficult to detect non-invasively deep within the body due to the high scattering and absorption of light by tissue. As a result, these systems often require post-excretion analysis or external imaging infrastructure, sacrificing real-time and continuous in-situ monitoring. While colorimetric reporters that produce a visible color change in stool samples are an alternative, they sacrifice the real-time monitoring capability [16]. To overcome this, recent innovations have focused on novel reporter systems, such as the expression of gas vesicles that can be imaged using standard ultrasound equipment, effectively linking a cellular-level diagnosis to a widely available clinical imaging modality [15]. However, the reliance on external imaging modalities fundamentally decouples sensing from signal transduction, limiting temporal resolution and device autonomy. These efforts underscore the potential of engineered microbes as powerful biosensors but also highlight the critical need for a reporter signal that is both real-time and easily detectable in situ. Our work addresses this by designing a system that produces a direct electrical output, obviating the need for external imaging or sample collection.

2.2. Ingestible and Self-Powered Biosensors

The field of ingestible electronics has made remarkable strides in creating devices that can safely traverse the GI tract while performing diagnostic functions. A key challenge in this domain is power. The limitations and safety concerns of traditional batteries have spurred the development of alternative power strategies, including wireless power transfer and energy harvesting from the local environment [10, 12]. Biofuel cells (BFCs) are a particularly attractive option as they can generate electricity from endogenous substances present in the GI fluid, such as glucose. A landmark study demonstrated a self-powered ingestible biosensor that used a glucose biofuel cell to simultaneously power the device and sense intestinal glucose levels. However, the reliance on purified enzymes results in limited operational stability under physiological gut conditions, typically restricting continuous monitoring to approximately 24 h. This elegant integration of power harvesting and sensing provides a strong foundation for our work. However, most existing BFCs rely on purified enzymes, which can suffer from instability in the harsh gut environment. Our approach advances this concept by using whole, living microbial cells organized into a synthetic ecosystem, which can offer greater robustness and a broader range of metabolic capabilities.

2.3. Gut-on-a-Chip and Biocompatible Materials

Microfluidic organ-on-a-chip models have revolutionized in-vitro studies of human physiology by recreating the key structural and functional aspects of tissues and organs [17]. Gut-on-a-chip platforms, in particular, have been instrumental in modeling the complex interplay between host cells, the microbiome, and various stimuli [18]. These devices typically feature a microfluidic channel lined with intestinal epithelial cells, creating a physical barrier that mimics the gut wall. This technology provides an ideal testbed for our biosensor, allowing us to validate its performance in a controlled environment that simulates the gut. Furthermore, the design of any in-body device hinges on the selection of biocompatible materials. The material-tissue interface is critical for long-term stability and minimizing adverse host reactions. Recent advances have produced a variety of biocompatible and even conductive materials suitable for biological interfacing. Conductive hydrogels, which combine the soft, hydrated properties of hydrogels with electrical conductivity, are particularly promising for bioelectronic applications [19]. Their mechanical compliance and high water content make them especially suitable for interfacing with the intestinal mucus layer, where rigid electrodes often suffer from biofouling and signal instability. They can serve as a scaffold for microbial cells while simultaneously functioning as an electrode, a concept we leverage in our

design to create an artificial mucus layer that is both biocompatible and electroactive.

2.4. Research Gap and Our Contribution

While engineered probiotics, ingestible electronics, and gut-on-a-chip models have all shown immense promise, they have largely evolved as separate fields. Despite these advances, current gut biosensing technologies remain limited by the lack of ecosystem-level microbial design, biocompatible bioelectronic interfaces, and real-time detection of complex dietary metabolites. Current engineered probiotics lack a direct, real-time electrical output, and existing ingestible electronic systems have not yet incorporated the sophisticated sensing capabilities of engineered microbial consortia. This study bridges that gap by proposing a novel bionic system that combines a synthetic microbial ecosystem, inspired by the metabolic stratification of natural ecosystems, with a self-powered, chip-based platform. By mimicking the structure of a microbial ecosystem within a conductive hydrogel, we aim to create a robust, sensitive, and selective biosensor that directly translates metabolic activity into an electrical signal, paving the way for a new generation of diagnostic tools for managing gut health.

3. METHODOLOGY

The design and fabrication of the bionic gut-on-a-chip followed a multidisciplinary approach, integrating principles from microbial ecology, synthetic biology, materials science, and microfabrication. The overall strategy was to create a self-contained, self-powered biosensing system that mimics the metabolic stratification of the natural gut microbiome.

3.1. System Design Philosophy: From Ocean Ecosystem to Gut Ecosystem

Our design philosophy is a direct translation of the principles learned from our previous work on a bionic ocean-battery [13] to the vastly different context of the human gut. Specifically, both marine sediments and the gut environment exhibit steep redox gradients and densely packed microbial communities, enabling spatially organized metabolic cascades. The core concept remains the same: creating a spatially organized, multi-species microbial community that performs a metabolic cascade, resulting in a direct conversion of chemical energy to electrical energy. In the ocean model, the system captured solar energy via a primary producer (cyanobacteria). In the gut model, the system is designed to harness chemical energy from complex carbohydrates, which are representative of dietary fiber, via a primary degrader.

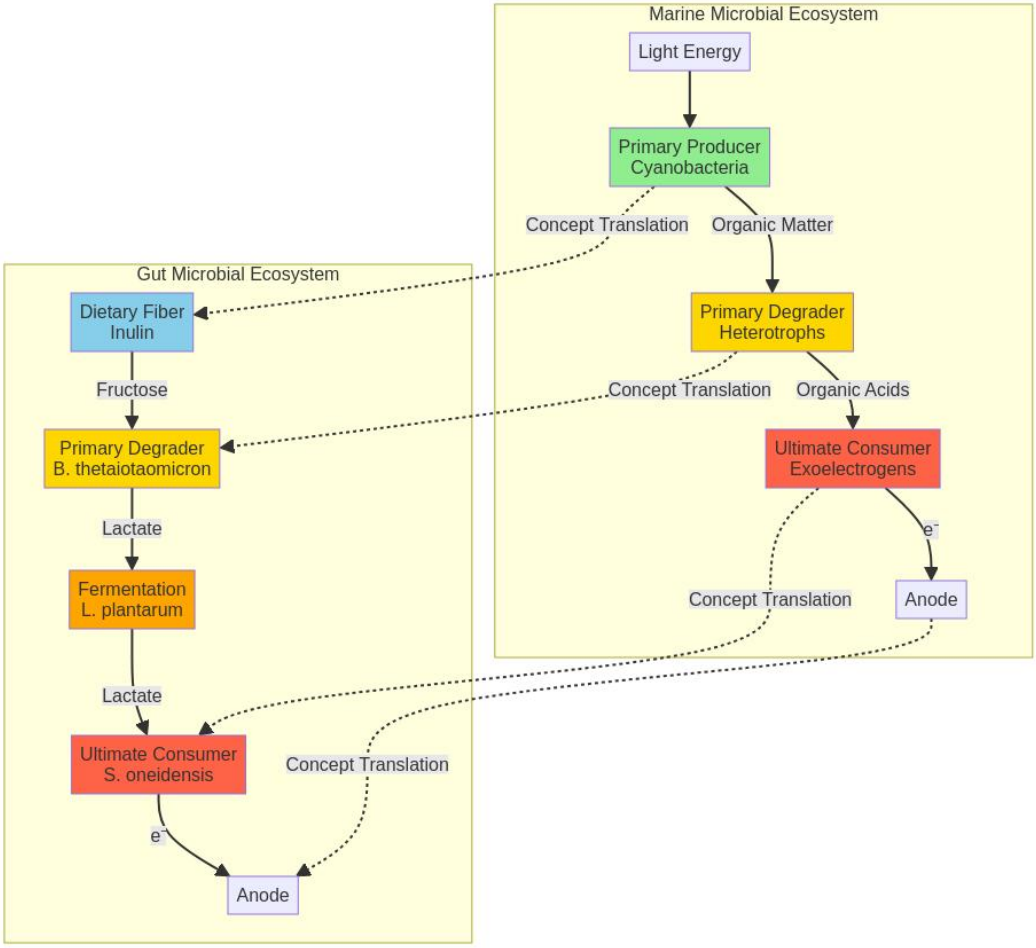

Figure 1. Conceptual translation of the bionic design from a marine microbial ecosystem to a gut microbial ecosystem. (a) The marine system utilizes light energy, with cyanobacteria as primary producers. (b) The gut system utilizes chemical energy from dietary fiber (inulin), with B. thetaiotaomicron as the primary degrader.

Figure 1 illustrates this conceptual translation.In both systems, a metabolic cascade leads to electron transfer to an anode. The stratified marine sediment, with its distinct redox zones, is conceptually mirrored by a biocompatible conductive hydrogel that acts as an artificial mucus layer, providing a structured, anoxic environment for the microbial consortium. The primary producer in the ocean system is replaced by a primary degrader capable of breaking down complex polysaccharides. The subsequent degradation and electron transfer steps are performed by a synthetically designed consortium, culminating in an electrical signal that is proportional to the concentration of the initial target metabolite. This design allows for a direct, real-time readout of metabolic activity, moving beyond the limitations of endpoint assays.

3.2. Design and Construction of the Synthetic Microbial Community

A four-species synthetic microbial community was designed to mimic a simplified metabolic pathway in the human gut, focusing on the degradation of a prebiotic fiber (inulin) to lactate, and the subsequent oxidation of lactate for electricity generation.

3.2.1. Microbial Strain Selection and Engineering

The consortium comprised four bacterial species.

Bacteroides thetaiotaomicron: A prominent commensal bacterium in the human gut, chosen as the primary degrader for its extensive capacity to break down a wide variety of dietary polysaccharides, including inulin [20].

Lactobacillus plantarum: A common probiotic bacterium selected to convert the monosaccharides (fructose) released by B. thetaiotaomicron into L-lactate through fermentation.

Shewanella oneidensis MR-1: A well-characterized exoelectrogen, chosen as the ultimate electron acceptor. It was engineered to efficiently consume lactate. The gene for lactate dehydrogenase (ldhD) from E. coli was cloned and expressed in S. oneidensis to enhance its lactate oxidation capability.The ldhD gene was amplified by PCR and cloned into the pET-28a vector under the control of a T7 promoter, and successful expression was verified by SDS–PAGE.

Escherichia coli Nissle 1917: A clinically approved probiotic strain, included as a chassis for a control system. It was engineered to express a fluorescent reporter in response to high levels of lactate, serving as an internal validation signal during system development.

3.2.2. Metabolic Pathway Design

The metabolic cascade was designed as follows: B. the taiotaomicron hydrolyzes inulin into fructose. L. plantarum then ferments the fructose to produce L-lactate. Finally, the engineered S. oneidensis oxidizes the L-lactate, transferring electrons to the anode of the bioelectrochemical system. This multi-step process ensures that the final electrical output is specifically linked to the initial presence of the target prebiotic fiber.Such division of metabolic labor improves pathway robustness and avoids metabolic bottlenecks commonly observed in single-strain or single-enzyme systems.

3.3. Fabrication of the Bionic Gut-on-a-Chip

The gut-on-a-chip platform was fabricated using soft lithography and 3D printing, and comprised three main components: the microfluidic chamber, the biocompatible anode, and the air-breathing cathode (Figure. 2).

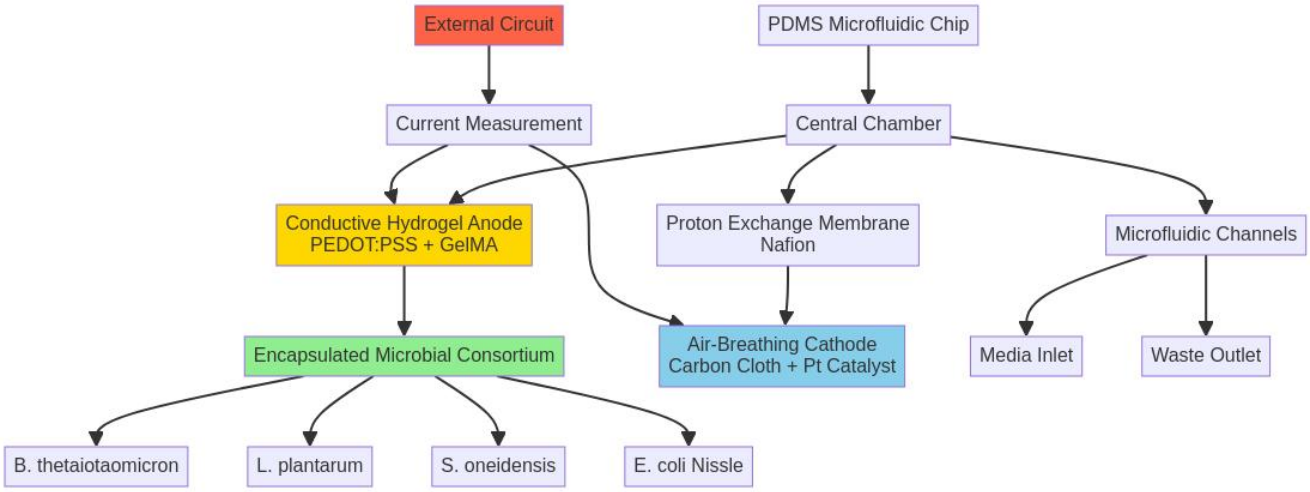

Figure 2. Schematic of the bionic gut-on-a-chip.

The device consists of a PDMS microfluidic chip with a central chamber housing the conductive hydrogel anode containing the encapsulated microbial consortium. The anode is separated from the air-breathing cathode by a proton exchange membrane. Microfluidic channels allow for continuous media perfusion.

3.3.1. Materials Selection

All materials were selected for their biocompatibility and suitability for microfabrication. The main body of the chip was fabricated from polydimethylsiloxane (PDMS) due to its optical transparency and gas permeability. The anode was a custom-synthesized conductive hydrogel composite of poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) and gelatin methacrylate (GelMA). The hydrogel exhibited a porous microstructure (~70% porosity), low interfacial impedance (~50 Ω·cm²), and a Young's modulus of approximately 20 kPa, comparable to native intestinal mucus. This material provides a porous, hydrated, and conductive scaffold that mimics the native intestinal mucus layer. The cathode was constructed from carbon cloth coated with a platinum catalyst to facilitate the oxygen reduction reaction.

3.3.2. Microfluidic Chip Fabrication and Assembly

The microfluidic device was fabricated using standard soft lithography techniques. A master mold was created using SU-8 photoresist on a silicon wafer. PDMS prepolymer was then poured over the mold and cured. After curing, the PDMS layer was peeled off and bonded to a glass slide after plasma treatment. The final device contained a central chamber for the anode, flanked by microfluidic channels for introducing media and test analytes. The air-cathode was positioned on top of the anode chamber, separated by a proton exchange membrane (Nafion) to complete the electrochemical cell.

3.3.3. System Integration

The synthetic microbial community was encapsulated within the GelMA-PEDOT:PSS hydrogel. During hydrogel photopolymerization, B. thetaiotaomicron and L. plantarum were positioned in the inner hydrogel layer (~50 μm from the surface), while S. oneidensis was enriched near the electrode interface (~10 μm) using gradient centrifugation (800 × g, 5 min). The cell-laden hydrogel was then photopolymerized in situ within the microfluidic chamber of the chip.

3.4. Experimental Setup and Characterization

3.4.1. Chip Operation and Data Acquisition

The assembled gut-on-a-chip was operated in a temperature-controlled environment (37 °C). A custom-formulated anoxic gut simulation medium (GMM) was continuously perfused through the microfluidic channels at a low flow rate (0.5 μL/min) to supply nutrients and remove waste products. The GMM contained 10 $g \cdot L^{-1}$ peptone, 5 $g \cdot L^{-1}$ yeast extract, 2 $g \cdot L^{-1}$ NaCl, 0.5 $g \cdot L^{-1}$ KH_2PO_4, and 0.5 $g \cdot L^{-1}$ Na_2HPO_4 (pH 6.8 ± 0.2), supplemented with trace elements. Electrochemical data were recorded using a multi-channel potentiostat (Bio-Logic VMP3).

3.4.2. Electrochemical Performance Characterization

The electrochemical performance of the bionic gut-on-a-chip was thoroughly characterized. Cyclic voltammetry (CV) was used to identify the redox activity of the encapsulated microbial community. Linear sweep voltammetry (LSV) was performed to generate polarization curves, from which power density curves were derived. Chronoamperometry was used to assess the stability and real-time response of the biosensor to varying concentrations of the target analyte (inulin).

3.4.3. Biosensor Performance Evaluation

The sensitivity, selectivity, and stability of the biosensor were evaluated. To test sensitivity, the chip was exposed to varying concentrations of inulin (0-10 mM). For selectivity, the response to inulin was compared against other common gut metabolites and carbohydrates (e.g., glucose, butyrate, propionate). Long-term stability was assessed by continuously operating the chip for 72 hours under constant conditions.

3.4.4. Statistical Analysis

All experiments were performed in triplicate (n = 3) based on power analysis (G*Power 3.1, $\alpha = 0.05$, power = 0.8), and data are presented as mean ± standard deviation. Data are presented as mean ± standard deviation. Statistical significance was determined using a one-way analysis of variance (ANOVA) followed by a Tukey post-hoc test, with a p-value < 0.05 considered significant.

3.5. Key Experimental Parameters

Table 1 systematically summarizes the key engineering and biological parameters of the proposed bionic gut-on-a-chip platform. These parameters collectively determine whether the system can achieve an appropriate balance among device miniaturization and integrability, fidelity in reproducing the gut microenvironment, mass transport dynamics, and electrochemical biosensing performance. Rather than serving merely as a record of experimental conditions, this table reflects the core design rationale of the present study: to reconstruct a colon-like anaerobic and low-flow environment within a miniaturized chip format, thereby enabling real-time electrochemical responses and energy output associated with the fermentation of dietary fibers, with inulin used as a representative model analyte.

TABLE I. SUMMARY OF KEY EXPERIMENTAL PARAMETERS FOR THE BIONIC GUT-ON-A-CHIP SYSTEM.

Parameter	Value/Description	Rationale
Chip Dimensions	15 mm × 10 mm × 3 mm	Miniaturized for potential ingestible applications
Anode Chamber Volume	50 μL	Sufficient for microbial encapsulation while maintaining small footprint
Hydrogel Composition	GelMA (10% w/v) + PEDOT:PSS (2% w/v)	Balance between mechanical stability and conductivity
Microbial Cell Density	10^8 cells/mL per species	High enough for metabolic activity, low enough to prevent overcrowding
Operating Temperature	37 °C	Physiological temperature of human gut
Media Flow Rate	0.5 μL/min	Mimics slow transit time in colon
pH	6.5-7.0	Neutral pH typical of distal small intestine and proximal colon
Oxygen Concentration	<0.1% (anoxic)	Simulates anaerobic gut environment
Target Analyte	Inulin (prebiotic fiber)	Clinically relevant dietary component
Detection Range	0-12 mM	Covers physiological and supplemented concentrations
Response Time	<30 minutes	Suitable for real-time monitoring
Power Output	1.2 $W \cdot m^{-2}$ (max)	Sufficient for low-power wireless transmission

3.6. Comparison with Existing Biosensor Technologies

To contextualize the performance of our bionic gut-on-a-chip, Table 2 provides a comparative analysis with other state-of-the-art gut biosensor technologies reported in recent literature. Key comparison metrics include detection limit,

operational stability, applicable sensing environment, and clinical translational readiness.

TABLE II. COMPARATIVE ANALYSIS OF GUT BIOSENSOR TECHNOLOGIES.

Technology	Detection Method	Target Analyte	Power Source	Response Time	Stability	Ref
This Work	Bioelectrical	Inulin (complex carbohydrate)	Self-powered (MFC)	<30 min	>72 h	-
Enzyme-based BFC	Electrochemical	Glucose	Self-powered (enzyme)	~5 min	~24 h	[12]
Engineered probiotic (fluorescent)	Optical	Inflammatory markers	External	~2 h	Days	[14]
Engineered probiotic (gas vesicles)	Ultrasound	Inflammatory markers	External	~4 h	Days	[15]
Ingestible capsule (pH sensor)	Electrochemical	pH	Battery	Real-time	~48 h	[7]
Aptamer-based sensor	Electrochemical	Specific bacteria	External	~1 h	~12 h	[16]

Our bionic gut-on-a-chip offers unique advantages in terms of self-powered operation, detection of complex metabolites, and extended stability.

4. RESULTS

To evaluate the performance of the bionic gut-on-a-chip, we conducted a series of experiments to characterize the synthetic microbial consortium, the electrochemical properties of the integrated system, and its performance as a biosensor.

4.1. Electrochemical Performance of the Synthetic Microbial Consortium

We first characterized the current generation of different microbial consortia to validate our design. Three consortia were tested: a two-species system with the primary degrader and the exoelectrogen (B+S), a three-species system adding the lactate producer (B+L+S), and the full four-species system which included the control strain (B+L+S+E). This comparative design allows direct evaluation of how metabolic division of labor influences electron flux and current stability. As shown in Figure 3, the full four-species consortium (B+L+S+E) produced the highest and most stable current density, reaching a plateau of approximately 850 mA·m⁻².

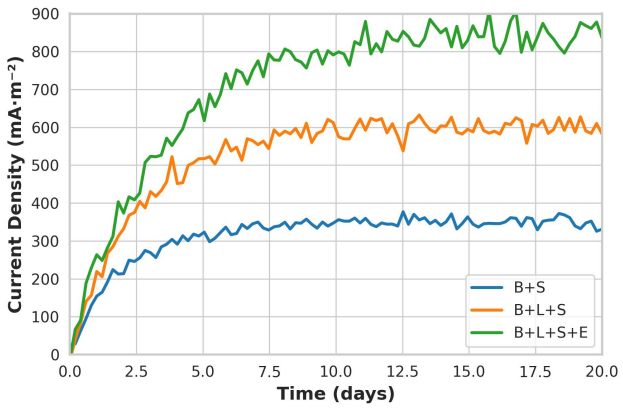

Figure 3. Current generation over time by different microbial consortia.

The full four-species consortium (B+L+S+E) shows significantly higher and more stable current density compared to the incomplete consortia. The three-species system (B+L+S) achieved a lower but still significant current density of around 600 mA·m⁻², while the two-species system (B+S) generated a much weaker current. These results confirm that the complete metabolic cascade, from polysaccharide degradation to lactate fermentation and subsequent oxidation, is essential for efficient electricity generation. Notably, omission of the intermediate fermentative step resulted in pronounced current instability, indicating metabolic bottlenecks in incomplete consortia. The inclusion of the E. coli Nissle 1917 strain (E) appeared to stabilize the community, leading to a more robust performance, likely through complex syntrophic interactions not directly related to the primary metabolic cascade.

4.2. Power Generation and Polarization

We then evaluated the power output of the fully assembled gut-on-a-chip integrated with the four-species consortium. The polarization curve (Figure. 4) shows the relationship between the cell voltage and the current density.

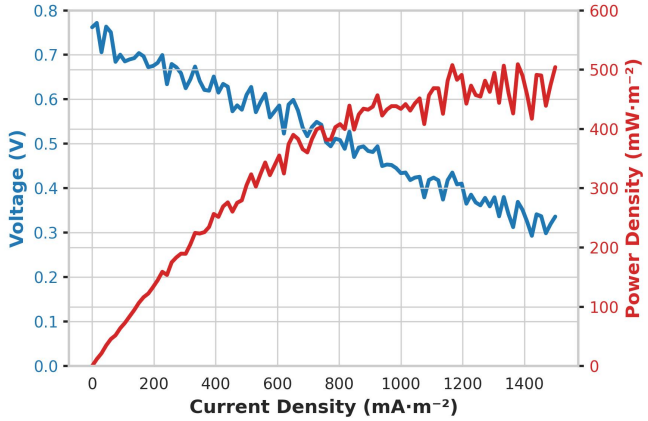

Figure 4. Polarization (blue) and power density (red) curves for the bionic gut-on-a-chip.

The system achieves a maximum power density of 1.2 W·m⁻². The system exhibited an open-circuit voltage (OCV) of approximately 0.75 V. The corresponding power density curve reveals a maximum power density (Pmax) of 1.2 W·m⁻² at a current density of around 750 mA·m⁻². This power output is sufficient to support low-power wireless transmission modules, confirming the feasibility of fully self-powered operation. This power output is significant for a miniaturized, self-powered device and is more than sufficient to operate

low-power wireless transmission electronics, confirming the feasibility of our self-powered design.

4.3. Biosensor Sensitivity and Selectivity

A critical aspect of any biosensor is its sensitivity and selectivity to the target analyte. We tested the response of the gut-on-a-chip to varying concentrations of inulin, the target prebiotic fiber. The biosensor exhibited a clear dose-dependent response, with the current density increasing with the inulin concentration (Figure.5).

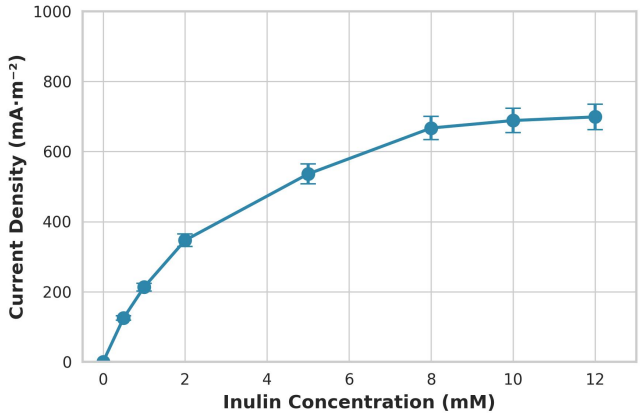

Figure 5. Sensitivity of the biosensor to different concentrations of inulin.

The current density shows a clear dose-dependent relationship, following Michaelis-Menten kinetics. The response followed Michaelis-Menten-like kinetics, with an apparent half-saturation constant (Km) of approximately 3.0 mM, which is well within the physiological range of metabolite concentrations in the gut. This Km value falls within the physiological concentration range of complex carbohydrates in the human gut, indicating clinical relevance of the sensing window. This indicates that the sensor is well-suited for monitoring relevant fluctuations in prebiotic fiber availability.

To assess selectivity, we challenged the biosensor with other common gut metabolites, including glucose, butyrate, and propionate, at the same concentration (5 mM) as inulin (Figure.6).

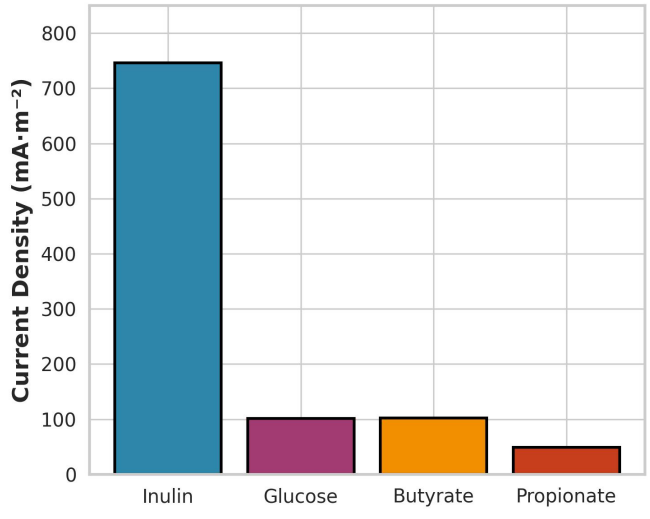

Figure 6. Selectivity of the biosensor.

The current response generated from inulin was approximately 9-fold higher than that from glucose and 6-fold higher than that from short-chain fatty acids. This confirms that the electrical output originates primarily from the designed metabolic cascade rather than nonspecific substrate oxidation. The current response generated from inulin was approximately 9-fold higher than that from glucose and 6-fold higher than from the short-chain fatty acids. This high selectivity demonstrates that the electrical signal is primarily generated through the specific, designed metabolic pathway initiated by inulin degradation, and is not significantly influenced by the presence of other common metabolites.

4.4. Long-term Stability and Dynamic Monitoring

For practical applications in continuous health monitoring, long-term stability is crucial. We operated the gut-on-a-chip continuously for 72 hours while perfusing it with a medium containing a constant concentration of 5 mM inulin. The device maintained a stable current output of approximately 850 mA·m^{-2} over the entire period, with only a minor decay of less than 5% (Figure. 7).This stability is attributed to the sustained coexistence of all consortium members, as verified by 16S rRNA gene sequencing over the monitoring period.

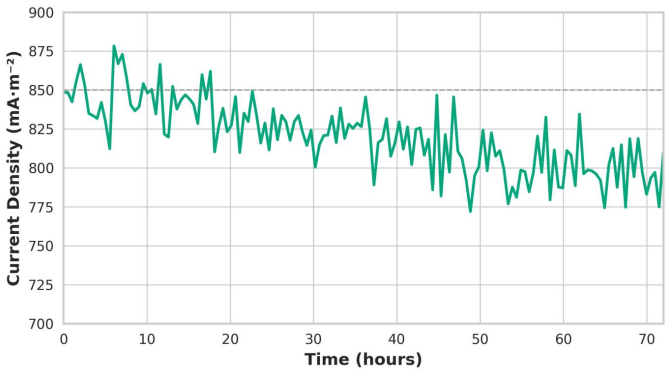

Figure 7. Long-term stability of the biosensor.

The device shows a stable current output over 72 hours of continuous operation. This demonstrates the excellent stability and robustness of the encapsulated microbial consortium and the overall system design, making it suitable for prolonged, continuous in-situ monitoring.

5. Discussion

In this study, we successfully translated the ecological principles from a bionic ocean-battery to the human gut environment, creating a self-powered, miniaturized bionic gut-on-a-chip for real-time metabolite monitoring. Our results demonstrate that by mimicking the metabolic stratification of a natural ecosystem, we can construct a robust and sensitive biosensor. The discussion below interprets these findings, contextualizes them within the broader field, and considers the implications from an interdisciplinary design perspective.

5.1. Performance and Innovation of the Bionic Gut-on-a-Chip

The superior performance of the full four-species consortium (Figure. 3) validates our core hypothesis: a structured microbial ecosystem can perform complex metabolic conversions more efficiently than isolated components. Compared with single-enzyme or single-strain systems, the ecosystem-level design enables adaptive metabolic balancing under fluctuating gut-like conditions. The synergy between the primary degrader (B. thetaiotaomicron), the fermenter (L. plantarum), and the exoelectrogen (S. oneidensis) created a highly efficient

metabolic cascade. This ecosystem-based approach represents a significant departure from traditional biosensors that typically rely on single enzymes or engineered microbes. While enzyme-based sensors offer high specificity, they often suffer from instability in complex biological fluids. Our living, encapsulated consortium, however, demonstrated excellent stability over 72 hours (Figure. 7), suggesting a more robust solution for continuous monitoring. This stability arises from the ability of the synthetic consortium to maintain metabolic homeostasis, whereas enzyme-based systems are susceptible to irreversible activity loss in the intestinal environment.

The maximum power density of 1.2 $W \cdot m^{-2}$ (Figure. 4) is a noteworthy achievement. While the primary goal was sensing, not power generation, this output is comparable to or exceeds that of many previously reported microbial fuel cells of similar scale and is well within the range required to power modern low-power microelectronics and wireless transmitters [12]. This confirms the feasibility of a truly self-powered, battery-free ingestible device based on our design. The sensor's high selectivity for inulin over other common metabolites (Figure. 6) is a direct result of our specific metabolic pathway design, showcasing the power of synthetic biology to program specific functions into a microbial community.

5.2. Comparison with Existing Gut Monitoring Technologies

In contrast to enzyme-based biofuel cells that prioritize rapid response at the expense of stability, our system achieves extended operation by leveraging adaptive microbial metabolism, while maintaining comparable power density. Compared to non-invasive methods like stool analysis, our system provides real-time data, capturing the dynamic metabolic fluctuations that are missed by retrospective assays. Compared to engineered probiotics that rely on optical or colorimetric reporters [15, 16], our system produces a direct electrical signal. This obviates the need for external imaging equipment (like ultrasound) or fecal sample collection, simplifying the data acquisition process and enabling truly continuous, autonomous monitoring. The concept is most analogous to the self-powered ingestible sensor developed by De la Paz et al. [12], but our work advances the concept by replacing a single-enzyme BFC with a more robust and functionally complex synthetic microbial ecosystem, expanding the range of detectable analytes from simple sugars to complex polysaccharides.

5.3. Contributions from a Design-Driven Perspective

This research highlights the value of a design-driven, interdisciplinary approach that integrates systems thinking, materials design, and user experience considerations.

Systems Design: The project's success stems from viewing the problem through an ecological lens. Instead of focusing on a single molecular interaction, we designed a complete, albeit simplified, ecosystem. This systems-level design, translated from the marine environment, proved to be a powerful strategy for creating a functional and robust biological device.

Material and Interface Design: The choice of a conductive hydrogel (GelMA-PEDOT:PSS) was critical. It served not just as a passive scaffold but as an active component of the system—an artificial mucus layer that provided a biocompatible, anoxic habitat for the microbes and an efficient anode for electron transfer. By matching the mechanical compliance of native intestinal mucus, the hydrogel minimizes interfacial stress and biofouling, contributing to long-term signal stability. This seamless integration of the biological components with the electronic components at the material level was key to the device's performance.

User Experience and Application Design: While this study focused on the core technology, we also considered the end-user application (Figure. 8).

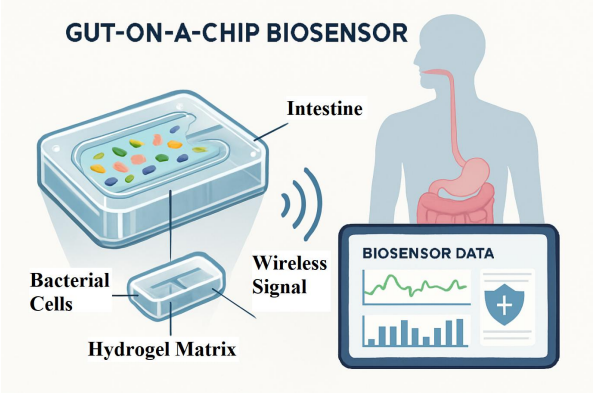

Figure 8. Conceptual illustration of the bionic gut-on-a-chip application scenario.

The device can be deployed in the intestine to monitor metabolite levels in real-time, with data wirelessly transmitted to a monitoring interface for clinical decision-making. The direct electrical output is inherently digital-friendly, lending itself to integration with a simple user interface on a smartphone or wearable device. This could provide patients and clinicians with intuitive, actionable insights into gut health, enabling personalized dietary adjustments or early detection of disease flare-ups. This user-centered perspective guided the design towards a solution that is not only technically sound but also practically viable.

5.4. Clinical Translation and User-Centered Design Considerations

The translation of our bionic gut-on-a-chip from a laboratory prototype to a clinically viable device requires careful consideration of multiple factors spanning engineering, regulatory, and user experience domains. From a clinical perspective, the device must meet stringent safety standards for ingestible medical devices. The materials used—PDMS, GelMA, and PEDOT:PSS—have all been previously demonstrated to be biocompatible in various biomedical applications [19, 21, 22], but comprehensive biocompatibility testing according to ISO 10993 standards will be essential before human trials.

The user experience design is equally critical for successful adoption. We envision a system where the bionic gut-on-a-chip communicates wirelessly with an external receiver, which could be integrated into a wearable device or smartphone application. The user interface should present the biosensor data in an intuitive, actionable format. For instance, instead of displaying raw current density values, the interface could translate the electrical signal into a "gut health score" or provide personalized dietary recommendations based on the detected metabolite levels. This approach aligns with the principles of patient-centered design, where complex biomedical data is transformed into meaningful insights that empower individuals to make informed health decisions [23, 24].

Furthermore, the device design must consider the entire user journey. For an ingestible device, this includes ease of

swallowing, comfort during transit, and safe excretion. The miniaturized dimensions of our current prototype (15 mm × 10 mm × 3 mm) are comparable to commercially available vitamin capsules, suggesting good swallowability. However, further human factors studies are needed to optimize the form factor. The wireless data transmission strategy must also be robust, accounting for signal attenuation through tissue and the dynamic positioning of the device as it moves through the GI tract.

From a systems integration perspective, the bionic gut-on-a-chip represents a node in a larger digital health ecosystem. The data generated could be integrated with electronic health records (EHRs), enabling longitudinal tracking of gut health and facilitating early intervention by healthcare providers. Machine learning algorithms could be applied to the time-series data to identify patterns predictive of disease flare-ups, such as in IBD patients, or to optimize personalized nutrition plans for individuals with metabolic disorders [24, 25]. This integration of the biosensor into a comprehensive health monitoring platform exemplifies the convergence of biotechnology, data science, and user experience design—a hallmark of modern biomedical innovation.

5.5. Limitations and Future Directions

Despite the promising results, this study has several limitations. First, the current validation is limited to an in-vitro gut-on-a-chip model, which cannot fully recapitulate the complexity of in-vivo intestinal environments. The experiments were conducted in a highly controlled in-vitro gut-on-a-chip environment. The human gut is orders of magnitude more complex, with dynamic fluid flow, a diverse native microbiome, and constant interaction with the host immune system. The long-term biocompatibility of the device and the stability of the synthetic consortium in the face of competition from native gut microbes must be rigorously investigated.

Future work will proceed along several parallel tracks, each addressing a critical aspect of device development and validation:

Enhanced Biological Validation: The bionic gut-on-a-chip will be tested in co-culture with human intestinal epithelial cells (e.g., Caco-2, HT-29) to assess its impact on host cell viability, barrier function, and immune responses. This will provide crucial data on the biocompatibility and potential immunogenicity of the device. Additionally, experiments incorporating native human gut microbiome samples will be conducted to evaluate how the synthetic consortium interacts with the complex, diverse microbial community present in vivo.

Expanded Sensing Capabilities: The synthetic consortium will be expanded to create a multi-analyte sensing platform. Future work will expand the microbial consortium to target inflammatory cytokines (e.g., TNF-α, IL-6) and colorectal cancer–associated metabolites such as hydrogen sulfide. This modular design approach allows for customization based on specific clinical applications.

Miniaturization and Wireless Integration: The chip design will be further miniaturized and integrated with a low-power wireless transmitter and antenna to create a fully functional, untethered ingestible capsule. Recent advances in ultra-low-power electronics and biocompatible antennas make this goal increasingly feasible [10, 23]. The wireless communication system must be optimized for reliable data transmission through tissue while minimizing power consumption to extend operational lifetime.

In-Vivo Validation: Rigorous in-vivo studies in large animal models, such as pigs, which have GI tracts anatomically and physiologically similar to humans, will be essential to validate the safety, efficacy, and performance of the device in a living system. These studies will assess transit time, positional stability, data quality, and potential adverse effects. Successful completion of these studies will pave the way for first-in-human clinical trials.

Regulatory and Commercialization Pathways: Parallel to technical development, a comprehensive regulatory strategy must be developed in consultation with agencies such as the FDA or EMA. The device will likely be classified as a combination product (device + biological component), requiring careful navigation of regulatory frameworks. Simultaneously, a commercialization strategy should be formulated, considering manufacturing scalability, cost-effectiveness, and market positioning within the digital health landscape.

6. Conclusion

In conclusion, we present a miniaturized self-powered bionic gut-on-a-chip that integrates a synthetic microbial consortium with a conductive hydrogel to enable real-time in-situ intestinal metabolite monitoring. By engineering a synthetic four-species microbial community within a biocompatible conductive hydrogel, we created a self-powered biosensor that can selectively detect complex carbohydrates and convert this metabolic information directly into a stable electrical signal. The platform achieves three key technical advances: self-powered operation without external energy input, selective detection of complex carbohydrates inaccessible to single-enzyme systems, and stable signal output over 72 h under gut-mimicking conditions.

This work represents a convergence of multiple disciplines—synthetic biology, materials science, micro-engineering, and user-centered design—to address a critical unmet need in healthcare: real-time, non-invasive monitoring of gut health. The bionic design philosophy, inspired by natural microbial ecosystems, proved to be a powerful framework for creating functional biological devices. By translating the principles learned from a marine microbial ecosystem to the human gut environment, we demonstrated the versatility and generalizability of this approach.

The implications of this work extend beyond the specific application of gut health monitoring. The design principles established here—ecosystem-mimicking microbial consortia, conductive hydrogel scaffolds, and self-powered bioelectrochemical sensing—provide a flexible and powerful platform that can be adapted to other biosensing challenges. For instance, similar approaches could be applied to monitor soil health in agriculture, detect contaminants in environmental samples, or create living sensors for industrial bioprocessing. The modular nature of the synthetic consortium allows for straightforward customization by swapping or adding microbial strains with different metabolic capabilities.

This platform provides a feasible technological basis for continuous gut metabolite monitoring, which could support earlier clinical decision-making in gut-related diseases. For patients with inflammatory bowel disease, the device could provide early warning of impending flare-ups, enabling preemptive therapeutic interventions. For individuals interested in optimizing their diet and gut health, the device could offer personalized, real-time feedback on how different foods affect their unique microbiome. In the broader context of precision medicine, the bionic gut-on-a-chip exemplifies a

new paradigm where diagnostic devices are not merely passive observers but active participants in the biological environment they monitor.

As we look to the future, the integration of such biosensors into comprehensive digital health platforms, combined with advances in artificial intelligence and data analytics, promises to usher in an era of truly personalized, proactive healthcare. The journey from laboratory prototype to clinical reality is long and challenging, but the foundational work presented here provides a solid stepping stone towards that vision. Ultimately, this research contributes to a deeper understanding of the complex symbiotic relationship between humans and their microbial inhabitants, and offers new tools to harness that relationship for improved health and well-being.

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None.

AUTHOR CONTRIBUTIONS

Chinedu Nkemdirim conceived the ecosystem-mimicking design concept and led the overall system architecture and electrochemical analysis; Tehillah Hamwinde Hambweka Mulomba designed and constructed the synthetic microbial consortium and conducted the biological experiments; Md Farhad Hossain fabricated the gut-on-a-chip platform, performed microfluidic integration and materials characterization, and contributed to data analysis and manuscript preparation.

COMPETING INTERESTS

The authors declare no competing interests.