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# AI-Based Gut-Brain Axis Digital Twins

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Abstract. More than 40% of the adult population suffers from functional gastrointestinal disorders, now considered disorders of the "gut-brain axis" (GBA) interactions, a very complex bidirectional neural, endocrine, immune, and humoral communication system modulated by the microbiota. To help discover, understand, and manage GBA disorders, the OnePlanet research center is developing digital twins focused on the GBA, combining novel sensors with artificial intelligence algorithms, providing descriptive, diagnostic, predictive or prescriptive feed-back.

Keywords. Gut-Brain Axis, Digital Twin, Artificial Intelligence, Smart sensors

#### 1. Introduction

The gut-brain axis (GBA) enables gastrointestinal homeostasis, but also has numerous effects on mood and mental health, cognitive functions, inflammation, allergy, neurological diseases, and metabolic health in general. Recent international studies show that more than 40% of the adult population suffers from functional gastrointestinal disorders [1], now considered disorders of "gut-brain" interactions. These interactions are intertwined in a complex bidirectional neural, endocrine, immune, and humoral communication system modulated by bidirectional signaling with the microbiota [2]. Although ongoing research is amassing strong evidence of the importance of these interactions, its intrinsic complexity poses a great challenge for its understanding and the development of precision health applications. A digital twin (or virtual twin) is a virtual representation of a real-world physical system or process (i.e., *physical* twin) with (near) real-time connectivity between the physical and the digital twin, and bidirectional flow of data, information and insights [3]. Digital twins of the GBA (DTGBA) could enhance the way we prevent and treat gastrointestinal disorders, allow us to influence our own behavior by providing us with an actual, continuous, and predictive status of the GBA. However, the GBA complexity poses a major challenge to the implementation of DTGBAs. The multiplicity of factors and scales in the biology of the GBA has prevented science to fully explain all involved processes mechanistically; sensors and actuators alone are not enough to implement a DTGBA. What if we could model some of these mechanisms in a data-driven fashion using artificial intelligence (AI) algorithms (e.g., deep and shallow machine learning, hybrid machine learning, Bayesian inference, mixed-effects models)? This is the question we are addressing at the OnePlanet Research Center (OnePlanet), a partnership between imec, Radboud University, Radboud University Medical Center, and Wageningen University and Research in the Netherlands.

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## 2. Methods

At OnePlanet, innovative sensors are developed to capture data on multiple biomarkers along the gastrointestinal tract (ingestible sensing and sampling sensors, smart toilet seat and urine sensors, wearables, food ingestion sensors, and Apps for human interactions). A digital health platform combines these data with lifestyle, nutrition, sleep, and stress data. These different sources of data are then combined and analyzed with various AI algorithms to derive information and new knowledge applied to early detection and disease prevention. The resulting insights are delivered in tailor-made interfaces, enabling bidirectional interactions between one's GBA and its virtual representation, allowing to keep track of the historical and real-time status of the GBA functions, recognize patterns, predict outcomes, and prescribe personalized measures to improve GBA, mental, and overall health in an interactive fashion.

## 3. Results, Discussion and Conclusions

In a DTGBA, novel sensors will provide data about the gastrointestinal tract function, microbiota, nervous system activity, and food or liquids consumed, and an App captures information about symptoms, mood, and the menstrual cycle. After the sensing interface combines these data, AI algorithms deliver descriptive analyses provided back to the physical twin (i.e., the person sensed) for monitoring. Further data processing based on AI algorithms offer diagnostic capabilities (e.g., indicating a possible flare up of inflammatory bowel syndrome), predictive capabilities (e.g., how symptoms will evolve if consuming certain food), and prescriptive capabilities (e.g., providing advice to manage symptoms) as actuating feed-back to the physical twin.

The digital twin platform applied to the GBA offers promising precision health abilities based on novel sensing and AI-based data analysis in a model allowing for (near) real-time feedback to help people prevent, detect, monitor, understand, and manage functional gastrointestinal disorders. This effort is limited to a selection of functions and components of the GBA, with a vision to progressively expand its coverage and capabilities. As powerful technology applied to human health, with tremendous potential but also concerns about possible unintended or unanticipated effects, research ethics and privacy protection are central in our work. In addition to performing trials assessed by research ethics committees, we strive for safe, effective, just, unbiased, and patientcentred AI applications, a complex issue we assess and address using principles for trustworthy (i.e., lawful, ethical, and robust) "responsible AI."

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