# Gastro-intestinal Implants

Valentine Delevaux Maroun Wakim Maximilian Grobbelaar

*Abstract*—**The gastrointestinal (GI) system plays a crucial role in digestion, nutrient absorption, and maintaining overall health. However, various disorders can impair its motility and function, leading to significant discomfort and health complications. Electrical stimulation therapies have emerged as a promising approach to modulate the GI system, offering potential treatments for conditions such as gastroparesis or obesity. This report examines the effectiveness of these therapies in restoring normal motility, alleviating symptoms, and improving the quality of life for patients. We also address the challenges and future directions for optimizing these therapies, including the development of more targeted and personalized approaches. Through an understanding of the underlying neurophysiological mechanisms and technological advancements, electrical stimulation holds great promise as a non-invasive or minimally invasive treatment for gastrointestinal disorders.**

## I. Introduction

### A. The Gastrointestinal System

The gastrointestinal system, also known as the digestive system, plays a key role in processing food to extract nutrients and energy for the body [1]. In addition to this, it serves a defensive function. Since the system provides an open pathway into the body, it must protect against potentially harmful external elements. This is achieved through physical and immune barriers [2]. Lastly, the gastrointestinal system has an endocrine function, as it regulates the release of hormones that control appetite and digestion.

The gastrointestinal system is made up of several different organs presented in figure 1. The esophagus transports food from the mouth to the stomach through rhythmic contractions known as peristalsis. The stomach furthers the mechanical digestion of food and uses gastric juices, including enzymes like pepsin, to break down proteins. Additionally, the stomach serves as a temporary storage site for food and controls its release into the intestine. The intestine consists of the small intestine and the large intestine, each with distinct roles in digestion. The small intestine, which directly follows the stomach, continues the process of nutrient absorption. The large intestine, also called the colon, absorbs water and electrolytes from undigested food. Finally, the rectum and anal canal serve as the exit points of the digestive system.

### B. The Electricity Under The Gastrointestinal System

Gastrointestinal motility is regulated by electrical waves known as "slow waves." These waves generate phasic contractions by altering the membrane potential of smooth muscle cells (SMCs). Slow waves originate in the myenteric plexus, a neural network located within the muscular layer of the gastrointestinal tract that spans the entire digestive system. The

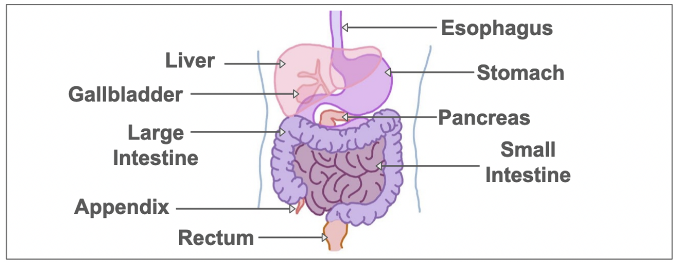


Fig. 1: **Gastrointestinal System Overview**

waves are initiated by interstitial cells of Cajal (ICCs), which serve as pacemakers for the digestive system [3]. The primary pacemaker zone is located near the greater curvature of the stomach, as seen on figure 2. The waves are then passively transmitted to SMCs via gap junctions connecting the cells. However, since SMCs cannot actively propagate these waves, the signal gradually diminishes as it spreads through the tissue.

The average physiological frequency of slow waves in the stomach is approximately 3 cycles per minute (cpm). In the pacemaker zone, located near the greater curvature of the stomach, the signal has a high amplitude and a fast velocity. The slow wave propagates effectively in the digestive direction but not in the anterograde direction, where the signal quickly diminishes in speed and amplitude. In the gastric corpus, the main storage region of the stomach, the velocity and the amplitude decrease. This is because the corpus primarily serves as a storage area and transmits the signal passively to more distal regions. Conversely, in the gastric antrum, which propels food into the intestine, the velocity increases again and the amplitude rises, reflecting the need for strong contractions in this region [4].

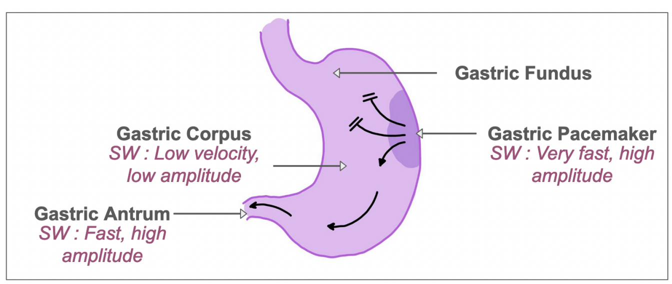


Fig. 2: **Slow Wave Propagation in the stomach**

Just as electrical dysfunction in the heart leads to various cardiac disorders, it is logical that gastrointestinal electrical dysfunction can result in localized motility disorders.

Thanks to these electrical properties, the gastrointestinal system can be studied and recorded using EEG. However, this technique captures overall activity and lacks the precision needed to distinguish between the activities of different stomach regions [1]. Since electrical activity generates corresponding magnetic fields, gastrointestinal electrical activity can also be studied using a magnetometer. However, the interpretation of this magnetic data is still under development.

### *C. The Diseases Linked To The Gastrointestinal System*

The digestive system is affected by various issues that can be classified into distinct categories like infectious conditions (such as gastroenteritis), inflammatory disorders (such as Crohn's disease), structural problems (such as hernias or obstructions), pain-related conditions (such as pancreatitis), and neoplastic diseases (such as cancers).

One notable category is functional gastrointestinal disorders (FGIDs). These are conditions that cause chronic symptoms, such as pain, bloating, diarrhea, or constipation, without any identifiable physical damage to the digestive system. FGIDs are often linked to disruptions in the gut-brain connection, abnormal gut motility, or heightened sensitivity in the digestive tract. Common examples include irritable bowel syndrome (IBS) and functional dyspepsia.

Another key category is motility disorders, which affect the movement of food through the digestive tract. One example is gastroparesis, a condition often associated with diabetes, where impaired muscle or nerve function slows the movement of food through the stomach.

### *D. The Traditional Treatments and Their Limits*

Traditional treatments for gastrointestinal disorders, including functional and motility issues, often involve a combination of medications, dietary adjustments, and stress management. For functional disorders, doctors may prescribe laxatives, antispasmodics, or antidepressants to alleviate symptoms such as pain or constipation. In the case of motility disorders like gastroparesis, prokinetic drugs can help enhance stomach emptying, while anti-nausea medications are used to reduce discomfort.

Despite their effectiveness in managing symptoms, these treatments have significant limitations. They typically address only the symptoms rather than the underlying causes of the condition. Additionally, medications can produce side effects, and some patients may not respond to them at all.

### *E. The Necessity of Stimulation Therapies*

Functional and motility gastrointestinal disorders can be treated with stimulation therapies, as both involve issues in nerve signaling and muscle coordination. These problems often stem from imbalances in the gut-brain axis or uncoordinated contractions. Techniques like vagus nerve stimulation (VNS) and gastric electrical stimulation (GES) help restore brain-gut communication, regulate motility, and ease pain by modulating nerve activity. By targeting the root causes, stimulation therapies offer a promising option for cases resistant to traditional treatments.

## II. The Stimulation Systems

Gastric electrical stimulation (GES) aims to apply external impulses to the gastrointestinal system [1]. There are several strategies, including low-frequency GES, high-frequency GES, and neural GES.

Low-frequency GES, also known as ”pacing” or ”long pulse stimulation,” seeks to replicate normal gastrointestinal activity by synchronizing slow waves in the proper direction (aboral) and improving motility in conditions like gastroparesis [8]. The pulse duration ranges from 10 to 600 ms, matching the smooth muscle cells' long time constant of 100 ms, allowing it to influence slow wave activity. When the frequency is slightly higher than the physiological slow wave, it can pace the system to the stimulation frequency [9]. Conversely, using a higher frequency (more than 40% above the physiological slow wave) can induce dysrhythmia, reducing motility and gastric emptying, which may help treat obesity [7] [8].

High-frequency GES ( 14 Hz), also called ”short pulse stimulation,” is much higher than the physiological slow wave frequency. This stimulation primarily targets the enteric nervous system rather than directly influencing the gut, alleviating symptoms like nausea or vomiting [9].

Finally, neural GES targets nerves such as the vagus nerve, sacral nerve, or spinal cord, using short pulses to match the fast response of neurons, which do not respond to long pulses [9].

### *A. Different Methods of Implantation*

Endoscopic and percutaneous stimulation are two implantation approaches in gastric electrical stimulation (GES) [18]. Endoscopic stimulation has the benefit of being minimally invasive, as it has the ability to utilize a standard endoscope within a gastrointestinal (GI) lab. Endoscopic stimulation allows for fast assessment and uses already available supplies [18]. However, it does require sedation, which can be of concern for people, and could potentially pose a risk of wire dislodgement. Percutaneous stimulation allows for extended evaluation periods due to the secure placement in the abdominal wall. It removes the factor of nasal wires and allows for the placement of multiple electrodes, which enhances the capabilities for recording. However, it is limited in that it is more invasive, and involves a more complex procedure that could disrupt gastro-jejunal extensions, and in addition has a risk of gastric perforation during lead placement [18].

Percutaneous stimulation will offer benefits such as extended use, secure placement, and recording capabilities [18]. However, it has increased invasiveness when compared to endoscopic methods, such as an increased risk of perforation. Endoscopic stimulation may provide a less invasive approach for initial assessment, however, a percutaneous method will be better suited for extended evaluations [18]. The choice between the techniques will depend on patient factors and specific clinical objectives set out by the physicians.

### B. The Electrical Systems Underneath

The electrical circuit of gastrointestinal implants like any implant generally is composed of 3 parts: the stimulating/ recording circuit, the power receiver and power management circuit, and lastly the controller circuit that is responsible of controlling the different parameters of stimulation and recording.( [10], [5])
The very first goal of those implants was intended to understand the biological signals that control the digestive system. So many of the first implants were only focused on recording rather than stimulation. This paper [11] has also proposed a multichannel system to monitor the propagation across the membrane. The recording circuit used was an instrumental amplifier followed by multiple stages of filters that are fed into the ADC of microcontroller and stored into memory.
As the signals became established, some papers ( [10], [5]) have implemented different stimulation techniques to understand the means of creating a response. The paper [5] has demonstrated that such systems require a lot of versatility depending on the location of stimulation with range of pulse widths varying from 3ms down to 0.3ms.
Furthermore the only means of powering the devices is using wireless charging. The human motion could affect the location of the implant, and so to solve that a paper [5] has proposed using NFC with an amplifier to transmit the power. Using NFC for wireless charging has demonstrated to be able to provide constant power with more spatial freedom from normal inductive coupling coils by using a closed loop feedback system for power compensation.

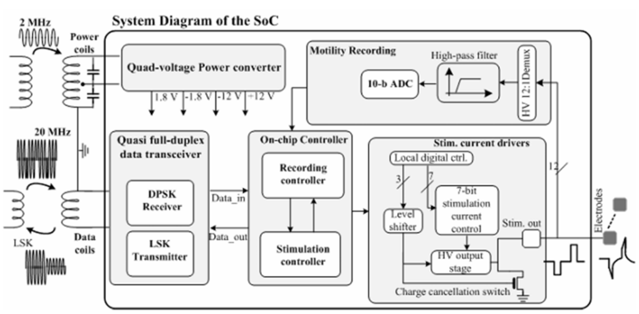


Fig. 3: Block diagram of the system proposed by [5]

Lastly, current research is all working on means to miniaturize the electronics as most designs were bulky [5]. A miniaturized design proposed [5] had an electrode array with an area of 4.3 cm by 8mm. This paper used a regular inductive coil one for charging, and one for data as the implant was fixed in place in vivo without any movement using a 2MHz, and 20MHz frequency respectively. It is important to take the necessary precautions when designing such system to the FCC limit of SAR which represents the limit of absorbed radiation. This paper still believes for the need to find the optimal stimulation parameters that is dependent on the region.

## III. Applications of Gastro-intestinal Implants

### A. Gastroparesis

Gastroparesis is a gastric motility disorder, often caused by dysfunction of stomach muscles or poor vagus nerve connection. In this condition, the slow waves may become faster, slower, or irregular. Treatment involves gastric stimulation to normalize the slow waves using electrodes on the stomach. Two types of stimulation are used: long pulse stimulation (milliseconds, physiological frequency) to reduce gastric dysrhythmias, and short pulse stimulation (microseconds, high frequency) to alleviate nausea, which may be mediated by the vagus nerve [7].

### B. Obesity and Diabetes

Obesity prevalence is increasing and is often linked to other conditions, such as diabetes. Current treatments, including lifestyle changes and medications, frequently fail to provide long-term weight loss. Surgical interventions are effective but come with risks of morbidity and mortality. Electrical pacing of the gastrointestinal tract is a safe, minimally invasive, and effective alternative. It also allows for combining different treatments. The goal of this therapy is to slow gastric emptying, which delays food passage from the stomach to the intestine, leading to an enlarged stomach that reduces hunger, lowers hunger hormone release, and increases satiety hormone release. Two types of stimulation are required, with only high-amplitude stimulations (10V) being effective; those under 5V have no impact.

The Transcend® stimulator is implanted laparoscopically near the lesser gastric curvature, with the procedure taking less than an hour. The stimulator is activated 30 days after surgery. The first type of stimulation uses short pulses and high frequency to target the vagus nerve. This alters the afferent vagus nerve transmissions, reducing hunger and food intake, while inhibiting efferent vagus nerve transmissions, which affects hormone release and reduces gastric tone, thus slowing gastric emptying.

The second type uses long pulses with low frequency. This stimulates gastric functions directly, in a retrograde manner, interfering with the natural slow waves to inhibit gastric emptying [7].

## IV. Available Technology

A summary of commercially available devices that have show efficacy in treatment of obesity and gastroparesis can be seen in Table. I.

## V. Current limitations and future innovations

The current limitations of gastro intestinal implants are bounded by the physiological structure and location [5]. This is because when an action potential propagates on the small intestine, it must have one complete path. Meaning that if more than one site was damaged then we need to place multiple stimulators across the whole intestine increasing the invasiveness of the procedure and the complexity of the design.

| Device Name | Subject Group | Developer | Description of the Device | Stage of Development |
|---|---|---|---|---|
| Enterra Therapy System [12] | 32 patients with idiopathic gastroparesis, unresponsive or intolerant to conventional prokinetic and antiemetic medications. | Medtronic Inc. | The system employs high-frequency, low-energy electrical stimulation to the stomach with 5 mA current, 14 Hz frequency, and a pulse width of 330 microseconds. It consists of two intramuscular leads and a neurostimulator device. | Enterra has had Humanitarian Device Exemption (HDE) since March 2000. Enterra is in an advanced stage of development, having already received FDA approval under the HDE program. |
| Transcend® IGS [13] | 20 morbidly obese patients, consisting of 12 females and 8 males, with a mean age of 40.3 years. The mean Body Mass Index (BMI) of the participants was 40.9 kg/m², with a range from 33.9 to 48.2 kg/m². | Transneuronix Inc. | It consists of a stimulation lead implanted in the gastric wall, which is then connected to a subcutaneous IPG. Electrical stimulation to the stomach at with 10 mA amplitude, with a 208 microseconds pulse width, and a frequency of 40 Hz. | The device was validated in a non-randomized clinical trial known as the Laparoscopic Obesity Stimulation Survey (LOSS), and was effective in inducing weight loss when compared to other non-invasive devices. |
| VBLOC [14] | 31 obese patients with a Body Mass Index (BMI) ranging from 35 to 50 kg/m². | EnteroMedics Inc. | VBLOC aims to block vagal nerve impulses with electrodes implanted on vagal trunks, connected to a subcutaneous IPG. It delivers 5000 Hz and an amplitude of 6 mA, alternating between 5 minutes on and 5 minutes off for 12 hours daily. | Underwent clinical trial. An open-label, prospective, baseline-controlled trial was conducted at three centers to assess the feasibility, safety, and preliminary efficacy of the device. |
| NCP VNS Device [15] | Eight adult obese Göttingen minipigs, divided into two groups: one receiving active VNS and the other receiving sham treatment. | Cyberonics, Inc. | The VNS device targets vagus nerves with electrodes connected to stimulators delivering pulses of 2 mA, 30 Hz, with a 500-microsecond pulse width. The stimulation is applied in a pattern of 30 seconds on and 5 minutes off. | The device from Cyberonics was tested at a preclinical trial stage, testing the feasibility in an animal model before application in humans. |
| DIAMOND® GES [16] | 61 patients with type 2 diabetes who were resistant to oral antidiabetic medications, with hemoglobin A1c (HbA1c) levels between 7% and 10.5%. | MetaCure Inc. (operations ceased in 2019). | DIAMOND® GES uses bipolar electrodes to deliver non-excitatory pulses to enhance intestinal contractility. | In a clinical evaluation; it showed positive results for glycemic control and weight reduction. |
| Abiliti® [17] | 160 patients with obesity, a mean age of 39 years, and a mean Body Mass Index (BMI) of 43 kg/m². | IntraPace, Inc. | The device delivers electrical stimulation in response to food intake, using an IPG laparoscopically implanted. | Abiliti® is in clinical evaluation. This study was conducted over 12 months and was to compare the efficacy of CLGES versus LAGB. |

TABLE I: Commercially available devices that have been used towards the treatment of obesity and gastroparesis.

Additionally, current devices have been claimed to be bulky and many current research is revolving around the miniaturization of the technology. Ingestible devices have recently emerged as a promising future prospect in minimally invasive gastrointestinal stimulation.

The recent publication on the ingestible, battery-free, and tissue-adhering robotic interface (IngRI) has demonstrated a significant advancement in addressing certain challenges such as poor electrode-tissue contact, navigation into the gastrointestinal sysyem, retention, and power supply [19]. The IngRI uses near-field inductive coupling to deliver electrostimulation, which demonstrating the potential it has in regulating appetite and treating endocrine conditions, which it does by modulating plasma ghrelin levels in a swine model [19].

Furthermore, the Vibrating Ingestible BioElectronic Stimulator (VIBES) pill is a promising approach to controlling obesity by causing the activation of gastric stretch receptors, in order to elicit satiety signals. VIBES effectively reduces the desire for food intake, and slows weight gain in animal models through the induction of a hormonal response similar to that of a fed state [20].

IngRI and VIBES highlight the move from traditional treatment strategies, towards minimising invasiveness, which serves to prioritise the safety of patients.

## VI. Conclusion

Gastric electrical stimulation is a promising treatment for gastrointestinal problems like gastroparesis, obesity, and diabetes. By using different types of stimulation, we can help restore stomach movement, regulate slow waves, and reduce symptoms like nausea and vomiting.

Improvements in implantation methods have made GES devices more accessible and flexible, allowing both short-term and long-term use. However, the choice of method should depend on

balancing invasiveness and effectiveness based on the patient's needs.

From an engineering point of view, GES systems require complex circuits for stimulation, recording, power management, and control. New wireless charging methods offer more freedom in implant placement. Despite these advancements, challenges remain in finding the best stimulation settings, improving device compatibility with the body, and making devices smaller and more practical for patients.

In the future, ongoing improvements in GES technology, along with a deeper understanding of gastrointestinal physiology and electrical stimulation, could lead to more effective and less invasive treatments for various gastrointestinal conditions. Integrating GES into personalized treatment plans could improve outcomes for many patients.

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