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Part IV Research Project

Final Report

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Pacemakers for Gastrointestinal Diseases

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Declaration of Originality

This report is my own unaided work and was not copied from nor written in collaboration with any other person.

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Abstract

The exploration and innovative implementation of a real-time algorithm for the detection of gastric Interstitial Cells of Cajal (ICC) activations bring forth a new paradigm in the field of biomedical signal processing, especially pertinent to gastroelectrical disturbances. This research delves into the intricate process of identifying and analysing gastric slow wave events amidst the challenge of a noisy environment, utilizing an embedded system to ensure accurate and timely detection of ICC activations in gastric myoelectrical activity. Developed based on the methodologies proposed by Marr and Vanpraseuth, the algorithm meticulously progresses through stages of adept filtering and strategic removal of artificial pacing artifacts and employs a Falling Edge Variable Threshold (FEVT) method for precise ICC activation detection. Implemented on the DE1-SoC board, and utilizing C/C++ for software development, the algorithm not only manages to proficiently discern activations within signals containing pacing artifacts but also demonstrates noteworthy reliability and specificity across varying datasets with different Signal-to-Noise Ratios (SNR). While the algorithm manifests commendable Positive Predictive Values (PPV), Sensitivity, and Accuracy across several datasets, certain challenges such as suboptimal artifact removal and cubic spline-induced false positives highlight avenues for further refinement and adaptation. The inherent delay, necessitated by the FEVT method, introduces a variable yet workable in real-time applications such as pacemaker synchronization. In the realm of gastric signal processing, particularly within the context of conditions like gastroparesis, this pioneering work stands poised to offer enhanced treatment modality options, bridging technological advancements with practical medical applications. The successful deployment of this algorithm within an embedded platform underscores its potential, warranting further exploration and optimization in mitigating limitations and expanding its applicability to a broader spectrum of biomedical signal analysis.

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1. Introduction

Gastrointestinal (GI) motility, crucially governed by the Interstitial Cells of Cajal (ICC)—pacemaker cells orchestrating bio-electrical "slow waves"—is fundamental to digestion and waste elimination[7, 8]. These slow waves, typically around three cycles per minute (CPM), are vital for digestive system function and are implicated in various GI motility disorders like gastroparesis and chronic unexplained nausea[1-4]. Gastroparesis, in particular, results from slowed gastric waves, causing symptoms like nausea and vomiting, thus diminishing life quality[2, 5]. Gastric Electrical Stimulation (GES) has been shown to improve symptoms and the overall well-being of gastroparesis patients[7,8]. Currently, due to a restricted understanding of gastric versus cardiac electrophysiology, no closed-loop FDA-approved pacemakers for the gut are available. Existing open-loop pacing of the GI tract, aiming to modulate dysrhythmic patterns, is seen as suboptimal[6].

While research endeavours, such as those executed by Wang et al., have begun paving the pathway towards addressing these GI motility disorders through GES, the journey towards an optimised, applicable solution is still dotted with challenges [5,6,11,12]. The pacemaker developed by Wan et al. failed to perform as expected in animal experimentation. The main reason for this was the inefficiency of it to work in a noisy environment. Thus, there is no model running on an embedded platform that addresses this issue.

With the goal of exploring beyond the extant limitations and innovating within the expansive domain of GI electrophysiology and GES, this project aspires to develop a robust, closed-loop GES system runnable on an embedded platform, which is capable of accurately sensing and modulating ICC network activity. Combining research and advanced prototype development, this work succinctly explores methodological approaches and innovative practices in gastrointestinal electrophysiology and motility disorder interventions, offering an insightful overview through critical analyses.

2. Research Intent & Literature Review

2.1 Gastrointestinal System and its Motility:

The GI System, with its vital function in food digestion and waste elimination, is maintained and regulated by an elaborate network consisting of nerves, hormones, and muscles, notably the Interstitial Cells of Cajal ICC. The GI Tract, extending from the mouth to the anus, encompasses several organs essential for digestion and nutrient absorption, playing key roles in motility as food traverses its pathway. GI motility, vital for optimal digestion, begins with smooth muscle contractions, controlled partially by bio-electrical events or slow waves, which are generated and propagated by ICC cells, while the smooth muscle cells produce phasic waves. The enteric nervous system (ENS), with intricate interactions among neural, hormonal, and mechanical factors, orchestrates smooth muscle contractions to drive food through the GI tract[13].

2.2 Gastric Electrical Stimulation

Bilgutay et al. laid the pioneering foundation in gastric-intestinal (GI) pacing, revealing the nuanced impact of electrical stimulation on gastric slow waves and symptomatology [10].

The utilisation of gastric electrical stimulation has shown promising results in ameliorating the effects of gastroparesis. Studies, notably between 1998 and 2000, have indicated that gastric pacing can significantly alleviate symptoms such as nausea and enhance gastric emptying time [8]. With an 89% improvement in symptoms among a subset of patients and associated reduced hospitalisations and ER visits, GES becomes a compelling intervention, offering reductions in symptomatology, enhanced gastric emptying, and improved patient quality of life compared to other treatments [22,23]. This GES is done in the gut by a gastric pacemaker. One such GES device created by Alighaleh et al. [18] achieved entrainment in all animals during trials, effectively modulating slow waves in pigs wirelessly. While promising, noted limitations such as the absence of consideration for current slow-wave patterns spotlighted the potential of closed-loop systems that should be FDA-approved [18,24]. Though simulated models have been developed, they often fall short in testing due to utilising ideal signals and not accounting for real-world variations and noise in gastric slow wave signals. Efforts to leverage artificial pacemakers have illuminated promising but temporally limited results , prompting exploration into sustainable, implantable GES devices[25].

2.3Mechanics Of Gastric Pacemaker by Wang et al:

Wang et al. crafted a closed-loop GES system[5,6,11,12] aimed at regulating gastric slow waves, with a pivotal element being the detection algorithm within its feedback loop, which oversees their periodicity, elaborated further in [12]. While simulations yielded positive results, experimental trials encountered challenges. The team suggested that the GES address bradygastria, arising from anomalous initiation and conduction block, by identifying and managing the disruptive extracellular potentials, subsequently pacing in a closed-loop format. The GES algorithm introduces a mechanism to filter these extracellular potentials and identifies slow wave activation employing a real-time slope and threshold technique. It leverages high-fidelity 2D ICC network models as noise generators to affirm the proposed GES algorithm's effectiveness. The strategy also involves using multiple leads to detect any unforeseen decelerations, and this pacing approach also administers modulated dysrhythmia via pacemakers through various leads to manage dysrhythmia.

The single-channel GES algorithm[21] is conceived to perceive and modulate an irregular ICC network, utilising extracellular potential amplitude and timing measurements, akin to the modus operandi of cardiac pacemakers. Under typical conditions, conduction transpires when an ICC network is captivated by its most rapid cell, referred to as the Lowest Rate Interval (LRI). To pinpoint abnormalities, the GES algorithm scrutinises extracellular potential levels for slow wave activations, equating them to LRI and identifying deviations by contrasting activation times elapsed since the previous one to this interval. If no activation is perceived within this timeframe, an external pace is applied to amend the abnormal conduction. GES functions by calculating its base time, denoting when the ICC near the probe first activates. The discrepancy between this base time and the current time facilitates the identification of abnormal slow-wave activation patterns. If slow wave activations recur within Gastric Repolarization Interval (GRI) or LRI intervals, it's deemed normal, resetting the base time; otherwise, if no activation transpires after the LRI period, an external pace is applied, perpetually correcting abnormal conduction within GES.

Addressing a slow wave conduction block might necessitate multi-lead pacing, requiring GES to sense and pace across several channels[5,6,11,12]. The GES pacing algorithm developed by Wang et al.[21] identifies slow wave activation and, if requisite, applies pacing to modulate the delay. Every channel has individual LRI and GRI timers and offsets for non-dominant cells are accounted for. The algorithm initiates pacing if no activation materialises within the LRI period plus the respective offset for each channel.

2.4Gastric Slow Wave Dynamics and Detection Techniques:

An in-depth exploration into gastric slow wave signal processing has laid a solid foundation for understanding and innovating gastrointestinal (GI) activity measurement methods, especially focusing on detecting dysrhythmia through specific signal properties [6]. Notwithstanding, a notable challenge persists in the form of noise, originating from various external factors such as sleep, digestion, and stress, which has historically impeded efficient signal analysis. A study by [15] critically evaluated four digital filters in gastric slow wave recordings, each offering unique advantages and drawbacks in extracting extracellular potentials.

The discernment of slow wave propagation within Interstitial Cells of Cajal (ICC) is paramount for the engineering of Gastric Electrical Stimulators (GES) as it is the prime feature being monitored

[17]. The slow waves exhibit an intrinsic frequency of approximately 3 CPM, and disorders like bradygastria and tachygastria are attributed to aberrations in these slow wave patterns [1-4,14]. While human detection of these slow wave events has proven relatively clear, the challenge lies in mechanising this detection and doing so in a real-world, non-simulated environment.

Thus, accurate detection techniques, after meticulous signal processing, are vital to delineate signal features, which are subsequently extracted and applied to an automated closed-loop model. The algorithmic criterion for ICC activation detection, especially in the system proposed by Wang et al. [12], necessitates real-time online capability, low computation cost, and minimal power consumption, to effectively function in a closed-loop with the GES device while ensuring implantability and patient convenience. Although online systems for automatic cardiac signal detection are prevalent [16], analogous systems for GI slow-wave activation detection remain scarce and warrant further exploration and development. A comparison of such algorithms is done by Marr and Vanpraseuth [28,29].

The derivative-based algorithm employed in [12], originally proposed in [17], was modified for online usage by Wang et al., serving as a pioneering solution with acceptable accuracy before [17]. Several areas for refinement were identified, including mitigating false positives on "bad channels" caused by noise, ensuring the extraction method for activation features is noise-immune, developing a mechanism to disregard artificial pacemaker-induced artefacts, and addressing potential issues of threshold lowering leading to additional false positives.

Bull et al. [16] tackled several of these issues, applying additional filtering and utilising a non-linear energy operator (NEO), among other techniques, reporting a positive predictive value of more than 90 per cent. Notwithstanding, they acknowledged challenges with false positives in instances of large gaps between activations. Notably, previous research in automatic detection primarily rooted in cardiac electrophysiology employed various methods, including wavelet transforms, and diverse machine-learning strategies [19-20]. However, applicability often hinged on the availability of extensive databases for training, which is not a present luxury in GI slow-wave research, due to the financial and labor-intensive nature of procuring such data. The utilisation of the Falling Edge Variable Threshold (FEVT) algorithm, highlighted by Du et al. [17] , Bull et al. [16], and Marr [28], provides a viable path for GI slow-wave applications, meriting its selection as the chosen method for this project, by balancing computational and power demands suitably for a closed-loop pacemaker device.

In conducting this review and developing subsequent analyses, it is pivotal to acknowledge that our insights and applications are drawn directly from a diverse array of foundational works.

2.5 Embedded Systems For Medical Devices

The development of embedded system devices for gastrointestinal pacemakers represents a significant advancement in the field of medical technology. These innovative devices harness the power of miniaturised electronics and microcontroller units to regulate and stimulate the smooth muscle contractions of the gastrointestinal tract, offering new hope for patients with debilitating motility disorders. Embedded systems, prominently exemplified by the cardiac pacemaker, have demonstrated profound impacts in the medical field. Low power consumption underscores a pivotal constraint in developing implantable devices, ensuring longevity and minimising invasive procedures for battery replacements. By seamlessly integrating with the human body and providing precise control over gastric and intestinal movement, these embedded systems have the potential to revolutionise the treatment of conditions such as gastroparesis and chronic intestinal pseudo-obstruction, improving patients' quality of life and enabling more effective management of their health.

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3. Research Methods

This project unfolds a strategic algorithm, ingeniously melding the methodology propounded in [20] with adaptations of pacing artefact removal tactics as explored in [28,29], tailoring them to the unique demands of gastric slow wave signals and for the embedded system implementation. The synthesised approach is succinctly captured in Figure 2, providing a visual summary of the implementation.

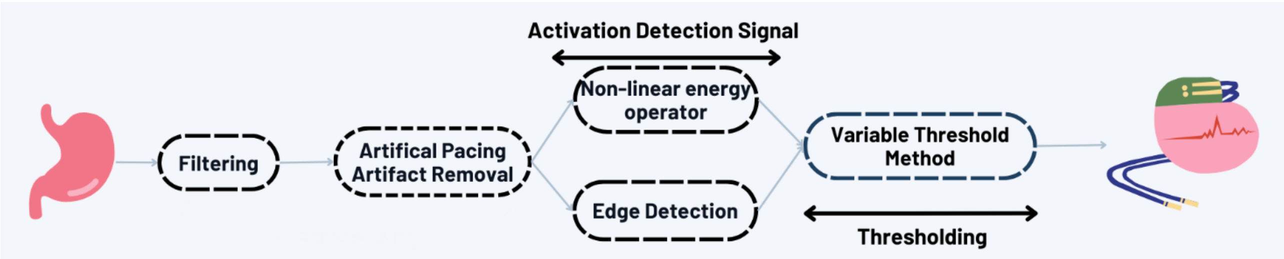

Figure 1 Novel Activation Detection Phases [28][16].

3.1.Filter

3.1.1. Low Pass Filter

High-frequency noise was mitigated using a low-pass Finite Impulse Response (FIR) filter, where the cutoff frequency was strategically established at 3Hz [5,28]. Implementation of a lowpass filter is applied to a padded data stream, invoking the renowned "filtfilt"[26] technique, often employed to alleviate phase distortion by applying a forward and reverse filtering mechanism.

3.1.2. High Pass Filter

The signal was passed through a high-pass filtering via direct convolution with pre-defined filter coefficients,finite Impulse Response (FIR) filter, set with a cutoff frequency positioned at 0.32Hz to eliminate baseline drift[28]. The coefficients used here were calculated by Marr and Vanpraseuth [28,29].The C execution of code is designed to execute high-pass filtering on an input signal of 1001 samples. It first pads the input signal to avoid border artifacts during the convolution operation, embedding it within a larger array '*padded lowpass*'. Subsequent convolution between the padded signal and filter kernel results in a high-pass-filtered signal, stored in a '*highpass signal'*. After convolution, padding produces the final filtered output, '*output signal'*.

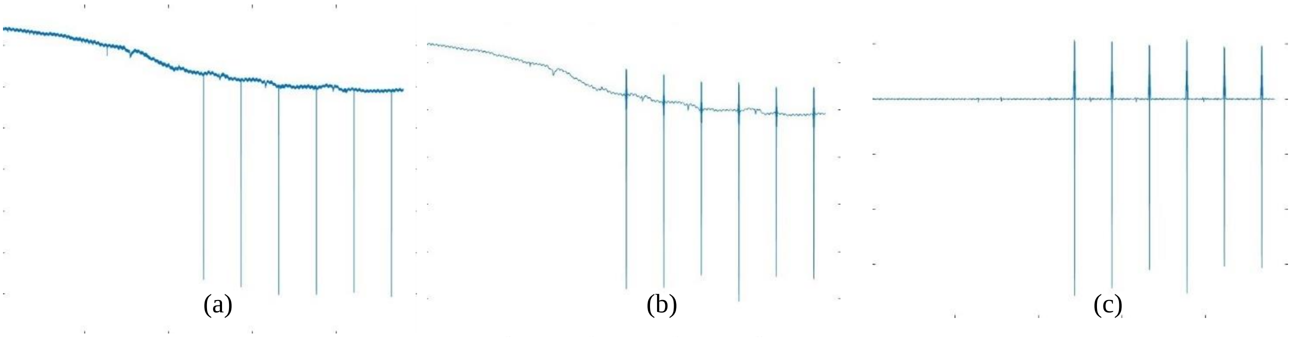

Figure 2 Signal Processing: a) Orignal Signal, b)Lowpass Filtering, c) Highpass Filtering

3.2. Pacing artifact removal

The approach to artifact removal entailed the identification and substitution of abrupt amplitude fluctuations within the signal, specifically by utilising a cubic spline. Artificial pacing artifacts, recognisable as nearly square pulses with an amplitude markedly larger than the natural signal features, were morphed into a sinc curve post-filtering. The final design of Thresholding based on amplitude[28,29], which leveraged this substantial amplitude difference for reliable artifact detection was implemented in C. The breadth of the artifacts has consistently ranged from 50-60 samples across various datasets[28]. Therefore, the signal undergoes analysis in segments, each encompassing 100 samples. We implemented a cubic spline interpolation to replace an artifact between the points '**x1'** and '**x2'**, within a given **window** of signal data of size 101 and storing the result in **output**. The logic is structured to derive cubic spline coefficients from the slopes at the segment's edges, constructing a smoothed representation over the identified artifact, while preserving the rest of the signal data [27,28].

- Initially, edge slopes and spline coefficients are computed utilising the signal values and differentials at **x1** and **x2**.
- The cubic spline polynomial is evaluated across a new array *'pol_data'*, representing points between **x1** and **x2**, generating replacement data *'replace data'* for the artifacted segment.

- The final output is constructed by stitching the original signal segments (before **x1** and after **x2**) with the interpolated *'replace data'* in between, ensuring a smoothly interpolated artifact replacement within the original *'window'* of data.

3.2.1 Artifact Detect

For artifact removal, the location identification of it is necessary which is done in artifact detection.

  - The function computes the absolute values of all entries in the input signal window '*signal_window'* (of length 101) and stores them in '*absolute_signal_window'*.
  - It iterates through '*absolute_signal_window'* to find the *max value* and its location (*index*).
  - If *max value* exceeds a provided threshold, the function returns the location of the artifact. If not, it returns '*NaN'* (Not a Number), indicating no artifact was detected.
  - The function checks for the presence of '*NaN*' values in the signal window and identifies the first non-NaN value's index.
  - The search for the maximum value (potential artifact) only begins from the first non-NaN value, preventing erroneous results due to invalid data points.

3.3.Neo Transform And Moving Average

The Non-linear Energy Operator (NEO) emphasises abrupt amplitude alterations in biomedical signals post artificial pacing artifact detect mitigation. Executed in C code via `NEO_transform`, it processes signal (`input`) to highlight rapid events through energy calculation, utilising $NEO(Vi) = V_i \; * V_i - V_{i-1} * V_{i+1}$ where (*Vi*) signifies the signal at index (i). The method squares each sample value, subtracts the product of adjacent samples, and records in `output`, thereby accentuating abrupt changes, assisting in natural activation identification in the purified biomedical signal. This methodology provides a base for additional signal analyses and understanding.The `*moving_average_1s_window*` function computes a 1-second moving average of an `input signal` length *N*, employing a sample rate to establish the window size `M`. Iterating from 0 to `N - M`, the function averages `M` subsequent values, placing the result in `*output*`. Positions from `N - M` to `N` in `output` are set to 0. This technique smoothens the NEO-transformed signal, mitigating brief fluctuations and underscoring longer-term trends.

3.4. Edge Detection

The edge detection method here has been proposed by Marr[28]. After filtering to remove unwanted noise and artifacts, the signal is subject to an edge detection operation to pinpoint regions where abrupt changes in the signal occur—these are typically indicative of events or characteristics of interest. Specifically, the signal is convolved with an edge detection kernel, which is mathematically akin to taking its first derivative, thereby creating a new signal[28,29], E_t, that emphasises abrupt gradients by presenting them as peaks. Here, notably, the negative gradients (i.e., downward spikes in the original signal) are of interest; thus ,a kernel of k=−1[1,0,−1] is employed. Then E_t and S_t (signal from neo transformed), are multiplicatively combined element-wise, yielding a detection signal D_t that embodies the instantaneous changes from both preceding signals. This resultant signal aids in detecting significant events in the original signal by spotlighting instances where both rapid amplitude changes and steep gradients occur concurrently, making it a potent tool for identifying physiological events like muscle activations in biomedical signal analysis.

The implemented edge detection code on an Embedded device processes a digital signal to identify and amplify abrupt changes, which is crucial for specific signal processing analyses. Initially, a buffer size of 1050 is defined, and arrays for detection signals and other variables are initialised. First, the input signal '*artifacts removed*' undergoes convolution with a kernel to accentuate abrupt amplitude changes, outputting results to '*convolution Result*'. Subsequently, negative values are nullified, and resultants are squared to emphasise larger signal changes. The squared convolution result is modified by another signal, '*output[idx]',* creating the '*detection Signal'*. To eliminate noise, the mean value of *'detection signal'* establishes a baseline, suppressing elements below it. This approach ensures

$$D_t = \left\{ \begin{array}{ll} E_t S_t, & \text{if } E_t S_t \geq 0 \\ 0, & \text{if } E_t S_t < 0 \end{array} \right\}$$

focused analysis on substantive signal changes while minimising interference from non-essential components.

3.5 Falling Edge Variable Threshold

The Falling Edge Variable Threshold method is used to discern activations from the detection signal, employing both online applicability via a buffer and mean absolute deviation (MAD) calculations of the signal. The MAD was substituted with a simpler mean calculation to save computational resources and time, according to certain research findings[29]. This value was multiplied by a scalar and determined to be 5.9[29]. Consequently, to mitigate issues like high threshold calculation values and missed slow wave events, testing dictated that the baseline for removal needed to be increased, revealing that multiplying the scalar 5.9 by a factor of 10 and setting this as the baseline reduced false positives and eliminated additional noise effectively[29].

In the C code implementation, an adaptive activation detection approach is implemented, whereby a dynamic threshold (computed as the mean of signal **f_t_sig** scaled by 5.9) identifies signal regions of interest, marking where the detection signal '*f_t_sig*' exceeds this threshold and appending identified locations to the '*locs*' array. The detection loop manages processing windows and laps by incrementing the indices '*i'*, *'j'*, and '*shift'*, ensuring sequential signal analysis. Concurrently, the code computes an '*activation threshold'*, detects surpassing '*detection signal'*, reallocates memory for storing these activations in an array, and enforces one activation per window with a proximity check (<500). This methodology ensures resource-efficient, real-time signal analysis by dynamically managing memory and leveraging an adaptive threshold for activation detection.

3.6 Pacing

The Gastrointestinal Electrical Stimulation (GES) algorithm identifies deviations in slow wave activations relative to the Lowest Rate Interval (LRI) and enforces external pacing when necessary. In instances where activations do not reoccur within established (GRI) or LRI intervals, indicating an abnormality, the GES triggers an external pace, ensuring the perpetuation of normalised conduction.

3.6 Developmental Tools

For the proposed GES embedded system, the DE1-SoC board is selected, leveraging its ARM processor and FPGA chip, which is programmable to implement custom logic, effectively making the board adaptable across numerous applications. Noteworthy is the DE1 board's prevalence in academic and research institutions as a tool for digital system design, backed by documentation and resources from Terasic Technologies. It stands out as a comprehensive platform for designing, testing, and validating digital systems in the medical domain, especially given the stringent requirements for reliability and precision in physiological interventions. Software development will leverage C /C++, languages revered for their efficiency, low-level hardware access, and portability in embedded systems. Moreover, their reliability and extensive developer community render them especially pertinent for crafting robust, dependable systems for medical applications where system failure can have dire consequences.

4. Assessment Techniques and Evaluated Metrics

The methodology applies a binary classification framework, wherein each signal point is categorised either as an activation (positive) or non-activation (negative). The model's performance is evaluated by utilising standard metrics derived from the confusion matrix[28]: true positive (TP), false positive (FP), true negative (TN), and false negative (FN). *Accuracy*, computed as $\frac{TP+TN}{TP+TN+FP+FN}$, gauges the overall correctness of both activation and non-activation predictions.[28]

- *Sensitivity* or the true positive rate, calculated as $\frac{TP}{TP+FN}$, assesses the model's aptitude in accurately identifying activations.[28]
- *Specificity*, derived as $\frac{TN}{TN+FP}$, evaluates the capability to correctly identify non-activations.[28]
- *Positive Predictive Value (PPV)*, calculated as $\frac{TP}{TP+FP}$, is introduced as a crucial metric, indicating the probability that a detected activation is indeed a true activation, mitigating potential pitfalls associated with FP detections in this particular application.[28]
- *Execution Time*: In real-time system computations, the Worst-Case Execution Time (WCET) represents the maximum time required for a function or program to execute, ensuring stringent adherence to time constraints. Utilising WCET as a referential execution time ensures that system operations remain within permissible temporal bounds, safeguarding against potential time-critical failures and preserving system integrity during operations. In this case, a histogram was plotted for multiple runs to find the worst execution time
- *Dataset:-* In the conducted experiments, two data sets were analysed. Data without a pacemaker, i.e. pig 37 and 41 datasets, devoid of artificial pacing artifacts[28], consisted of data from trials without a pacemaker at 30 Hz, exhibiting a higher Signal-to-Noise Ratio (SNR) and ease in distinguishing activations from noise[28].

The second set of entailed data (exp 10 and 16) from pacemaker-conducted trials, recorded at a higher frequency (512 Hz), but presented challenges like low SNR, artificial pacing artifacts, and equipment glitches.

Bad channels in both sets, characterised by indiscernible activations and noise dominance, were omitted from the evaluation. Manual marking of activations was executed for each dataset to facilitate testing, explicitly excluding artifacts and glitches in experiment 10 [28].

5. Exploratory Findings and Results

To illustrate the functionality of each phase of the algorithm, outputs are depicted in Figures 3 to 8,utilising a channel from the pig37 experiment dataset for these visualisations. These show the processing of the signal at each stage.

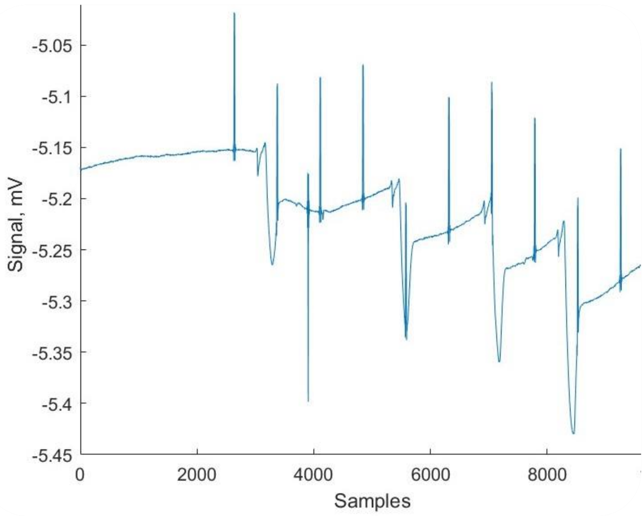

Figure 3 Low Passed Signal

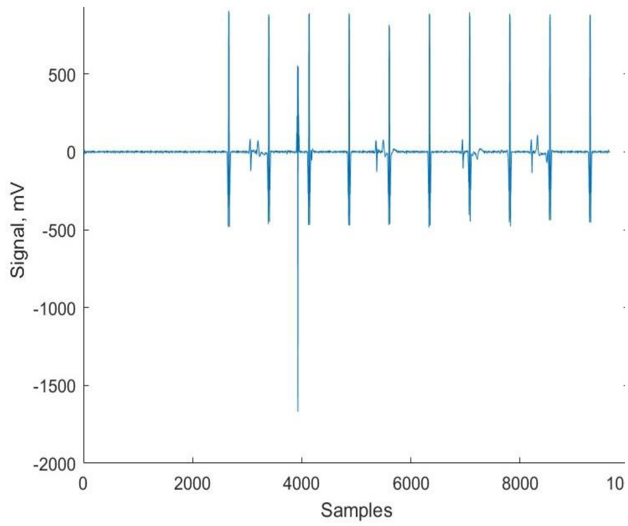

Figure 4 High Passed Signal

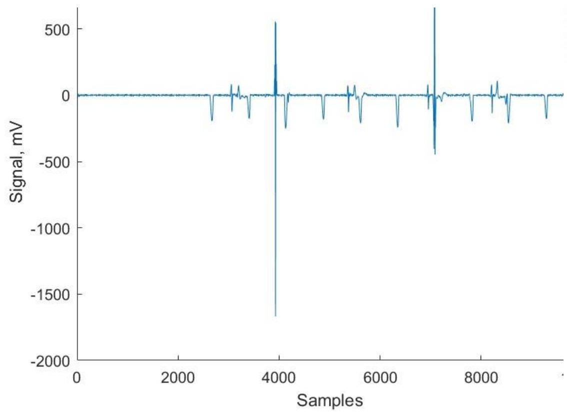

Figure 5 Artifact removed Signal

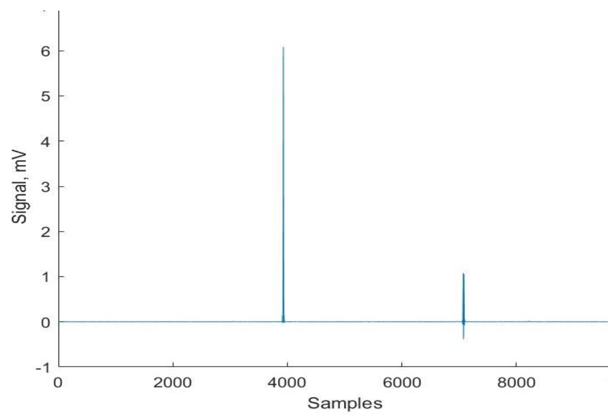

Figure 6 Neo Filtered Signal

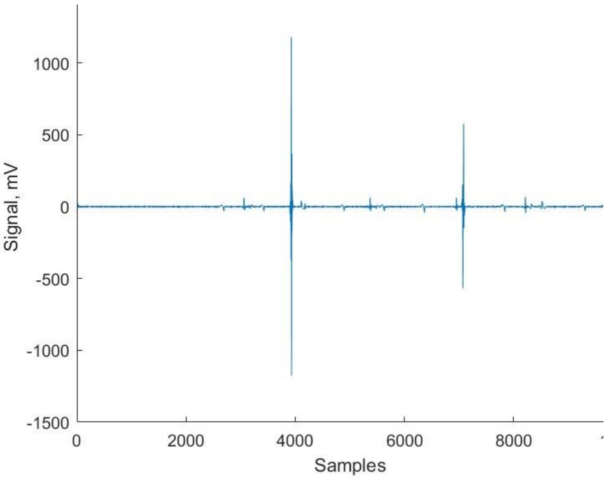

Figure 7 Edge Detection Signal

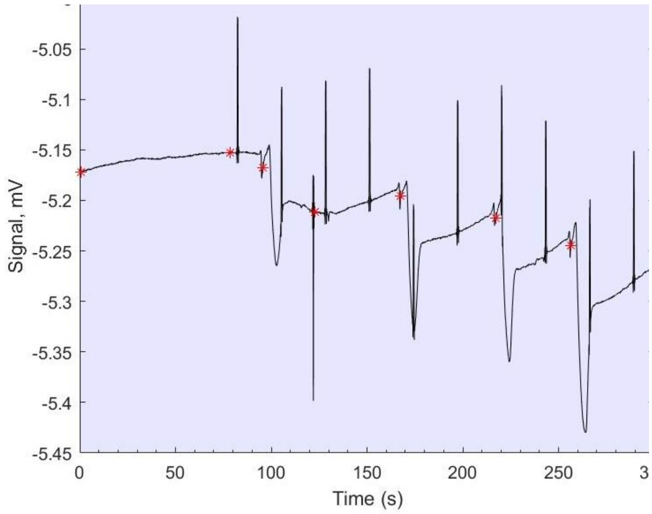

Figure 8 Signal with activation Detections

In the process of compiling the outcomes, channels that were unreadable were frequently encountered, about 38.5 per cent in without paced data and 54.4 per cent on paced data, as mentioned by Vanpraseuth [29]. These bad channels were omitted from result counting.

The project performance is evaluated in without the Pacemaker and with the Pacemaker datasets against the metrics mentioned in section 4.The performance for these datasets is tabulated in Tables 1 and 2, respectively.

Table 1Performance From Signals without Pacemaker

Experiment	TP	TN	FP	FN	Accuracy	Specificity	PPV	Sensitivity
Pig 37	154	796195	1	10	0.99998	0.99	0.939	0.993
Pig 41	596	565130	37	14	0.99	0.99	0.94	0.97
Overall	750	1361325	38	24	~99.4%	~99%	~93.9%	~98.1%

Table 2 Performance For Signal having Pacemaker

Experiment	TP	TN	FP	FN	Accuracy	Specificity	PPV	Sensitivity
Exp 16	294	786758	197	66	0.999	0.99	0.59	0.816
Exp 10	78	239873	104	24	0.99	0.99	0.44	0.765
Overall	372	1026631	301	90	~99.4%	~99	~51.4	~79.05

Timing Analysis

The algorithm, after 200 sample runs, exhibited a noteworthy processing time, with its most prolonged execution duration approximating 1.5 seconds for 1000 samples. However, it's crucial to highlight that an inherent delay is introduced due to the requisite buffering of the data, specifically, a delay of 31.25 to 33.3 seconds for downsampling at 32 HZ or 30 Hz is introduced as the algorithm necessitates 1000 samples for processing, requiring buffering of the data before execution.

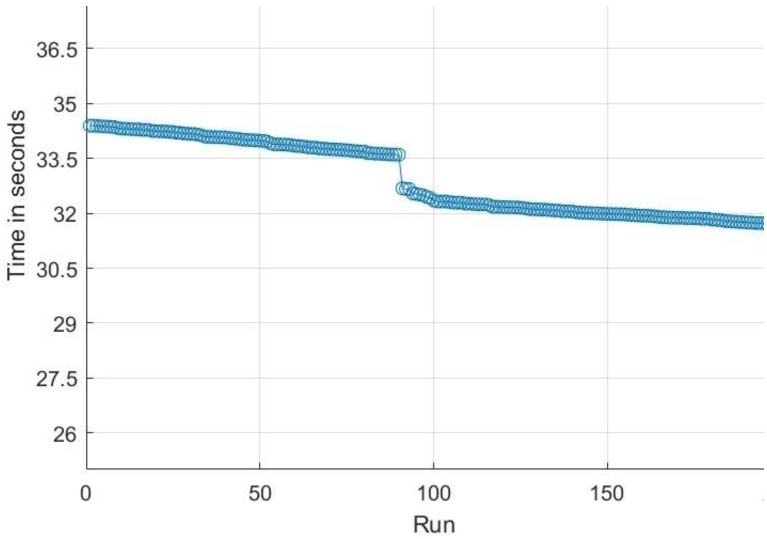

Figure 7 Runtime On Embedded Device

6. Discussion

6.1 Analytical Overview and Comparative Findings

The in-depth analysis yielded both merits and demerits in the implemented algorithm in the Embedded platform.

Mirroring the comparative findings of Bull et al. [16] and Marr [28], which illustrated a PPV of 0.92 for both and a sensitivity of 0.95 and 0.98, respectively, for the online system, our algorithm under analogous testing conditions demonstrated a PPV and sensitivity of 0.93 and 0.98 respectively for pig 37 and 41 data. The parallelism in these results underscores shared reliability in environments bearing semblance in SNR and signal characteristics.

While signal experiments on the data set mentioned before echoed the literature, confirming a high true positive hit rate and minimised false results, the algorithm's performance in experiment 10 didn't performed well. Notably, experiment 16 exhibited an appreciable positive predictive value, near 0.59, but in experiment 10, it was 0.43. These results are close to Vanpraseuth [29] except for experiment 16, which may be due to our elimination of more bad signals and channels for the result. The runtime for us was quite good, with only 1.5 seconds required to process data and a delay of 33.3 added to it. So, the worst execution time was 34.8 seconds.

5.2 Recognising Limitations

Delving deeper, one critical limitation was the artifact removal methodology, particularly regarding the removal of artificial pacing artifacts. Suboptimal removal not only inflated the FPs but also bolstered FNs, attributed to the driving up of the variable threshold by the artifact, thereby occluding activations with smaller amplitude in the detection signal.

The employment of a cubic spline to supplant the artifact unveiled a challenge[28]. The method, while utilising the y-value and derivative of endpoints to avert discontinuities, exhibited susceptibility to forming a sharp, spike-like curve in scenarios involving steep gradient endpoints. This attribute led to a large NEO signal amplitude, misconstruing splines as activations, which was also warned by Vanpraseuth in his finding[29].

In our initial endeavours to implement low-pass filtering, we employed a Butterworth filter, adhering to the literature and established a passband from 0.02Hz to 1Hz [12, 28]. Despite the theoretically sound basis, practical implementation heralded complications such as phase shifts. Thus, the Butter-style filter, characterised by its unique coefficients, was further refined through 'filt-filt' techniques to alleviate phase shifts and presented a viable solution. The potential for superior performance via better implementation of the ‘filtfilt’ technique and alternative filters, such as a more polished version or perhaps employing a Chebyshev variant, lingers as an avenue for future exploration and comparison.

It is pivotal to note that experiment 10 and 16 datasets may not epitomise signals from a well-optimized closed-loop pacemaker. The observed pacing artifacts, stemming from an obsolete algorithm, would be markedly reduced in a functioning pacemaker, which might naturally boost PPV scores by reducing FP counts.

5.3 Achieving Objectives and Overcoming Delays

The overarching goal of implementing a real-time ICC activation detection algorithm that can proficiently navigate through a noisy environment was achieved with some concessions.

A delay exceeding ~31 seconds, prompted by the necessity of numerous samples[28], introduces a variable to be considered in clinical applications such as pacemaker synchronisation despite its aptitude for real-time applications. The algorithm can change its buffer size to reduce time delay, but it has to evaluate its efficiency against the dataset.

An avenue that warrants further exploration is the improvement of the algorithm's reliability. With a respectable TP rate across tested data, the notable presence of FPs in certain channels delineates a crucial area for refinement, potentially through alternative pacing artifact removal techniques or spline calculation adjustments. Testing is not done on limited channels of a signal, and other datasets should be used for experimental testing to get more insight into the algorithm.

5.5 Evolution in Methodology and Algorithm Application

In confronting challenges like artifact removal, a departure from cubic splines to explore alternative substitutes could provide a potential remedy, adjusting for signals with diverse peak-to-peak ranges. A smoothing spline or a low-tension spline might be a viable solution to explore. Both of these approaches aim to achieve a balance between fitting the data closely and maintaining a smooth, manageable curve.

Moreover, filtering methodologies were subject to adaptation, moving from the initially intended

Butterworth filter to utilising ‘filtfilt’ technique.

This project also illuminates the necessity of exploring adaptive filters, considering the inherently dynamic nature of gastric signals, an aspect acknowledged yet still unoptimised in the field [15].

7. Conclusion

We have successfully implemented an innovative algorithm proposed by Marrr and Vanpraseuth [28,29] capable of detecting gastric ICC cell activations in real-time, particularly within noisy, slow wave signals containing pacing artifacts, which marks a noteworthy advancement in the realm of real-time gastric signal processing. This novel algorithm navigates through three pivotal stages: proficient filtering, strategic removal of artificial pacing artifacts, and a precise detection method aligning closely with the design propounded by Bull et al. [16]. Notably, the removal of detected artifacts, managed by substituting them with cubic splines, assists in preserving signal integrity.

Despite its commendable performance metrics like positive predictive scores of 0.93, 0.94, 0.93, and 0.44 for data from pig 37, pig 41, exp 16, and exp 10, respectively and maintaining high accuracy and specificity scores above 0.99 across all sets, challenges were encountered particularly with exp 10, attributed to the spike-like shape of cubic splines, potentially inciting false positive readings. Moreover, the delay of 30 seconds, mandated by the sample requisition for optimal FEVT method performance, still befits the operational prerequisites of a closed-loop pacemaker, ensuring deliberate synchronisation of artificial paces with the slow wave rhythm.

In the context of gastroparesis, a condition is notoriously known for detrimentally impacting the quality of life, the real-time algorithm not only fills a technological void but also offers a tangible solution transcending the capacities of current treatment modalities like dietary alterations and rudimentary, open-loop gastric pacemakers, which notably lag in functionality, design, and accessibility. Navigating through the intricacies of the problem, this algorithm, conceived to function within a closed-loop system, has decisively met the preset project objective of having an embedded system for testing.

Interweaving critical innovations, namely the ‘filtfilt’ filter implementation, has not only enhanced the project’s robustness but also placed it a notch above predecessors by applying the FEVT method in the embedded system to elevate the baseline, thus attenuating noise and ensuring a meticulous artifact removal which significantly curtailed the rate of False Positives (FP) in low-resolution results.

8. Future Work

The partial attainment of the project’s objective elucidates the room for several pivotal advancements and refinements in the developed algorithm and its practical implementation.

Automating Bad Channel Omission:

The manifestation of bad channels, albeit infrequent, significantly affects the experiment and, hence, the overall reliability of the detection algorithm. The removal of them was mentioned in previous works but still not done[28]. Innovating an automated system that accurately identifies and flags incoherent signals, potentially through a window analysis method, could enhance the functionality and reliability of the algorithm, especially in a real-time application where manual intervention is impracticable.

Incorporation of Machine Learning (ML):

Though initially omitted due to a lack of results and developmental difficulties, machine learning emerges as a viable future pathway. Especially when dealing with complex signals, ML models, if fed with adequate and accurate data, can become adept at identifying abnormalities and nuances that might be otherwise neglected by conventional filtering and detection methods.

Advanced Preprocessing Techniques:

In the realm of embedded systems, particularly where the algorithm is implemented in C and runs on Linux, exploring and developing advanced preprocessing techniques to facilitate more accurate and efficient real-time analysis becomes paramount. Given the inherent constraints of embedded systems, such as computational and memory limitations, innovating lightweight yet efficacious preprocessing methodologies that can seamlessly integrate with the existing algorithm can significantly enhance its real-time applicability and performance.

Automated Adaptation to Varied Signal Characteristics:

Tailoring the algorithm to automatically adapt to varied gastric signal characteristics, thereby enhancing its generalisation capability across diverse datasets and scenarios, will amplify its utility and applicability across a broader spectrum of gastric signal processing applications.

Security and Safety Protocols:

As the algorithm may potentially be embedded within medical devices like pacemakers, developing and integrating robust security and safety protocols is essential to safeguard against malicious intrusions and ensure reliable and safe operation.

9. Contribution

- Implementing FIR filters in C(both Lowpass and Highpass)
- Implementing Artifact removed and detected Logic in C
- Executing edge detection filter in C
- Implementation of the NEO transform and averaging filter
- Implementing Edge detection and detection algorithm in C
- Runtime calculation (with Glacer)
- Visualisation

References

[1] R. A. Hinder and K. A. Kelly, "Human gastric pacesetter potential: site of origin, spread, and response to gastric transection and proximal gastric vagotomy," Am. J. Surg., vol. 133, no. 1, pp. 29–33, 1977

[2] W. J. Lammers, L. Ver Donck, B. Stephen, D. Smets, and J. A. Schuurkes, "Origin and propagation of the slow wave in the canine stomach: the outlines of a gastric conduction system," *Am. J. Physiol. Gastrointest. Liver Physiol.*, vol. 296, no. 6, pp. G1200–G1210, 2009, doi:10.1152/ajpgi.90581.2008.

[3] J. U. Egbuji, G. O'Grady, P. Du, et al., "Origin, propagation and regional characteristics of porcine gastric slow wave activity determined by high-resolution mapping," *Neurogastroenterol. Motil.*, vol. 22, no. 10, pp. e292–e300, 2010, doi:10.1111/j.1365-2982.2010.01538.x.

[4] G. O'Grady, P. Du, L. K. Cheng, et al., "Origin and propagation of human gastric slow-wave activity defined by high-resolution mapping," *Am. J. Physiol. Gastrointest. Liver Physiol.*, vol. 299, no. 3, pp. G585–G592, 2010, doi:10.1152/ajpgi.00125.2010.

[5] L. Wang, A. Malik, P. S. Roop, L. K. Cheng, and N. Paskaranandavadivel, "A formal approach for scalable simulation of gastric ICC electrophysiology," IEEE Transactions on Biomedical Engineering, vol. 66, no. 12, pp. 3320–3329, 2019.

[6] L. Wang, A. Malik, P. S. Roop, L. K. Cheng, N. Paskaranandavadivel, and W. Ai, "A novel approach for model-based design of gastric pacemakers," Computers in Biology and Medicine, vol. 116, p. 103 576, 2020. 21

[7] H. P. Parkman, W. L. Hasler, and R. S. Fisher, "American Gastroenterological Association technical review on the diagnosis and treatment of gastroparesis," Gastroenterology, vol. 127, no. 5, pp. 1592-1622, 2004.

[8] J. Forster, I. Sarosiek, R. Delcore, Z. Lin, G. Raju, and R. McCallum, "Gastric pacing is a new surgical treatment for gastroparesis," The American Journal of Surgery, vol. 182, no. 6, pp. 676–681, 2001.

[9] G. Farrugia, "Interstitial cells of Cajal in health and disease," Neurogastroenterology & Motility, vol. 20, pp. 54–63, 2008.

[10] A. M. Bilgutay, R. Wingrove, W. O. Griffen, R. C. Bonnabeau Jr, and C. W. Lillehei, "Gastro-intestinal pacing a new concept in the treatment of ileus," Annals of surgery, vol. 158, no. 3, p. 338, 1963.

[11] L. Wang, A. Malik, P. S. Roop, L. K. Cheng, N. Paskaranandavadivel, and W. Ai, “Design of a closed-loop gastric pacemaker for modulating dysrhythmic conduction patterns via extracellular potentials.,” in 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), IEEE, 2020, pp. 2504– 2507.

[12] L. Wang, A. Malik, P. S. Roop, L. K. Cheng, and N. Paskaranandavadivel, “A framework for the design of a closed-loop gastric pacemaker for treating conduction block,” Computer Methods and Programs in Biomedicine, p. 106 652, 2022.

[13] J. B. Furness, "The enteric nervous system and neurogastroenterology," Nat. Rev. Gastroenterol. Hepatol., vol. 9, no. 5, pp. 286-294, 2012

[14] I.-H. Huang, J. Schol, R. Khatun, et al., “Worldwide prevalence and burden of gastroparesis-like symptoms as defined by the United European Gastroenterology (ueg) and European Society for Neurogastroenterology and motility (ESNM) consensus on gastroparesis,” United European Gastroenterology Journal, 2022

[15] N. Paskaranandavadivel, G. O’Grady, P. Du, and L. K Cheng, “Comparison of filtering methods for extracellular gastric slow wave recordings,” Neurogastroenterology & Motility, vol. 25, no. 1, pp. 79–83, 2013.

[16] S. H. Bull, G. O’Grady, L. K. Cheng, and A. J. Pullan, “A framework for the online analysis of multi-electrode gastric slow wave recordings,” in 2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, IEEE, 2011, pp. 1741–1744

[17] P. Du, W. Qiao, G. O’Grady, et al., “Automated detection of gastric slow wave events and estimation of propagation velocity vector fields from serosal high-resolution mapping,” in 2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, IEEE, 2009, pp. 2527–2530.

[18] S. Alighaleh, L. K. Cheng, T. R. Angeli, et al., “A novel gastric pacing device to modulate slow waves and assessment by high-resolution mapping,” IEEE Transactions on Biomedical Engineering, vol. 66, no. 10, pp. 2823–2830, 2019

[19] E. J. D. S. Luz, W. R. Schwartz, G. C´amara-Ch´avez, and D. Menotti, “Ecg-based heartbeat classification for arrhythmia detection: A survey,” Computer methods and programs in biomedicine, vol. 127, pp. 144–164, 2016.

[20] B. T. Lee, S. T. Kong, Y. Song, and Y. Lee, “Self-supervised learning with electrocardiogram delineation for arrhythmia detection,” in 2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), IEEE, 2021, pp. 591–594.

[21] L. Wang, "Gastrointestinal Electrophysiology Modelling and Closed-loop Gastric Pacemaker Design," PhD dissertation, ResearchSpace@Auckland, 2022.

[22] T. Abell, R. McCallum, M. Hocking, K. Koch, H. Abrahamsson, I. LeBlanc, G. Lindberg, et al., "Gastric electrical stimulation for medically refractory gastroparesis," Gastroenterology, vol. 125, no. 2, pp. 421-428, 2003.

[23] R. W. McCallum, Z. Lin, J. Forster, K. Roeser, Q. Hou, and I. Sarosiek, "Gastric electrical stimulation improves outcomes of patients with gastroparesis for up to 10 years," Clin. Gastroenterol. Hepatol., vol. 9, no. 4, pp. 314-319, 2011.

[24] F. T. Sun and M. J. Morrell, “Closed-loop neurostimulation: The clinical experience,” Neurotherapeutics, vol. 11, no. 3, pp. 553–563, 2014.

[25] Z. Lin, R. McCallum, B. Schirmer, and J. Chen, “Effects of pacing parameters on entrainment of gastric slow waves in patients with gastroparesis,” American Journal of Physiology-Gastrointestinal and Liver Physiology, vol. 274, no. 1, G186–G191, 1998.

[26] A. de Cheveigné and I. Nelken, "Filters: when, why, and how (not) to use them," *Neuron*, vol. 102, no. 2, pp. 280-293, Apr. 2019.

[27] R. M. Rangayyan, *Biomedical Signal Processing and Signal Modeling*. Wiley-IEEE Press, 2015.

[28] L. Marr, D. Vanpraseuth, A. Malik, and P. Roop, "Pacemakers for Gastrointestinal Diseases," *Dept. Electrical, Computer, and Software. Eng., University Of Auckland, New Zealand,* Project 7, 2022.

[29] D. Vanpraseuth, L. Marr, A. Malik, and P. Roop, “*Machine Learning and Signal Processing for the Human Gastric System”*, Department of Electrical, Computer and Software Engineering, *University Of Auckland, New Zealand,* Project 7, Oct. 14, 2022.