

Open Mind Neuromodulation Interface for the CorTec Brain Interchange (OMNI-BIC): an investigational distributed research platform for next-generation clinical neuromodulation research

Hanbin Cho ^{1,1}, Jeffrey G. Ojemann ², and Jeffrey Herron ²

¹University of Washington

²Affiliation not available

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Abstract

The rise of adaptive stimulation approaches has shown great therapeutic promise in the growing field of neuromodulation. The discovery and growth of these novel adaptive stimulation paradigms has been largely concentrated around several implantable devices with research application programming interfaces (APIs) that allow for custom applications to be created for clinical neuromodulation studies. However, the sunseting of devices and ongoing development of new platforms is leading to an increased fragmentation in the research environment- resulting in the reinvention of system features and the inability to leverage previous development efforts for future studies. The Open Mind Neuromodulation Interface (OMNI) is a previously proposed solution to address the weaknesses of the DLL-driven API approach of past neuromodulation research by utilizing an alternative gRPC-enabled microservice framework. Here, we introduce OMNI-BIC, an implementation of the OMNI framework to the CorTec Brain Interchange system. This paper describes the design and implementation of the OMNI-BIC software tools and demonstrates the framework's capabilities for implementing customized neuromodulation therapies for clinical investigations. Through the development and deployment of the OMNI-BIC system, we hope to improve future clinical studies with the Brain Interchange system and aid in continuing the growth and momentum of the exciting field of adaptive neuromodulation.

Open Mind Neuromodulation Interface for the CorTec Brain Interchange (OMNI-BIC): an investigational distributed research platform for next-generation clinical neuromodulation research

Hanbin Cho
Department of Electrical and
Computer Engineering
University of Washington
Seattle, WA USA
hcho5@uw.edu

Jeffrey Ojemann
Department of Neurological Surgery
University of Washington
Seattle, WA USA
jojemann@uw.edu

Jeffrey Herron
Department of Neurological Surgery
University of Washington
Seattle, WA USA
jeffherr@uw.edu

Abstract— The rise of adaptive stimulation approaches has shown great therapeutic promise in the growing field of neuromodulation. The discovery and growth of these novel adaptive stimulation paradigms has been largely concentrated around several implantable devices with research application programming interfaces (APIs) that allow for custom applications to be created for clinical neuromodulation studies. However, the sunsetting of devices and ongoing development of new platforms is leading to an increased fragmentation in the research environment- resulting in the reinvention of system features and the inability to leverage previous development efforts for future studies. The Open Mind Neuromodulation Interface (OMNI) is a previously proposed solution to address the weaknesses of the DLL-driven API approach of past neuromodulation research by utilizing an alternative gRPC-enabled microservice framework. Here, we introduce OMNI-BIC, an implementation of the OMNI framework to the CorTec Brain Interchange system. This paper describes the design and implementation of the OMNI-BIC software tools and demonstrates the framework’s capabilities for implementing customized neuromodulation therapies for clinical investigations. Through the development and deployment of the OMNI-BIC system, we hope to improve future clinical studies with the Brain Interchange system and aid in continuing the growth and momentum of the exciting field of adaptive neuromodulation.

I. INTRODUCTION

Symptoms associated with a variety of neurological and psychiatric disorders have been shown to improve with stimulation therapy [1], [2], [3]. However, these current open-loop stimulation methods are still limited by efficacy and efficiency. Tradeoffs of open-loop stimulation include side effects, such as paresthesia and dysarthria [4], [5]. Additionally, variations in symptoms between clinical visits can result in

partial efficacy since patients are often limited in their ability to adjust settings until a clinician adjusts their stimulation.

To address the weaknesses of current open-loop methods, there is increased motivation to investigate adaptive neuromodulation and characterize patient specific biomarkers that may serve as indicators to signal when therapeutic stimulation should be delivered. Various clinical studies have shown the promise of adaptive stimulation methods for improving therapy efficacy [6], [7], [8]. With implantable neuro-stimulators (INS) now capable of modifying stimulation parameters in real-time using neural sensing, there has been greater interest in developing more complex and customizable stimulation paradigms to investigate in neuromodulation research. Fully implantable research neuromodulation systems, like the Summit [9], [10] and DyNeuMo [11], have demonstrated system feasibility of closed-loop stimulation in clinical populations. However, there are a diverse array of adaptive algorithms of interest that utilize approaches not currently supported by available devices, such as the application of time-dependent processing [6]. Additional distributed system development has started to address current device shortcomings by providing flexibility to researchers to create more customized and complex stimulation algorithms of interest. Application programming interfaces (APIs) have been integral to this development as they simplify communication with implantable systems and allow users to interface with system-unique functionalities such as stimulation and recording. As more research tools are released into the field, software incompatibilities between systems pose a higher risk to rewriting research software, a burdensome and time-consuming task that potentially limits researchers’ abilities to take advantage of novel features of up-to-date technology. Additionally, efforts to pursue replication or expansion works are less robust due to possible differences in technical foundation of re-written software.

To minimize fragmentation and development barriers while expanding the support for clinical systems oriented towards

research purposes, the Open-Mind Neural Interface (OMNI) architecture [12] was introduced. OMNI is an architecture that aims to accelerate neuromodulation research by establishing a common technical foundation while still enabling INS-specific functionalities. The programming-language agnostic framework employs gRPC (gRPC Remote Procedure Call), an open-source remote procedure call framework that enables communications across different programming languages [13]. By enabling software interoperability, research groups can utilize preferred programming languages, easing the translation of new investigational devices towards research applications. Additionally, the gRPC microservice runs in its own sandboxed instance, providing a layer of security by which user-mode code errors or crashes are isolated from implant-interfacing code in the server. Ensuring an isolated environment to run application code maintains stability and improves robustness by minimizing potential security threats to the system.

This paper introduces the application of the OMNI framework to the design and implementation of a microservice for the Brain Interchange (BIC) system, named here as the OMNI Brain Interchange or “OMNI-BIC”. We will describe the current design and features of the Brain Interchange and how the gRPC protocol is being applied to create a flexible research ecosystem using our OMNI-BIC framework. We will then demonstrate examples of distributed adaptive paradigms not currently well serviced by existing research platforms to assess the infrastructure and examine various metrics to evaluate performance. While these examples are benchtop assessments, we anticipate this work to establish the feasibility and robustness of the system to perform time-dependent adaptive stimulation algorithms for future clinical studies.

II. METHODS

A. CorTec Brain Interchange (BIC) System Overview

The Brain Interchange is a wireless investigational system that consists of an implant, external communication unit, and personal computer as shown in Fig. 1. The implant consists of a power receiving coil and electrode connections that can contain up to 32 electrocorticography (ECoG) channels that are designed for stimulation and recording up to a 1 kHz sampling rate. The implant connects to a communication unit via a magnetic head piece which provides power inductively and communicates via broad-band radio. This external communication unit connects to a personal computer via USB

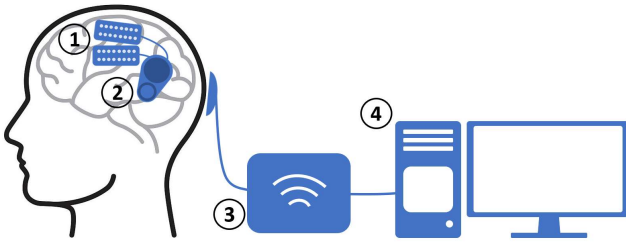


Fig. 1 CorTec Brain Interchange Overview: Intended use diagram for the OMNI-BIC for cortical stimulation. The implant consists of a 1) cortical grid that supports up to 32 contacts and an 2) electronics unit for power and communication. The 3) external unit supplies power and connects to a 4) PC with the custom API.

where data can be streamed and logged. Fig. 1 presents the Brain Interchange system setup expected in an implanted patient. The Brain Interchange has accompanying APIs compatible with C, C++, and Python. These APIs enable custom design of stimulation algorithms and monitoring of neural data, alongside other system diagnostics like power, temperature, and humidity.

B. Design and Implementation of OMNI-BIC

To create the OMNI-BIC framework, shown in Fig. 2 a) we used the provided C++ API to control the Brain Interchange device. Defined through prior work [12], OMNI provides an API framework definition for common features available across different INS devices. The services are divided into the Bridge API, Device API, and Info API. The Bridge services provides an abstraction layer for telemetry-related functionality such as device discovery and communication status. The Device service enables an application to access the implanted device’s configuration and control stimulation. Finally, the Info API supplies information about the microservice itself including version number and supported devices. This microservice structure has several advantages such as allowing developers more flexibility to avoid getting locked into outdated technology and sandboxed execution environments to prevent user-code related application crashes from impacting critical implant interfacing software. Additions to the protobuf file, which provides the programming-agnostic definitions microservice-provided functions and messages, beyond the general OMNI specifications allow the use of the Brain Interchange’s specific functionalities which includes status monitoring, sensor streaming, data logging, and stimulation.

To perform stimulation with the CorTec API, we first created a waveform definition request. We subsequently created pulse functions with characteristics such as amplitude and period that can then be added to the waveform. Once the waveform of interest was populated with the desired pulse functions, the waveform was then enqueued before a start stimulation command was sent to the system. The Brain Interchange has different stimulation enqueueing modes including persistent function, allowing selection of a specific pulse function of a waveform for delivery, persistent command, where a stimulation waveform is sent and the same waveform is retained for subsequent stimulation, and volatile command, where after delivery of the stimulation waveform the initial waveform is reset and must be defined again prior to subsequent stimulation. In approaching the implementation of various stimulation paradigms, we used the persistent command preloading method as all enqueued functions delivered.

Desired data processing steps, such as thresholding and filtering, can be integrated into the microservice through C++ to isolate and detect neural biomarkers of interest. Additional microservice features include missing data interpolation to account for missing data caused by communication dropouts, client-side stimulation waveform definition, and reporting of system characteristics such as temperature and humidity.

C. Microservice-implemented Stimulation Algorithms

To demonstrate the versatility of the OMNI-BIC we implemented several example neuromodulation paradigms

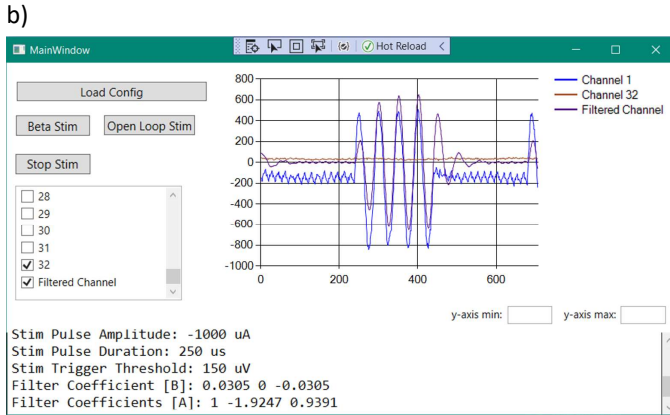
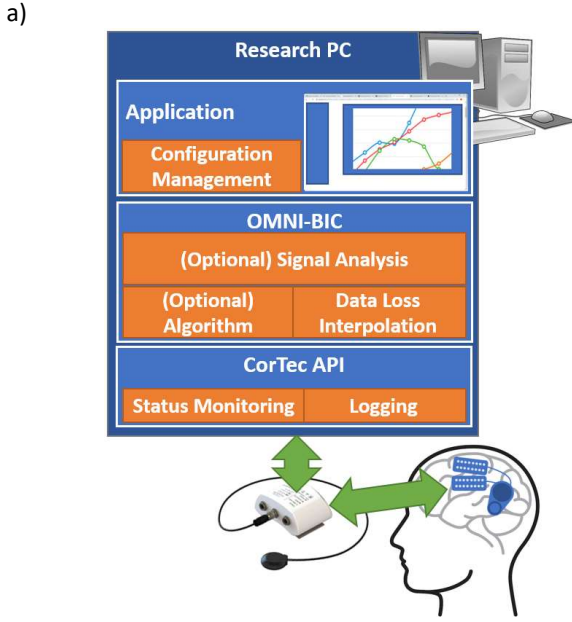


Fig. 2 Software Block Diagram: a) Block diagram of the features of the software components. b) The client application the user interacts with to load configuration parameters and monitor incoming and filtered data.

based on previously published work by integrating the required functionality directly into the microservice. By choosing to integrate stimulation triggering and adaptive algorithms into the microservice directly, system developers can ensure that their operation is uninterrupted by user-mode application crashes. Implemented paradigms include open loop stimulation and two investigated adaptive stimulation algorithms: a beta burst paradigm [6] and a phase-locked stimulation paradigm [14].

As the Brain Interchange system does not have an innate open-loop stimulation functionality, we designed an open-loop subcomponent in the microservice. To implement open-loop stimulation, a 20Hz waveform with a maximum of 255 repetitions was defined to ensure that our open-loop stimulation pattern will run as long as possible each time stimulation is triggered. The waveform definition encompassed defining the stimulation pulse and an interpulse interval indicative of the overall frequency of the desired stimulation. This pattern was then uploaded as a persistent waveform. Given our targeted open-loop frequency of 20Hz and using the maximum of 255 waveform repetitions, we continuously delivered open-loop stimulation by using a dedicated thread which stops stimulation

on a stimulation frequency-defined interval before re-triggering the delivery of this repeated waveform. While this results in short periods of inactivity between each trigger, these periods where no stimulation was sent did not significantly impact the overall delivery of open-loop stimulation given the overall high duty-cycle.

The beta burst paradigm [6] aimed to detect bursts of beta activity, neural oscillations typically ranging between 12 and 30 Hz, and respond with a burst of stimulation for the duration of elevated beta activity. Characterizing online beta activity used a moving average filter followed by rectification, smoothing, and thresholding, functionalities not currently available in clinical systems. To replicate this paradigm, incoming neural samples from a selected channel were processed using a two-pole IIR bandpass filter with a passband frequency of 15-25 Hz. This filtered data was then rectified and smoothed using an IIR low pass filter. The resulting processed signal was then monitored to identify when it was above a certain threshold and responded with a burst of stimulation. When the processed signal was below the set threshold, stimulation was discontinued.

The phase-locked paradigm [14] targeted the depolarizing phase of ongoing oscillatory beta activity for stimulation. Neural activity was band-pass filtered to isolate oscillations of interest and a dual time-amplitude window discriminator helped generate triggers for stimulation on specific phases of the filtered oscillations. Current clinical systems are limited to spectral analysis and are unable to apply additional temporal processing needed for this algorithm. To implement the phase-locked paradigm with the OMNI-BIC, data was similarly filtered using an IIR bandpass filter with a passband frequency of 15-25 Hz. The maxima of the filtered signal were then identified and used to trigger stimulation output. The maxima were used to account for time delays of the system to ensure stimulation delivery during the proper phase of the filtered waveform.

D. Custom Application Development

A client application, as seen in Fig. 2b), was developed to provide an interface where users can interact with the implemented features of the OMNI-BIC. The application was written in C#, for flexibility and versatility, and accepts JSON files to configure parameters characterizing features such as filtering and stimulation. Modifiable stimulation variables include amplitude and duration values for each pulse in a biphasic waveform, and the channels that sense neural activity and observe stimulation output. While the stimulation characteristics are determined by a user, the distributed algorithm determines the timing of the stimulation pulse through processing and identification of key biomarkers. Processing parameters, such as filtering coefficients and thresholding values, can also be set through the imported configuration file. The customization of implemented processing functionalities through multiple JSON configurations allows various control paradigms to be explored and tuned for patient specificity. The application is also capable of logging raw and interpolated data, in addition to timing data

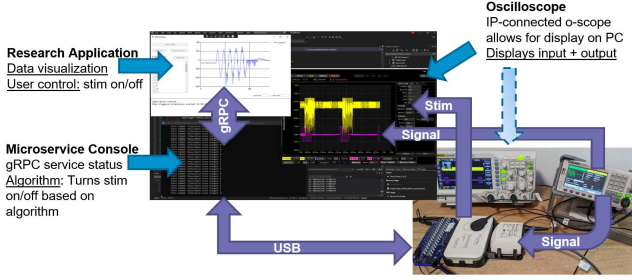


Fig. 3 Benchtop Demonstration: The client application and microservice are started, allowing a user to load configuration parameters and monitor incoming and filtered data. A signal generator connected to the Brain Interchange provides a sine wave input. The PC (not shown) determined the stimulation control paradigm. Meanwhile, an oscilloscope monitored the stimulation output and an in-phase but higher amplitude version of the original input into the system.

to allow synchronization between data logged by the CorTec API and interpolated data from the microservice.

E. Testing Methods

The benchtop experiment used to assess performance of the system is pictured in Fig. 3. A signal generator served as neural input to the system and delivered bursts of 20 Hz sine waves into a channel on the Brain Interchange’s breakout board, which utilizes a resistor-capacitor based model to replicate biophysical properties of neurons, replacing a tissue phantom model. An oscilloscope was connected to observe stimulation output alongside a second sine wave generated in-phase, but with higher amplitude, to the original input to assess timing. Upon starting the client, a JSON configuration file designated the sensing and output channels, the stimulation waveform parameters, and the filtering coefficients for a 15-25 Hz bandpass filter. This test setup was used to evaluate the performance of the open loop stimulation and adaptive stimulation algorithms implemented into the OMNI-BIC; specifically, the system’s ability to identify specified biomarkers of interest and respond with stimulation.

Another facet of system performance assessed was communication robustness. As the Brain Interchange is a wireless system, we were interested in characterizing packet loss during system operation. We compared packet loss by categorizing packets into two categories. First is a critical loss, which is an instance when there are more than 9 consecutive missing packets. This threshold was selected as interpolating more than 9 lost data points at the system’s native sampling rate of 1KHz results in an effective Nyquist rate below a desired minimum of 50Hz which ensures an oversampling of the beta frequency range of interest by at least two. The second category is a recoverable packet loss, which is when there are 9 or fewer dropped packets, in which case linear interpolation is used to preserve signal processing and filtering functionality despite the lost data.

III. RESULTS

A. Stimulation Performance

Open loop stimulation and the two adaptive stimulation paradigms were tested and the output of the OMNI-BIC system for each is shown in Fig. 4. The top subplot in each figure shows

TABLE I.
COMPARISON OF COMMUNICATION LOSS FOR 10 MIN PERIODS OF
DIFFERENT STIMULATION PARADIGMS

Condition	Total Packets	Critical Events	Recoverable Events	Average Loss per Event
Recording only	664500	0	6509	1.99
Open-loop	678600	0	28898	1.57
Beta-burst	666700	0	27091	2.46
Phase-locked	669199	0	15892	1.83

data logged by the OMNI-BIC system while the bottom subplot shows the observed measurements from the oscilloscope. Recordings from the OMNI-BIC were time synchronized with data collected by an oscilloscope. Input signals and stimulation output aligned between the data streams, verifying the reliability of the system’s data collection abilities. Approximately 10 min sessions were performed for each paradigm and the recorded input signal was then compared to the recorded active stimulation signal to assess system performance. For all paradigms, there were periods of absent or irregular stimulation output. Encountered exceptions were logged for all three paradigms and time-aligned to determine the result of encountered exceptions during stimulation. Two types of DLL exceptions were logged: type I and type II. Type I exceptions were returned when the device is in an invalid state and cannot start stimulation due to a recent stop stimulation command. Type II exceptions were reported when there is no response (a timeout) from the device when trying to start stimulation.

For the open-loop paradigm, there were 124 exceptions encountered during testing. 121 instances of Type I exceptions were logged while 3 instances of Type II exceptions were recorded. In all cases, the system was able to automatically retry the stimulation command to resolve the issue and continue with open-loop stimulation.

The beta burst algorithm was assessed only if triggering points resulted in stimulation. Of 619 triggering points, 618 elicited a burst of stimulation. Latency between the triggering point and onset of stimulation was characterized by having a median of 22.75 ms. Most latencies ranged between 21.81 ms and 23.99 ms. 2 exceptions were logged, and all were recorded as type II. Bursts of stimulation affected by exceptions were observed to have fewer than the expected number of pulses.

For the phase-locked stimulation paradigm, identified peaks did not always trigger a stimulation response. In a recording with 3830 identified peaks, 3818 of those peaks triggered a stimulation response. The stimulation responses were then subdivided into hits (stimulation delivered during the depolarizing phase) and misses (those that were delivered past the depolarizing phase). 3372 peaks were classified as hits while 446 peaks were classified as misses. OMNI-BIC’s performance of the phase-locked paradigm was further assessed through characterizing latency between a triggering peak and onset of stimulation. The median latency for the phase-locked paradigm was 21.80 ms with most latencies ranging from 20.06 ms to 23.34 ms. Five type II exceptions were logged.

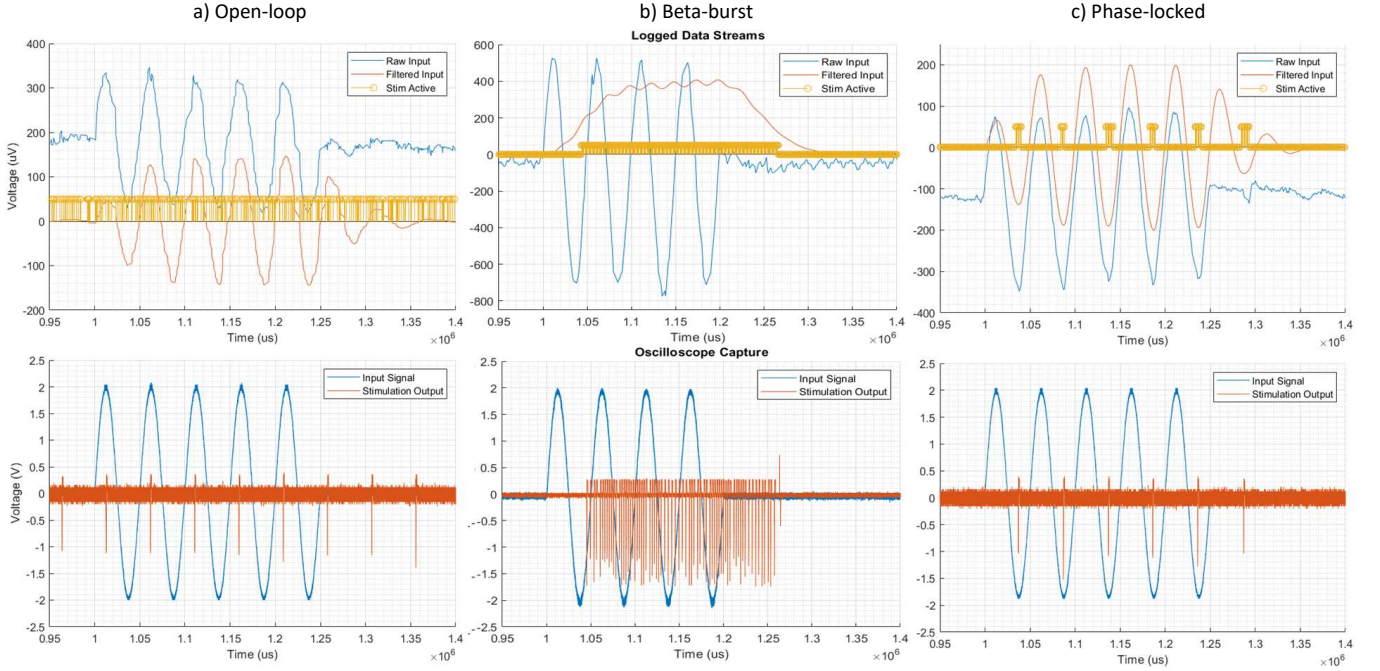


Fig. 4 Stimulation algorithm demonstration: Time synchronized data as reported by the OMNI-BIC system and recording oscilloscope are shown in the top and bottom plots respectively for the a) open-loop, b) beta-burst, and c) phase-locked paradigms. The sine wave input connected to the oscilloscope was in-phase with the input into the OMNI-BIC system but of higher amplitude in order to assess timing.

B. Communication Robustness

Packet loss characterization for all stimulation paradigms and passive recording was assessed. While there is packet loss due to the wireless communication nature of the system, there is also loss expected during stimulation. For every stimulation pulse, 2 packets are lost. However, as the number of lost packets is below the threshold for data interpolation, these samples are recovered. A distribution of the types of losses observed is shown in Table 1. While conditions were performed in 10 min sessions, the total time, including setup and shutdown, sometimes resulted in 11 min recordings being used for communication analysis. Across all paradigms, no critical events were observed, indicating that all data loss was minor enough to be mitigatable through interpolation. The passive recording session observed about 1.94% of total packets as interpolated packets. For the open-loop paradigm, 6.67% of total packets were interpolated. In the beta-burst paradigm, 9.99% of total packets were interpolated. The phase-locked paradigm observed 4.35% of total packets as recoverable.

IV. DISCUSSION

Further expansion of promising research tools for the neuromodulation sphere provides opportunities for future studies to investigate novel adaptive paradigms. Specifically, providing the means to test temporal driven methods towards closed-loop stimulation diversifies the approaches to selective and effective stimulation therapy. Developing the OMNI-BIC has shown successful application of the OMNI architecture to the CorTec Brain Interchange for high performance of time sensitive processing for closed-loop neuromodulation. OMNI offers standardized functionalities to interface with devices while still allowing customization to realize unique applications

and algorithms, allowing researchers to replicate and build off previous work.

While our experience working with the preliminary development kit for the Brain Interchange system showed it is generally robust for adaptive stimulation applications, there are still technical limitations to be considered when designing system software for the Brain Interchange device. As observed with the beta burst and phase locked paradigms, there was a delay between data received and the stimulation response. Furthermore, we identified instances where stimulation commands were rejected or dropped by the API, resulting in no stimulation pulses generated despite a request. However, these instances are rare and, as the system is able to recover and eventually send stimulation, do not significantly impact the regularity of accurate stimulation delivery. Wireless communication dropouts such as these are common across implantable devices and system developers must take care to evaluate the proper actions to take upon an API function's time-out. However, the choice by the BIC developers to stream 1000Hz neural data with one data point per packet at low-latency (which include all 32 channels at each sampled time point) allows for easy interpolation of lost data in the case of a short drop-out to preserve processing functionality. While data interpolation was high in the case of the beta-burst paradigm, packet loss is expected to vary depending on stimulation activity of the system, as demonstrated by interpolation observed in the open-loop and phase-locked paradigms.

Although some of these development hurdles are addressed by applying the OMNI framework, there is still user effort required to develop algorithms of research interest. Functionalities embedded into the Brain Interchange system are limited, so features that are not already implemented in the

OMNI-BIC microservice or provided applications will require user effort and familiarity with the CorTec API before running OMNI-BIC with the desired abilities. Still, OMNI-BIC has the potential to ease developer effort in other ways by allowing researchers to create applications with their programming languages of choice and to provide greater opportunity for sharing and reusing code.

It should be noted of course that the demonstrations performed with the OMNI-BIC utilized benchtop equipment, and do not fully encompass the system's technological capabilities as a neuromodulation research platform. Utilizing this system in vivo will help better characterize system performance, such as stimulation artifact, and potential barriers that would not be encountered when using benchtop instruments. Future work will focus on evaluating the system in a saline tank environment using upcoming application-specific electrodes prior to using the system with a patient. Conditions from additional testing within a saline tank will more likely match those when performing recordings in a patient. Testing and observing the results in saline can potentially serve as feedback to see how well the OMNI-BIC system would perform in a patient and how to improve the performance when the OMNI-BIC is used with a patient. Additionally, while the stability of wireless communication in the demonstration is robust, there is room for stability variability between recording sessions. The use of data interpolation to recover dropped packets preserves the integrity of recorded data and helps counter the impact of dropped packets, however so far, we have only implemented linear interpolation and more sophisticated interpolation methods may further improve the quality of signal processing during minor data loss events. Future updates to the Brain Interchange, such as system configurations allowing selection of the most stable frequency channel for wireless communication further reduce packet loss.

By implementing various stimulation paradigms in a single system, we have demonstrated the flexibility of the OMNI-BIC system to explore novel stimulation approaches. We believe the OMNI-BIC has great potential in enabling research opportunities for algorithms that have yet to be explored in current implantable systems. In addition, the OMNI-BIC presents avenues to incorporate additional sensors for more complex data collection and processing. Previous literature [11], [15] has shown the therapeutic application of sensor data in closed-loop stimulation. Integration of sensor data is feasible through additions to the microservice or custom user application and could be used to expand the feedback utilized to deliver stimulation beyond neural biomarkers. Furthermore, due to the low latency of the system from current processing, additional steps can be added to our processing pipeline. We believe that stimulation artifact rejection algorithms can be applied as data is streamed to maintain the stability of neural recordings. Minimization of the effect of stimulation artifact can enable more precise delivery of closed-loop stimulation and ease post-collection analysis of data.

We have developed a distributed neuromodulation system and demonstrated its versatility in realizing various neuromodulation paradigms. The above work is the first demonstration of software tools to interface with the CorTec

BIC system and its feasibility to implement temporal processing techniques to direct simulation. By ascertaining the potential of OMNI-BIC, this work establishes the system as a potential research tool for future neuromodulation studies that aim to investigate and assess variations of closed-loop paradigms not previously supported in upcoming clinical studies.

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