The Bionode: A Closed-Loop Neuromodulation Implant

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Implantable closed-loop neuromodulation devices for use in long-term chronic studies in a lab or clinical trial are expensive to acquire and difficult to modify for specific use cases. This article documents the design and fabrication of a wireless implantable device using only commercially available off-the-shelf (COTS) components. This device, called the Bionode, can record and transmit up to four channels of biopotential data while simultaneously providing biphasic constant-current stimulation. The Bionode is a viable, low-cost, reusable, and easily modifiable research tool with clinical implications that has gained widespread use in various research projects at Purdue University.

CCS Concepts: • **Hardware** → **Bio-embedded electronics**; *Wireless devices*; • **Computer systems organization** → *Firmware*;

Additional Key Words and Phrases: Implantable biomedical devices, wireless communication, wireless powering, biocompatibility

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1 INTRODUCTION

Wireless implantable devices with the ability to record biopotential signals and electrically stimulate the nervous system have been used to study and treat a wide variety of neurological and neuropsychiatric disorders in humans including epilepsy, Parkinson's disease, depression, and drug addiction [1–5]. To research these disorders in rodent models, various miniature wireless implantable devices have been developed [6–10]. To achieve a small size and reduce power requirements, many of these devices rely on application-specific integrated circuits (ASICs), specifically designed packaging methods, and/or proprietary technologies. While these techniques can produce small and power-efficient devices, the ability to reproduce them in typical laboratory settings is often prohibitively difficult and expensive. Additionally, the application-specific nature of such devices introduces problems when adapting them to alternate applications. This article documents the design and deployment of a miniature wireless implantable device for rodent through clinical models called the Bionode. The Bionode features customizable recording and stimulation channels in a flexible, modifiable, and re-useable package to accommodate a wide variety of use cases.

The Bionode was developed over four years at the Center for Implantable Devices (CID) at Purdue University. With the ability to record four differential signals and provide up to 1 mA of biphasic constant current electric stimulation, its capabilities and performance exceeds that of currently available implantable devices for rodent models [6, 9, 11]. Furthermore, the ability to fully implant the Bionode in rodents greatly increases its versatility when compared to larger implantable devices and non-implantable rodent head-stages [12]. Each input channel contains gain and filtering stages that can be modified to accommodate a variety of input signals. Bidirectional communication between the implant and external systems allows for the real-time specification of stimulation wave-forms, providing a platform for closed-loop recording and stimulation studies. Additionally, all components used to construct the Bionode are available as commercial off-the-shelf (COTS) components with the intent that any and all aspects of the Bionode's design can be reproduced by a typical university laboratory or small medical device company.

Over the past four years, the Bionode has been used by researchers at Purdue University to study epilepsy, Parkinson's disease, glaucoma, urinary incontinence, and vagus nerve stimulation for modulation of the inflammatory reflex and gastroparesis. Throughout the course of these studies, 76 Bionodes have been successfully implanted. The methods used to encapsulate the Bionode have been refined to increase its ease of use and re-use.

This article is organized in sections that document the design challenges and solutions for the various systems on the Bionode. When applicable, *in vivo* results are reported and discussed in each section. These sections include descriptions of the Bionode's recording channels, stimulation circuitry, bidirectional communication scheme, communication antenna design, wireless power capabilities, and packaging techniques. The challenges outlined in these sections have been thoroughly studied by current and past members of the CID at Purdue University. The unforeseen difficulties presented by these challenges have motivated the detailed documentation of their various solutions in this article in the hopes that they will be of use to others designing and utilizing electroceutical devices.

2 IMPLANT SYSTEM OVERVIEW

The Bionode implant consists of three printed circuit board assemblies (PCBAs): The Bionode mainboard, the Pownode, and the Feedthrough board. The Bionode mainboard contains all circuitry for the recording and stimulating channels as well as a microcontroller, radio, and antenna for data transmission and reception (Sections 3–6). The Pownode provides power rails

Fig. 1. Bionode implant assembly (left) and four-channel Bionode fully packaged inside glass packaging with electrodes attached and rechargeable batteries included (right).

Fig. 2. Bionode settings are updated and acquired data is displayed on a PC via Bionode DataView, a custom designed cross-platform graphical user interface. Bidirectional communication is facilitated via the Base Station, which also provides the wireless power source that drives the WPT chamber. The WPT chamber houses the implanted rodent and carries the circulating magnetic field that powers the device.

to the Bionode mainboard (Section 7). Electrodes are connected to the Bionode mainboard via the Feedthrough board (Section 8). Fully assembled and fully packaged Bionodes are pictured in Figure 1. We implant Bionodes like the one shown in Figure 1 in the subcutaneous space on the side of rats.

The Bionode is supported by various external systems as seen in Figure 2. A Wireless Powering Transfer (WPT) chamber provides both power to the Bionode and a living space for the implanted rodent (Section 7). All data transmitted to and from the Bionode passes through an external Base Station that provides a communication interface between the Bionode and a PC via a Wi-Fi link (Section 5). A custom-designed cross-platform application provides a graphical user interface allowing users to view and save data transmitted by the Bionode as well as specify various settings (i.e., stimulation waveform parameters) on the Bionode.

3 BIOSIGNAL ACQUISITION

To acquire small electric signals generated by biological processes, an analog front end (AFE) is needed to amplify and filter the signals before they can be digitized.

3.1 AFE Design Considerations

The AFE features high differential input impedance, low noise, a high common mode rejection ratio (CMRR), and sufficient gain and bandwidth. The gain and bandwidth are specified for each input channel to properly condition the various signals that may be sensed by the AFE (i.e., electrocardiogram (ECG), electrocorticogram (ECoG), electromyogram (EMG), local field potential (LFP),

Fig. 3. Signals are acquired via an analog frontend consisting of front-end filtering and two amplification stages. Front-end filters provide passive bandpass filtering prior to amplification. The first stage differentially amplifies the signal using an instrumentation amplifier. The second stage provides additional gain and active bandpass filtering.

compound nerve action potential (CNAP), thermocouple sensor inputs, or pressure sensor inputs). While this AFE can filter out noise generated by typical sources (i.e., nearby radiated signals, motion artifacts, and other biological signals), it also can filter out high frequency RF noise injected into the signal from the WPT chamber (Section 7).

3.2 AFE Design Overview

The Bionode has two parallel dual ended AFEs; one for each input channel. Two additional channels can be added to the Bionode via an expansion board. Each AFE consists of passive front-end filtering followed by two stages of gain amplification (Figure 3). The two stages of gain amplification include a first stage of differential amplification and a second stage that provides bandpass filtering and additional gain. These parallel AFEs are dual ended with $\pm 0.9V$ rails to allow the AFE to have a zero dc bias voltage. This is necessary, because the stimulation circuit requires that the negative stimulation electrode is connected to the Bionode's ground (Section 4). If the AFE had a non-zero dc bias voltage, then a static potential would exist between the recording electrodes and the negative stimulation electrode, causing possible tissue damage, electrode erosion, and unwanted stimulation performance. Alternatively, inputs and outputs can be ac coupled, but that introduces different signal processing challenges for stimulus artifact cancellation in the recorded signal and lowers the CMRR for the AFE.

3.3 Front End Filtering

The optional passive front-end filters allow for the inclusion of a high pass filter, low pass filter, or bandpass filter before the first stage differential amplifier. While adding these filters reduces the CMRR and differential input impedance of the AFE (Table 1), they have been found to be necessary under certain conditions. When directly sensing biosignals with differential leads (i.e., ECG, ECoG, or EMG), a drifting dc offset voltage has been observed, which can cause the inputs to the first stage to drift out of the dc voltage input range of the instrumentation amplifier. To avoid this issue, we populate a passive high-pass filter in the front-end filtering stage of the AFE and leave it out for smaller and higher frequency recording where high CMRR is paramount. A similar issue is also observed when providing power to the Bionode using a high frequency inductive link. High frequency RF noise can couple onto the leads and traces of the Bionode when inductively powering.

Table 1. Measured Performance Characteristics of the Bionode AFE

	No front-end filters	Low-pass front-end filter	Bandpass front-end filter	Units
<i>Gain</i>	60	60	59.9	dB
<i>High-pass cutoff</i>	10.47	4.9	6.0	Hz
<i>Low-pass cutoff</i>	1,410	1,480	1,460	Hz
<i>CMRR</i>	100	43	72	dB
<i>Input Impedance</i>	100,000	3.61	2.03	M Ω
<i>Input-referred noise</i>	51.85	101	97.3	nV/ $\sqrt{\text{Hz}}$

We remove this noise by populating a passive low-pass filter in the front-end filtering stage of the AFE. If operating the Bionode under conditions where both problems may occur, then we populate a passive band-pass filter. Alternatively, we can bypass all of the front-end filtering section by populating the R_1 and C_1 pads with zero-ohm resistors and not populating the R_2 or C_2 pads; providing input channels with much higher differential input impedance and CMRR. When recording small signals requiring high differential gain, maximized CMRR is necessary to cancel noise common to both differential inputs. Additionally, high CMRR is needed when stimulation artifact cancellation is required, because the stimulation artifacts are common to both differential inputs.

3.4 First Stage Differential Gain

The first stage consists of an instrumentation amplifier (INA333) that differentially amplifies its input signal. The INA333 is used because of its high input impedance (100 G Ω) and low current draw (50 μA). We typically set the gain of the INA333 to 20 dB by setting R_G to 11 k Ω . For higher CMRR, higher first-stage gain settings should be used.

3.5 Second Stage Gain and Filtering

The second stage consists of an inverting band-pass filter [13] using an operational amplifier (OPA2313). The OPA2313 is used because of its sufficient gain bandwidth (>1MHz), low noise (25 nV/ $\sqrt{\text{Hz}}$), and rail-to-rail output. The OPA2313 has the added benefit of being available in a dual-package form factor allowing one IC to be used for both AFEs. The gain and bandwidth of this stage can be set individually by choosing appropriate component values for R_S , C_S , R_P , and C_P [14]. The gain for this stage is typically set to between 20 and 50 dB. Table 2 contains values for all of the passive components in the AFE that we have used when measuring respiration (via a thermocouple), ECG, ECoG, and CNAP signals. Note that for neural signals, we chose a high-pass filter to remove motion artifact for the specific application of seizure detection. Typical neural recordings, which require sub-1Hz recordings can be achieved by altering C_S and R_S . Also, using smaller values for R_1 would help reduce input referred noise.

The outputs of the each of the AFE's are routed directly into two of the NRF51822 microcontroller's ADC inputs. The NRF51822 is powered at the same (± 0.9) voltages that power the AFEs, which remove the necessity for the outputs of the second stages to be transformed into single-ended signals. This allows them to be routed directly into the ADC inputs of the microcontroller. Depending on desired device size, and sensitivity to noise at the input, these supply voltages can be generated jointly or separately for AFE and microcontroller. The NRF51822 microcontroller's ADC can be configured to acquire samples at either 8-bit or 10-bit resolution with a total sample rate of up to 25kHz, which is selectable by the user via the bidirectional communication interface (Section 5).

Table 2. Passive Component Values for Desired Gain and Bandwidth for Various Biosignals

	Respiration	ECoG	ECG	CNAP	Units
<i>Desired Gain</i>	70.5	60	54	60	dB
<i>Desired Bandwidth</i>	0.53–371.6	3.62–1,400	3.62–1,500	15–2,500	Hz
R_1	10	20	20	Short	k Ω
C_1	Short	100	100	1,000	nF
R_2	Open	1,000	1,000	100	k Ω
C_2	1	0.1	0.1	Open	nF
R_G	11	11	11	11	k Ω
R_S	30	20	20	10	k Ω
C_S	10,000	2,200	2,200	1,000	nF
R_P	10,000	2,000	1,000	1,000	k Ω
C_P	0.039	0.047	0.1	0.053	nF

Fig. 4. Wirelessly acquired biopotential signals from freely behaving rodents. (a) Respiration signal acquired using a thermocouple implanted in the nasal cavity of a rat. (b) ECoG signal acquired from the cortex of a rat at the end of a seizure using a differential pair of helical leads. (c) ECG signal acquired four days after implantation. (d) ECG signal acquired twenty days after implantation.

Two more AFE channels can be added to the Bionode implant by via a two-channel AFE daughterboard containing two AFE channels. The daughterboard's AFE outputs are connected to two additional ADC inputs on the microcontroller on the Bionode mainboard.

3.6 In Vivo Results

Twenty-seven rats have been implanted with 4-input-channel Bionodes configured to record respiration, ECoG, and ECG signals in the lead I and lead II positions. Examples of signals acquired during these studies can be seen in Figure 4. All signals depicted in Figure 4 were acquired wirelessly from freely behaving rats.

4 STIMULATION

Many open-loop implantable systems have been designed to either record biological signals [15] or to produce a physiological response by means of electrical, mechanical, or optical excitations

[16, 17]. For a closed-loop study, however, both capabilities are required. Therefore, the Bionode is designed with a flexible single electrical stimulation channel to supplement its recording capabilities. Alternatively, the stimulation channel can drive an LED for optogenetic stimulation if desired [18].

4.1 Stimulation Circuit Design Considerations

When designing an electrical stimulator, the specific type of stimulation that is needed must be considered. Constant voltage stimulation between a reference and counter electrode is relatively easy to implement but suffers from the drawback of variable charge injection due to the capacitive nature of the electrode/body interface, leading to variable and therefore unreliable stimulation efficacy. Constant current (galvanostatic) stimulation is more difficult to implement but has the advantage of attaining a consistent and knowable charge injection throughout a stimulation pulse [19]. We implement a constant current stimulator on the Bionode using a Howland current source to ensure stimulation consistency and efficacy.

Another consideration in electrical stimulation is the flexibility of the stimulation waveform generated. Stimulation parameters such as amplitude, pulse width, frequency, and charge balancing are adjusted to meet the safety and efficacy needs of a given study. For example, while using a monophasic pulse train stimulus will likely result in an increased amount of action potential responses in nerves, this stimulus waveform will also likely cause tissue damage and electrode erosion over time. This might be sufficient for short-term acute studies, but for long-term chronic experiments, a charge-balanced biphasic pulse train is more appropriate to prevent future tissue and electrode damage in the subject. The tradeoffs of efficacy and safety in stimulation protocols are studied at length in the literature [20]. The Bionode allows the stimulation amplitude, pulse width, and frequency to be defined by an outside user in real time using its bidirectional communication capabilities (Section 5). For the long-term safety reasons mentioned previously these parameter choices force the stimulation to be biphasic and charge balanced, although a simple firmware change will allow for non-balanced and/or mono-phasic stimulation if needed or desired.

A final important consideration in electrical stimulation is the accuracy and precision of the output of the stimulation circuit. Safe stimulation requires an accurate delivery of the desired stimulation waveforms. Unbalanced pulses, inconsistent pulse delivery times, and DC offsets on the stimulation waveform can cause unintended damage to the nerve and compromise electrode integrity. The Bionode is measured to have an acceptable charge balance ($\leq 0.3\%$ error) and has the added safety of a stimulation glitch switch built in to prevent unintended charge release during device startup.

4.2 Stimulation Circuit Design

We construct the constant current stimulation waveform using a current source (LT6375) driven by a DAC7551 digital to analog converter (DAC) as seen in Figure 5.

The LT6375 improved Howland current source (HCS) converts a control voltage provided by the DAC into a current waveform to achieve constant current stimulation [21]. We prefer the HCS topology over other topologies like current mirroring or electrode polarity switching (where the positive and negative electrodes are physically switched), because the HCS can generate reliable symmetric bipolar current pulses. It is difficult to achieve symmetric pulses using current mirroring topologies due to part tolerances, and electrode polarity switching can sometimes create asymmetric responses in stimulated nerves due to the physical change in anodic and cathodic electrode placement.

Fig. 5. Constant current stimulation is generated via an LT6375 Howland current source. The output of the Howland current source is set by the microcontroller on the Bionode via a 12-bit digital-to-analog converter (DAC7551). A comparator connected to the output of the DAC7551 compares the DAC output to ground, which allows the microcontroller to automatically compensate for DC offset errors presented by the DAC7551. A normally grounded control switch is used to ensure that unwanted stimulation does not occur during the Bionode power-on sequence. To ensure true biphasic stimulation, the positive stimulation electrode swings around the negative stimulation electrode, which is directly tied to the Bionode's ground. The positive stimulation electrode is AC coupled to the stimulator output through a DC-blocking capacitor (C_D) to ensure that unwanted DC stimulation is blocked. During startup and between stimulation pulses, the output of the stimulator circuit is grounded via a normally closed switch, which discharges C_D , and shunts any unwanted stimulation output to ground.

In the LT6375, the output current I is related to the control voltage V_{CTRL} by the equation:

$$I = \frac{V_{CTRL}}{R_S}. \quad (1)$$

Here, R_S is a current limiting resistor, which we choose while populating the Bionode PCB such that the specified stimulation current amplitude and precision are met. For example, let us say the Bionode is designed to provide a maximum stimulation current of 1mA through a 10kΩ electrode impedance. Because the output voltage range for the DAC, which provides V_{CTRL} is -0.9 to 0.9 V, R_S is set to 800 Ω; allowing the HCS to provide current outputs ranging from -1.125 to 1.125 mA. To drive this current across a 10 kΩ electrode impedance, the HCS is powered by a ± 10.5 V supply allowing a maximum voltage of 10.5V to appear at the output terminal.

Stimulation waveforms are created by the 12-bit DAC7551 DAC, which is controlled by the Bionode's onboard NRF51822 microcontroller via a serial peripheral interface (SPI). These stimulation waveforms are biphasic rectangular pulses defined by the user in terms of amplitude, pulse width (T_{PW}), interphasic delay (T_{IPD}), and pulse repeat time (T_{PRT}) (Figure 6).

The user defines these parameters using the Bionode DataView application (Section 5), which subsequently instructs the Bionode to set interrupt registers in its onboard NRF51822 microcontroller. These interrupt registers define the stimulation waveform by specifying when DAC output voltage updates must occur.

A single-pull double-throw (SPDT) switch between the DAC output and the HCS input avoids a documented start-up glitch on the output of the DAC that appears when the DAC is first powered on. If not avoided, then this glitch will cause the HCS to output an unwanted stimulus pulse every time the Bionode is powered on. This switch is controlled by the onboard NRF51822 microcontroller and has a pull-down resistor attached to the control line, which ensures that the switch is in position 0 even when the microcontroller is powering on. When at position 0, the switch connects the V_{CTRL} line of the HCS to ground, causing the stimulator to not output any current. When

Fig. 6. The biphasic stimulation waveform is defined in real time by the user via the Bionode's bidirectional communication interface. The aspects of the stimulation waveform that are settable by the user are its amplitude, pulse width (T_{PW}), interphasic delay (T_{IPD}), and pulse repeat time (T_{PRT}).

Table 3. Performance Characteristics of the Bionode Stimulator

	Value	Units
Voltage headroom	10.5	V
Current amplitude ¹	0.005–1.050	mA
Current amplitude resolution	4.4	μ A
Pulse width (T_{PW})	50–8.36e6	μ s
Pulse width resolution	1	μ s
Pulse rate	1e-5–20	kHz
Charge balance error ²	<0.3	%

¹Over a 10k Ω load.

²PW = 200 μ s, amplitude = 500 μ A.

at position 1, the switch connects the output of the DAC to V_{CTRL} , allowing the DAC to control the current output of the stimulator circuit. For safety reasons, the switch is only set to position 1 when the user has specified that stimulation should occur. Table 3 shows a list of key performance specifications for the stimulator.

Initially, the comparator, blocking capacitor (C_D), and discharge switch seen in Figure 5 were not included in the stimulator circuit. We added these elements to the stimulator circuit after we observed unwanted DC offsets in the stimulator output. Some of these offsets were due to documented offsets that exist in the DAC7551. The comparator allows the microcontroller to determine if the DAC7551 is properly centered around ground by periodically reading the output of the comparator between stimulation pulses and updating the DAC output to compensate. We added the blocking capacitor C_D to further ensure that no unwanted DC offsets in the stimulator are transferred to the positive stimulation electrode. Between stimulation pulses, the output of the stimulator is connected to ground via the discharge switch, which discharges C_D and shunts any unwanted stimulation output to ground. The discharge switch is normally closed, so unwanted stimulator circuit outputs experienced during startup are shunted to ground as well.

4.3 In Vivo Results

We tested stimulation and recording with the Bionode on a rat under isoflurane anesthesia [22]. Body temperature was controlled to 36.5–37.0°C. Twisted pair 125 μ m insulated stainless steel electrodes were placed in left fimbria and right CA1 stratum radiatum. In this configuration, the post-synaptic response is mediated by axons of CA3 pyramidal neurons on the left and is recorded as a negative wave lasting about 7ms. The six stimuli delivered at 20ms reveal the phenomenon of

Fig. 7. Evoked responses in the hippocampus *in vivo*. Responses recorded in the right hippocampal CA1 stratum radiatum evoked by stimuli to the left fimbria. Arrows mark the stimuli and grey circles mark the peak postsynaptic responses.

frequency potentiation, as expected for this pathway (Figure 7). Each stimulus pulse was of the form of a biphasic negative-leading pulse with an amplitude of 1mA, a pulse width of 100 μ s, an interphasic delay of 100 μ s, and a pulse repeat time of 50ms.

5 BIDIRECTIONAL COMMUNICATION

Bidirectional communication (the ability to transmit and receive data) greatly increases the flexibility and possible application use of an implantable device. Not only does the ability to transmit data remove the burden of on-board data storage from the implantable device, it also allows the device to communicate its current status and settings in real time. Furthermore, the ability to receive data allows the implantable device to be configured, calibrated, and instructed before, during, and after implantation; increasing its adaptability to varying circumstances. An implantable device that can both receive and transmit data has the added benefit of allowing an external user or system to reactively send instructions to the implantable device based on recorded data obtained by the implantable device, effectively creating a closed-loop system.

While the benefits of bidirectional communication are great, it poses some specific challenges to the design of a small, power-efficient implantable device. These challenges, namely, power consumption and data robustness, are addressed in the design of the Bionode, and our custom bidirectional communication system is described here.

5.1 Bionode and Base Station Firmware

The major challenge of implementing bidirectional communication in an implantable device is handling the increased power consumption introduced by radio communication circuitry. In many cases, including in the Bionode, the most power-hungry system on an implantable device is the transmit/receive radio. Power consumption for the Bionode is greatly reduced while transmitting and receiving data by tightly coordinating when data transmissions occur.

The Nordic NRF51822 microcontroller on the Bionode handles all data telemetry moving into and out of the device. This microcontroller was specifically chosen because of its low-power sleep states, small size, on-board radio, and on-board analog to digital converter (ADC). Because this microcontroller only draws 2 μ A of current when it is in sleep mode and draws 20mA of current when the radio is activated, an interrupt-driven firmware design was developed to keep the microcontroller in sleep mode with the radio deactivated as long as possible.

Bidirectional communication is achieved under this scheme by enforcing a coordinated handshake protocol with the custom designed external Base Station to facilitate all communication between the Bionode and any outside user (Figure 8). After the Bionode acquires 40 data samples from its ADC, the Bionode's microcontroller initiates a data-packet transmission to the base station

Fig. 8. The Base Station facilitates all communication between the PC and the Bionode. The user can specify Bionode recording and stimulation parameters or Base Station settings by sending an update packet to the Base Station via the PC application. The Base Station then relays the packet to either to its own register update or to the Bionode during the next Base Station handshake. All data recorded by the Bionode is packetized and wirelessly transmitted to the Base Station via the Bionode's onboard radio. These packets are then relayed to the PC the Base Station's Wi-Fi link to the PC. All incoming data to the PC can be stored on the PC's onboard hard drive.

using the onboard 2.4GHz ISM band radio. In most cases, the radio is only activated during this transmission, which lasts approximately 1ms. However, the 100th data packet initiates a handshake with the Base Station. Immediately after transmitting the 100th data packet, the Bionode sets its radio to receive mode, and listens for a data packet from the Base Station for no more than 10ms. This gives the base station an opportunity to send a single data packet to the Bionode. This data packet contains a 45-byte long payload, which is used to set firmware registers in the Bionode microcontroller that store data acquisition, stimulation, and communication settings. Because the payload contains values for all writeable firmware registers on the Bionode, the Bionode is fully configured and instructed during this single transmission.

This handshake driven communication scheme allows the Bionode to transmit acquired data rapidly, while maintaining the ability to receive data from an outside source with minimal radio activation time. For example: given a data acquisition sample rate of 5kHz, the Bionode's radio will transmit 125 data packets per second and initiate a handshake once every 800ms. Given the described radio on-time, bidirectional communication can be achieved with the radio being deactivated 86.7% of the time. If this handshake latency is too large for a particular application, then it can be reduced at any time by either increasing the sample rate or by reducing the handshake packet interval.

Another challenge in any wireless communication scheme is increasing data robustness. To properly analyze any data recorded by the Bionode, the ability to identify when data has been corrupted or lost is essential. Data can be corrupted or lost during wireless transmission if it is blocked by something that can absorb RF energy, if a nearby device communicating on the same frequency creates interference, or if the distance between the Bionode and the base station exceeds the transmission range of the Bionode. Data can also be lost if the Bionode suddenly loses power during data acquisition or transmission.

We design methods into the Base Station to detect corrupted or lost data packets. Before sending data packets to the Base Station, the Bionode appends a 2-byte cyclic redundancy check (CRC) to

Fig. 9. The Bionode DataView application provides access to all of the settings for the Bionode and Base Station. All incoming biopotential recordings can be displayed in real-time.

the end of the packet. The base station uses this CRC to determine the validity of all incoming data packets. Corrupted data packets failing this CRC are discarded by the Base Station. To make lost data packets detectable, the Base Station appends a time stamp at the end of all incoming packets. These time stamps can be used to determine not just if data samples are missing from the acquired data stream, but how many data samples are missing, which is crucial for data analysis.

Finally, the Bionode can request a re-transmission of a missed handshake by simply not incrementing its packet ID counter whenever an expected handshake is not received. This causes the Base Station to continually re-transmit the handshake packet until the Bionode indicates that it has received the handshake by incrementing its packet ID counter.

5.2 PC Graphical User Interface

Users communicate with the Bionode via the Base Station using a software application called Bionode DataView. This application is implemented in Python (Figure 9). We use Python, because it is open source and easily portable to Macintosh, Windows, and Linux operating systems, allowing the application to be built and deployed to a wide range of computing devices. To further increase the ease of deployment, we designed the base station to create its own Wi-Fi connection, which allows any device with Wi-Fi capabilities to communicate with the base station without the need of additional drivers. The Bionode DataView application provides a graphical user interface that displays all acquired data and current Bionode and Base Station settings in real time. The user interface allows the user to set Bionode stimulation parameters as well as initiate and terminate stimulation sessions. All incoming data packets can be recorded into a binary data file. These raw binary files can be either analyzed directly or exported as .wav files and easily imported by multiple data analysis tools (e.g., MATLAB, Spike2, etc.)

6 COMMUNICATION ANTENNA AND MATCHING NETWORK

Reliable wireless communication between the Bionode and the Base Station is essential to the Bionode's wireless bidirectional communication capabilities described in the previous section. Wireless

Fig. 10. The L-section matching network is located between the balun and the trace antenna.

Table 4. Antenna Driving Impedance Measured at 2.45GHz

Loading Condition	Measurement 1	Measurement 2
<i>No phantom</i>	$18.363 + j51.689$	$18.565 + j51.964$
<i>7mm above phantom</i>	$18.658 + j51.703$	$19.024 + j51.895$
<i>2mm above phantom</i>	$20.767 + j49.599$	$19.135 + j46.094$

communication with the Bionode is achieved with a system that exploits far-field radiation in the industrial-scientific-medical (ISM) band centered at 2.45GHz and involves hardware onboard the Bionode including the microcontroller's radio, a balun, a matching network, and an antenna. The 2.45GHz operating frequency offers suitable energy transmission through tissue [23] and permits antennas that conform to the physical constraints of the Bionode implant to operate with satisfactory efficiency. The balun and supporting components were implemented following recommendations by the manufacturer of the microcontroller. The antenna was implemented as a trace on the Bionode Mainboard with a length of 15.5mm, the best realizable approximation of the objective 18.4mm quarter wavelength of the fields to be radiated due to size constraints. The matching network was designed according to the analysis described in this section.

6.1 Matching Network Theory and Methods

Effective impedance matching between the antenna and the microcontroller's radio maximizes wireless communication capabilities by increasing reception sensitivity and total radiated power during transmission [24–26]. We implemented the matching network on the Bionode using an L-section design [26] using a pi-network (Figure 10). We designed the impedance matching network using traditional calculations [26] incorporating antenna driving impedance data that we obtained by experimental measurement using an Agilent E5071B vector network analyzer (VNA). We connected the VNA to a Bionode mainboard via an SMA connector with its center pin and grounded outer conductor connected to the antenna and ground of the PCB, respectively. We measured the driving impedance of the antenna at 2.45GHz under various conditions relative to a beef steak tissue phantom with 300g mass and 15mm thickness, designed to imitate typical loading conditions (Table 4). We used an averaged measured value of the antenna driving impedances to calculate the capacitance values, to implement the matching network demonstrated in Figure 10 [26].

The successful design of the antenna and matching network is demonstrated by the experimental measurement of the number of data packets dropped during a set duration of time. A Bionode was configured to transmit 10,000 data packets at a rate of 125 packets per second while being placed in three different orthogonal orientations within the WPT chamber. In all three orientations, the Bionode successfully transmitted over 99.7% of these packets.

7 POWERING

Active implantable devices requiring power in the milliwatt range are typically powered using wireless EM fields, batteries, or a combination of the two [27, 28]. Other powering methods such

Fig. 11. Each coil (modeled here by C_{coil} and L_{coil}) is connected directly to an impedance matching network, which maximizes power transfer efficiency. Acquired AC signals are then rectified using a dual-ended rectifier to produce positive and negative DC voltages. Both rectifier outputs are then passed through passive low pass filters to remove high frequency RF noise. Positive and negative power rails for the Bionode are generated by regulating the filtered outputs of the rectifiers. Higher voltages needed by the stimulator are generated by passing the filtered rectifier outputs through positive and negative voltage doubler circuits. Optional battery charging/discharging is handled by PMICs attached to the rectifier outputs.

as ambient energy harvesting, optical coupling, or ultrasonic excitation become difficult to implement when higher power is needed, deeper implantation sites are required, or small implant size is paramount [27]. Battery solutions offer a robust method for powering implantable devices by providing stable powering during the battery's lifetime. However, this solution comes at the cost of requiring a relatively large footprint that scales with capacity [29]. Furthermore, implantable devices relying on battery power have an inherently limited device lifetime.

7.1 Wireless Powering Systems

Our way of powering an implantable device is to generate a circulating magnetic field inside a WPT chamber using resonant cavity theory [30], which removes the necessity for any primary transmit coils, because the entire WPT chamber resonates. Secondary coils in the implantable device can harvest energy from the magnetic field as long as the device is appropriately oriented inside the WPT chamber. Thus, the WPT chamber provides a space where a freely moving implanted rodent can live while the implanted device is wirelessly powered [30]. Alternatively, an external wand can be used to generate a magnetic field to power and recharge the device when the WPT chamber cannot be used (e.g., when implanting a subject that cannot fit inside the chamber). The Bionode leverages either method of wireless powering through a custom designed powering module called the Powernode (Figure 11).

7.2 Powernode

The Powernode is designed as a modular board that can provide sufficient power to the Bionode. Figure 12 illustrates the typical power consumption of the Bionode while acquiring data at 5,000 samples per second.

To accommodate the powering requirements of the Bionode, the Powernode is designed to provide 16mW of average power with the ability to produce up to 60mW of peak power. This power is transferred to the Bionode through voltage rails that are used by the Bionode's acquisition and stimulation circuitry (Sections 3 and 4).

The Powernode uses two secondary coils oriented orthogonally to each other to collect energy from the circulating magnetic field inside the WPT chamber. The orthogonal orientation of these

Fig. 12. Power consumption greatly increases during the activation of the Bionode's onboard radio as illustrated in this figure between $t = 0$ and $t = 0.5$, and $t = 1.7$ and $t = 2.2$ ms. Power consumption also increases whenever the microcontroller on the Bionode initiates a sampling of the onboard ADC as illustrated by the periodic ~ 10 mW spikes in this figure.

two coils allows the Pownode to more consistently collect energy while the implant is in varying orientations within the WPT chamber. The power transferred to each coil is maximized via an impedance-matching admittance inverter network on the Pownode tuned to the resonant frequency of the WPT chamber (approximately 340MHz). This resonant frequency is determined by the geometry of the WPT chamber. This high frequency allows us to apply up to 2 Watts of power to the chamber while staying within SAR limits. The impedance matching network consists of two capacitors (C_P and C_S in Figure 11), which initially have values predicted by bandpass filter theory [31–33]. These capacitor values are further tuned based off of measured resonant responses of the system. Because the coils are perpendicular to each other and their rectifiers provide high reactance between the two coils, the coils minimally affect each other's energy transfer.

The AC voltages coupled onto each coil are converted into both positive and negative DC voltages using a full wave rectifier. High amplitude voltages coming out of the rectifier are clamped using Zener diodes to protect low-voltage circuitry on the Bionode. Furthermore, to provide stable voltage rails to the Bionode, we implement RC-based low-pass filters on both the positive and negative rectifier outputs to reduce coupled AC noise from non-idealities present in the rectifier. The rectified voltages are then fed into regulators to provide the digital and recording circuitry on the Bionode with accurate, low ripple voltage supplies. To supply the higher headroom voltage required by the Bionode's stimulation circuitry, we double both outputs of the full wave rectifier using a Texas Instruments TI7660 boost converter for the positive output and an inverting charge pump for the negative output. The outputs of these doubler circuits provide the voltages required by the Bionode's stimulation circuitry to drive its constant current stimulation output.

7.3 In Vivo Results

To determine the effectiveness of the Pownode's ability to provide power to the Bionode inside a WPT chamber, we analyzed the data gathered during a study involving a freely moving rat with an implanted Bionode. We placed the rat inside the WPT chamber for 1.6h, and continuously recorded two channels of biopotential data (ECG and respiration). During the recording, we manually tuned the driving frequency of the WPT chamber to maximize device on-time. PID and timestamp information (Section 5) in the recorded data file can then be used to determine that the Bionode was receiving sufficient power to acquire and transmit biopotential data 85.43% of the time. While the powering of the Bionode during this session is not perfect, it is sufficient to provide useable biopotential signals over the duration of the study (Figure 4).

This method of wirelessly powering implantable devices addresses many of the issues present with powering devices inside freely moving rodents. However, improvements to power transfer efficiency can still be made. Secondary coil misalignment created when the rodent is aligned in certain orientations within the WPT chamber's circulating magnetic field can cause insufficient coupling to either coil, resulting in insufficient power generation for the Bionode. Furthermore, the resonant frequency of the WPT chamber is modified when the rodent changes radial position within the chamber, causing the Powernode to become de-tuned, which reduces the power transfer efficiency of the system. These challenges are currently being addressed by incorporating dynamic impedance matching on both the WPT chamber power source as well as the Powernode to allow the system to dynamically tune itself in response to the rodent's radial motion [34]. No wireless powering scheme can provide 100% on-time, and so a determination of what is good enough falls to the application needs. For required on-times approaching 100%, rechargeable batteries are added to the Bionode as described below.

Two LIR1220 lithium-ion rechargeable coin-cell batteries can be connected to the Powernode to provide a supplemental power source. Each battery is connected between ground and either the positive rectifier output or the negative rectifier output via two Linear Technology LTC4071 power management integrated circuits (PMICs). These PMICs ensure that the batteries are connected to the outputs of the rectifier circuits whenever the coils are unable to provide sufficient voltage through the rectifier. Furthermore, whenever excessive power is provided to the Powernode through the coils, the PMICs direct this power to recharge the batteries. When equipping Bionodes with these backup batteries in chronic implant studies, we have achieved 100% on-times for over 3h at a time. These batteries also allowed us to successfully implant the Bionode into three pigs for a multi-week chronic study [35]. Because the pigs could not fit into the WPT chamber, we activated and charged the implanted Bionodes using the external wand.

8 MANUFACTURING/PACKAGING

Successfully fabricating and packaging a device for chronic implantable applications depends greatly on miniaturized form-factors and robust device encapsulation. All physical aspects of the Bionode implant are designed with the goal of creating an adaptable, inexpensive, robust, and fully implantable device with a form factor allowing for long-term chronic implantation in rodents or minimally invasive implantation in humans. These design considerations were further constrained by the desire to use only COTS components as well as a need to maximize manufacturing yield. The components of the Bionode that most define its form factor and manufacturability are its printed circuit board assemblies (PCBAs), electrodes, wireless powering coils, and packaging used to encapsulate the implant.

8.1 PCBA Considerations

The Bionode implant contains two PCBAs: The Bionode mainboard, and the Powernode. The mainboard contains the AFE, stimulator, microcontroller, radio, and antenna. The Powernode contains all circuitry necessary to provide power rails to the Bionode mainboard and wirelessly recharge battery if used (Section 7). Because these two boards were developed in a modular fashion, each board could be designed, optimized, fabricated, and tested independently. The ability to fabricate and test the two Bionode PCBAs separately made manufacturing defects easier to find and repair, which increased device manufacturing yield. This approach also allowed a modular design where different Powernodes (e.g., with and without rechargeable batteries) could be used in different applications.

Both PCBAs were optimized for size by selecting small component packages and laying out all pads and traces on the PCB using a minimum spacing and width of 0.127mm wherever possible.

The Bionode mainboard is a six-layer board, while the Povernode is a two-layer board. Both PCBs were fabricated by Advanced Circuits and hand-populated by researchers and technicians at the CID at Purdue University.

8.2 Electrode Considerations

A variety of electrodes and leads can be successfully used with the Bionode for both recording and stimulating including nerve cuffs, helical leads, pressure sensors, thermocouples, deep brain electrodes, and bone screws. All these electrodes connect to the Bionode by means of low-impedance commercial pins. This interface allows virtually any electrode to be terminated with a 0.46–0.51mm diameter pin and connected to the Bionode.

8.3 Coil Considerations

Both wireless powering coils (Section 7) were hand-wound by the authors at the CID using 22-gauge wire. The front-coil has a 7mm inner diameter and the top-coil has a 5mm inner diameter. These dimensions were constrained so that the coils could fit inside the cylindrical package described next. We optimized for number of turns and wire-gauge choice by iterative experimentation.

8.4 Packaging Considerations

To chronically implant the Bionode in a rodent model for any length of time, it must be encapsulated in a package that insulates it from tissue. Many materials including polymers, metals, ceramics, and glasses have been used in recent years for hermetic and non-hermetic implantable device packaging [36–39]. While metal packages with glass or ceramic feedthroughs have become popular for long term medical implants, the sealing processes often require highly controlled environments and expensive precision equipment (i.e., infrared lasers to melt glass or laser-beam welders to fusion weld metals). Metal packaging also may require powering coils and communication antennas to be placed outside of the packaging to avoid power and communication losses; further complicating the packaging process [36].

With these considerations in mind, the inexpensive and flexible option of using medical grade epoxy to encapsulate the Bionode was chosen, which has been successfully verified as a legitimate option in other research [37, 40]. Fully encapsulating the Bionode in medical grade (Hysol Loctite M-31CL) epoxy was achieved using a multi-step process illustrated in Figure 13. Prior to encapsulation, a custom 3D printed case is created to shield the Bionode from the epoxy. All electrode connections are made via a feedthrough board, which connects the electrode pins to the Bionode mainboard. The main function of the feedthrough board is to prevent leakage into the implant via faulty leads. Lead breaks are often a cause for implant failure [41]. The feedthrough board isolates the leads from the inside of the implant case, which ensures that broken leads do not provide a path for fluid to enter the implant.

The packaged Bionode is 3.5cm long with a diameter of 1.5cm and weighs 9g, which is comparable to other non-ASIC systems [42, 43]. This packaging method provides excellent reliability for short to medium term chronic studies. To date, using this packaging method, 76 Bionodes have been successfully implanted for chronic studies lasting up to 71 days. No packaging failures have been observed during these studies.

This packaging approach optimizes for customization and flexibility in the design and test cycle of the implantable device. Changes in the board shape, size, and architecture can be accommodated with quick changes to device casing and feedthrough board layout, providing for fast turn-around and implementation. In addition, the interconnects utilized by the feedthrough board can be modified to meet the ever evolving attributes of future devices [44], such as capacitive feed-through

Fig. 13. A cross-sectional view of the packaging of the Bionode. (A) A feedthrough cap containing electrode receptacles and mainboard connector is constructed. (B) A Bionode and Powernode is connected to the feedthrough cap, and a 3D printed case is glued to the feedthrough cap. (C) A plug is connected to the outside of the feedthrough cap and epoxy is used to create a well above the feedthrough cap. (D) A second coating of epoxy is applied around the entire 3D printed case and the plug is removed. (E) Electrodes are connected to the feedthrough cap, and the well above the feedthrough cap is insulated with a layer of silicone. Finally, the implant is fully encapsulated with one more layer of epoxy.

systems [45, 46]. Unlike other hermetic sealing examples [38, 47, 48] have used alternative materials and methods, the materials and tools used in this method are relatively inexpensive and easy to obtain.

In a recent study involving the long-term chronic implantation of the Bionode in rats, the 3D printed case was replaced with a glass cylinder. This reduced the amount of epoxy needed to seal the device, because the glass case does not need to be fully encapsulated in epoxy. One of these devices is pictured in Figure 1.

The use of removable packaging facilitates the ability to adjust and reuse explanted Bionodes. For devices that do not require any adjustments to the Bionode hardware, the top layer of epoxy surrounding the feedthrough well can be removed using a band-saw or rotary tool. Once the epoxy is removed, the old leads can be replaced with new ones, and the device can be re-encapsulated in epoxy. For devices needing adjustments to the Bionode hardware (e.g., devices needing different AFE passband values), the device can be completely removed from its packaging, adjusted, and then repackaged. To date, 15 Bionodes have been reused using this process, with some being reused multiple times.

9 CONCLUSION

The Bionode's verified ability to acquire chronic biopotential data from freely behaving rodents as well as concurrently stimulate and record from the nervous system has led to its widespread use in research projects at Purdue University and at other institutions. This widespread usage is further facilitated by proven fabrication and packaging methods that make the Bionode a viable low-cost, reusable, and modifiable research tool. Improvements to the wireless power transfer methods including the addition of dynamic impedance matching on both the Bionode and the external power source are currently being developed with the goal of improving powering performance. The use of only COTS components in the Bionode's design allows all aspects of the Bionode to be replicated and/or modified by a typical university lab. It is the authors' desire that the publication of the Bionode's design will enable more investigators to use implantable device technology in their electroceutical research.

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