Implantable Neuromodulation System

A Major Qualifying Project Report

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by

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Report Submitted to:

Professor Taskin Padir, Advisor, WPI

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Abstract

Neuromodulation, specifically spinal cord stimulation, has proven to be an effective treatment for treatment of various chronic pain symptoms. For this project, a prototype of a system capable of providing spinal cord stimulation through an implanted device was developed. The developed system was notable for its relatively small size and low power wireless communication using Bluetooth Low Energy. The implantable pulse generator is capable of providing biphasic pulses with amplitudes up to 25mA.

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Background

Neuromodulation Therapy

Neuromodulation is the process of controlling or modifying the function of the nervous system through the use of electrical stimulation. Therapeutic neuromodulation for the relief of pain was first documented by the researchers Wall and Sweet in 1967. They performed neuromodulation on a peripheral nerve. Researchers Shealy and Mortimer followed with stimulation of a nerves in the spinal cord that same year [1]. Modern applications of neuromodulation include pain relief and treatment of functional conditions like incontinence. It has become a versatile and attractive treatment option for clinical applications [2].

Spinal Neuromodulation for Pain Treatment

Neuromodulation provides pain relief through the mechanism of the Gate Control Theory of pain, published by Wall and Melzack. The theory states that two separate types of neural fibers carry sensory information to the brain. Thick fibers carry signals indicating sensations like touch, pressure, and vibration, while thin fibers carry pain signals. Pain relief is provided by stimulation of the thick fibers, which prevents pain signals from the thin fibers from being transmitted to the brain [3]. The gate control theory has proven over the course of more than 30 years to provide an excellent synthesis of many of the observations and theories of pain that have been developed [4].

Spinal cord stimulation has proven to be an effective method of pain relief for a variety of different types of pain. In one study of patients who suffer from failed back surgery symptom, more than 40% of the individuals who received spinal cord stimulation received at least 50% reduction in pain, as opposed to those who only received other conventional treatments, of whom only 9% received a 50% reduction in pain [5]. In a study evaluating treatment of patients experiencing chronic intractable pain treated with permanent implants which performed spinal cord stimulation, 52% of the patients experienced at least 50% continued relief of pain [6]. A literature review of many different studies on spinal cord stimulation "found that SCS had a positive, symptomatic, long-term effect in cases of refractory angina pain, severe ischemic limb pain secondary to peripheral vascular disease, peripheral neuropathic pain, and chronic low-back pain" [7].

Motivation

The goal of this project was to develop a prototype system demonstrating the capabilities required to provide wirelessly controlled neuromodulation from an implantable device capable of providing spinal cord stimulation. Many conventional systems rely on wired communication and are relatively high power. This system will aim to provide low power, wireless communication, and a small size implantable device. The system consists of two main components. The first component is a prototype of the implantable device with the capability to respond to wireless. The second major component was a device capable of sending wireless control signals to multiple stimulator devices, while providing a convenient interface for the user. A diagram of the desired system architecture appears below in Figure 1.

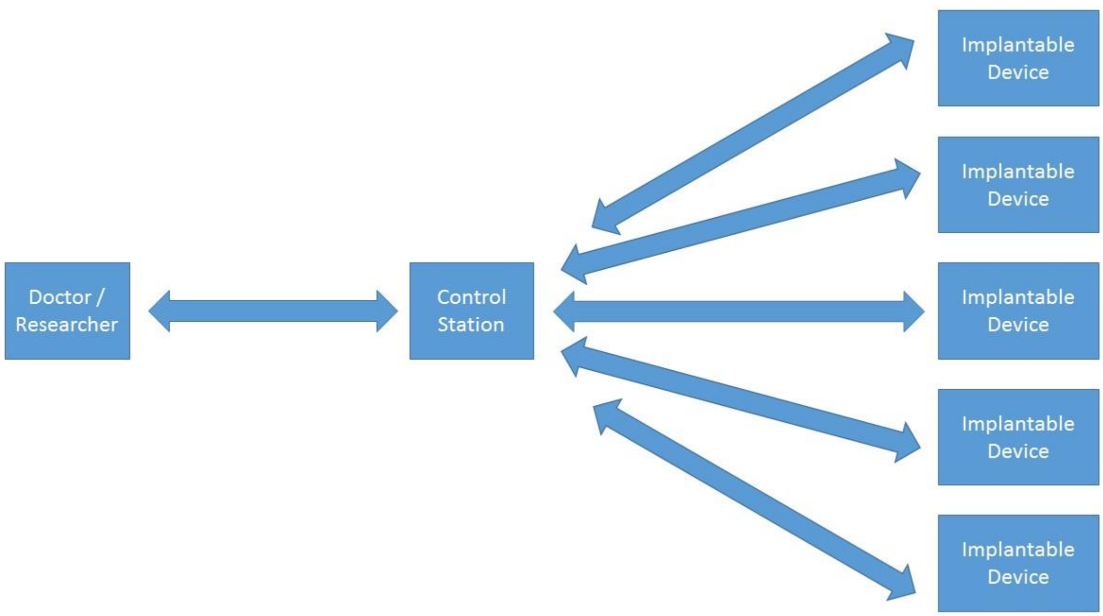

Figure 1: System Architecture Overview

Implantable Device Prototype

The goal of the prototype implantable device was to develop a self-contained unit displaying all the functionality necessary in an implantable neuromodulation device. Micro-Leads had chosen an ASIC for generating the neuromodulation waveforms, and chose TI's CC2650 microcontroller to provide wireless communication using Bluetooth Low Energy (BLE) and generate digital control signals for the ASIC. Creating the prototype would require implementation of TI's BLE stack software to establish the Bluetooth link, creating an appropriate message format for the wirelessly transmitted data, and designing a custom PCB.

Control Station Prototype

The control station prototype's function was to provide a method for wirelessly communicating with one or more of the implantable device prototypes over BLE. The goal was to include setting of stimulation parameters and device status information, and to provide the user with a convenient interface.

Design Methodology

Design of Implantable Device Prototype

Before the start of the project, Micro-Leads had acquired a test board for the ASIC to be used for the project from the ASIC manufacturer. This board featured the ASIC, an MSP430 microcontroller, and an FTDI USB to UART chip. A custom PC application, also provided by the ASIC manufacturer, communicated with the MSP430 via the FTDI chip, and in turn the MSP430 commanded the ASIC to generate appropriate waveforms.

Wireless Communication

The first step taken was to insert two CC2650 microcontrollers, incorporated in TI development kits, into the communication chain between the computer running the custom application from the ASIC designer and the MSP430 controlling the ASIC. One CC3650 development kit was connected to the computer, with an FTDI chip on the development kit board providing USB to UART communication from the computer to the CC2650. This development kit would transmit the data it received via UART over BLE to the second development kit. The second development kit then communicated the information to the MSP430 on the ASIC test board via UART. This process was undertaken to develop familiarity with the CC2650 and TI's BLE stack software, which was being used as a starting point for the project. An overview of this first system architecture is shown below in Figure 2.

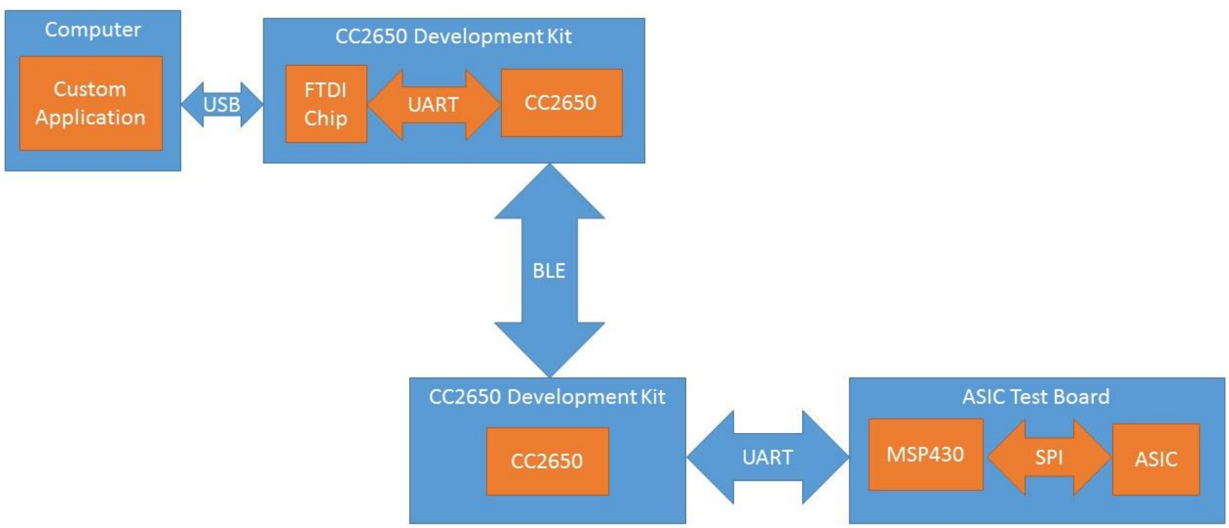

Figure 2: First System Architecture

The Bluetooth Low Energy stack from TI implements the framework defined by the Bluetooth Special Interest Group for Bluetooth Low Energy. This framework provides for two different types of devices, client devices and server devices. Client devices are responsible for issuing Generic Attribute Profile (GATT) commands and requests, and server devices respond to these requests. Server devices have one or more services, representing functions the device can perform. Services are groups of one or more characteristics, which are individual pieces of data related to performing the function of the service. These characteristics are read or written by the client device. Figure 3 below provides a visual illustration of the Bluetooth Low Energy architecture.

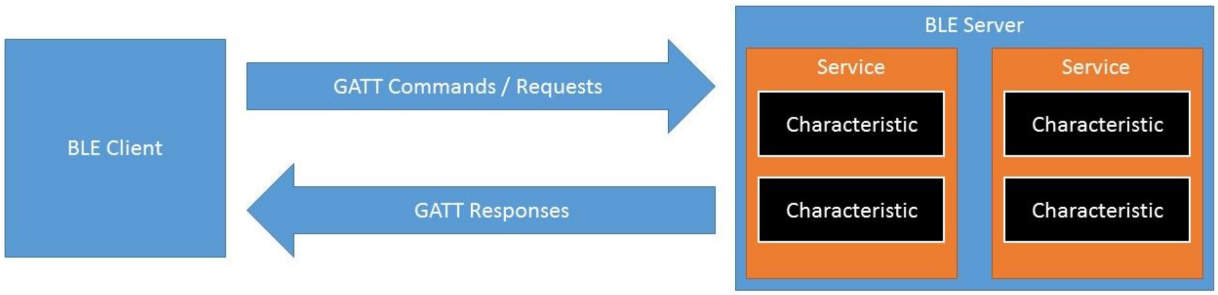

Figure 3: Bluetooth Low Energy Architecture

To provide a more concrete example of the Bluetooth Low Energy architecture, an illustration of an example architecture has been provided below. These figures demonstrate a cell phone communicating with a temperature sensor which provides the temperature based on an average of some number of recent temperature samples. Figure 4 shows an example of a GATT characteristic read request. The client (the cell phone in this example) requests to read the temperature characteristic. The server (the temperature sensor) responds with the temperature it has calculated. Figure 5 shows an example of a GATT write request. The client asks to write to the sample frequency characteristic, and the server responds with a message indicating the result of the operation.

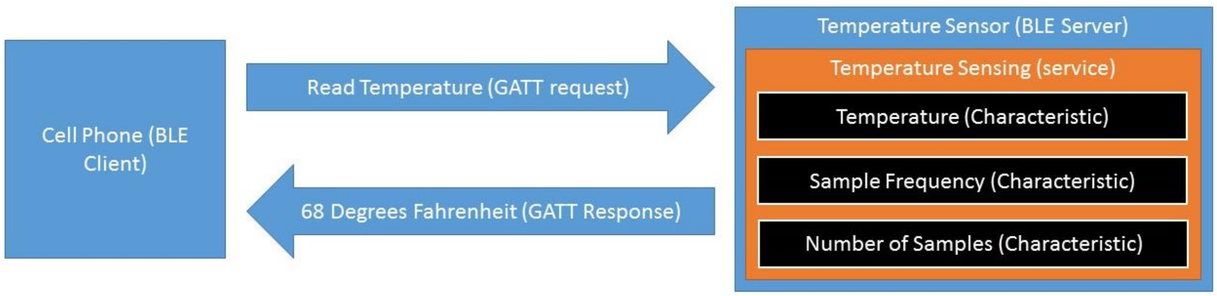

Figure 4: BLE Architecture Example – Read

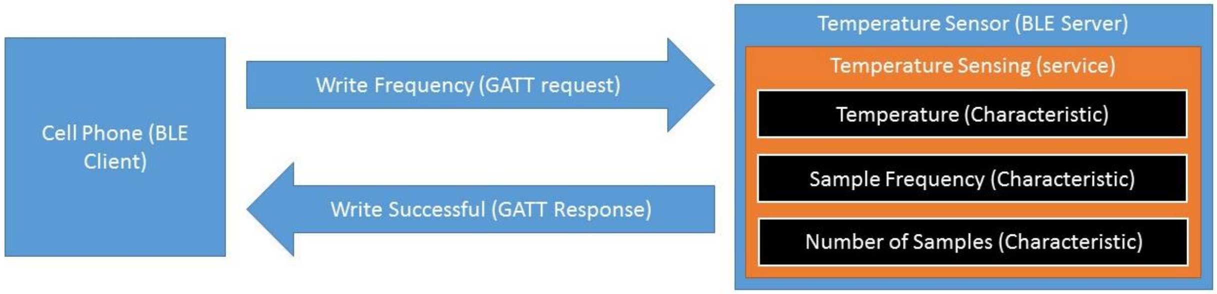

Figure 5: BLE Architecture Example - Write

For this project, a single custom service was implemented, which contained only one characteristic. The CC2650 development kit connected to the computer was set up as a client device, and the one connected to the ASIC test board was configured as a server device. The server implemented a custom service providing a single characteristic. The message generated by the custom application on the computer was written to this single characteristic by the client device. After the characteristic had been written, the server device relayed the message over UART to the MSP430 on the ASIC test board.

One significant challenge faced in the process of implementing this system was the size of the message generated by the custom PC application. The PC application generated a message that was several hundred bytes long. Bluetooth Low Energy has a maximum transmission unit (MTU) with a default value of 23 bytes. This required use of the GATT commands for long characteristic values, in which the messages include an offset field, indicating which segment of the characteristic each packet represents. However, the number of packets required to transmit an entire message proved problematic for the BLE stack architecture TI provides. The BLE stack architecture provided by TI operates using a FIFO queue of events that need processing. During testing of the transmission of the message from the CPU, it was discovered that holding up this queue for too long processing a single transmission event would cause the application to crash. In order to overcome this obstacle, a new structure for message transmission events was developed. Each event would result in the transmission of a single packet of the message. Then, if more message remained, the event would add another transmission event to the end of the queue. This “recursive” event generation method allowed for the transmission of sufficiently long characteristic values without tying up the event queue for too long.

After the wireless communication protocol had been debugged, software was written for the CC2650 to replicate the functionality of the MSP430 on the original ASIC test board. A new breakout board for the ASIC was acquired which featured the ASIC without a microcontroller to command it. The CC2650 evaluation board was connected to the computer by USB, and to this new evaluation board by jumper wires. No wireless communication was used for this step. The custom PC application was used to send messages to the CC2650 over UART, which in turn communicated with the ASIC using SPI to set waveform parameters. This setup was implemented in order to verify the ability to appropriately communicate with the ASIC, using the SPI bus and required control lines, without the added complication of implementing wireless communication at the same time. A diagram illustrating this second system architecture appears below in Figure 6.

Figure 6: Second System Architecture

Once the wireless communication and ASIC control projects had both been completed, the next step was to combine the two projects into one. In this iteration, the computer was connected to one CC2650 evaluation board via USB, and communicated with the CC2650 via UART. This microcontroller then transmitted the data it received from the PC to a second CC2650 via BLE. The second CC2650 was connected the new ASIC breakout board, and was responsible for controlling the ASIC to generate the desired waveforms. At this stage, the second CC2650 and ASIC were functioning as they would be expected to in the implantable device. An overview of this architecture is shown below in Figure 7.

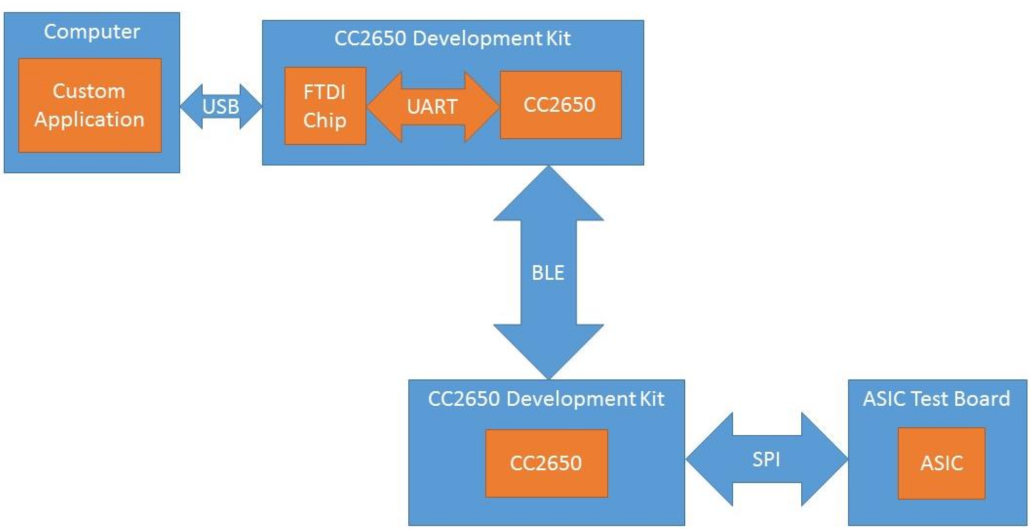

Figure 7: Third System Architecture

Printed Circuit Board Layout

Following development of appropriate software for an implantable device, a custom printed circuit board was designed. Included on the circuit board were the ASIC responsible for generating neuromodulation waveforms, the CC2650 microcontroller, and wireless power circuitry designed by an employee of Micro-Leads. This circuit board was designed to incorporate the functionality of the CC2650 development kit and the ASIC test board connected by SPI in the system architecture shown in Figure 7, in addition to providing for battery power of the device. The board was also designed with two different voltage regulation schemes available so that each could be tested for efficiency and effectiveness.

The two most significant challenges faced during design of this PCB were the design of the RF microstrip line to connect the CC2650 to its antenna and the goal of achieving a small size such that feasibility of implanting the device into humans or smaller animals could be demonstrated. For ease of implementation, an end-mount coaxial connector was chosen for the antenna for the board. This solution was determined because it was anticipated that it would be most likely to work without having to debug RF interference or trace antenna shape.

The design of the RF microstrip portion of the PCB was based on a reference design provided by TI. The reference design used was the CC2650EM-7ID. This design is for a 2 layer PCB that can be mounted onto the larger development kit board. The design also includes a trace antenna. A portion of the schematic for the design appears below in Figure 8. Shown below are the required power supply bypass capacitors, the 2 different required clock crystals, and the matching network for the antenna. All of these components were copied in the custom PCB.

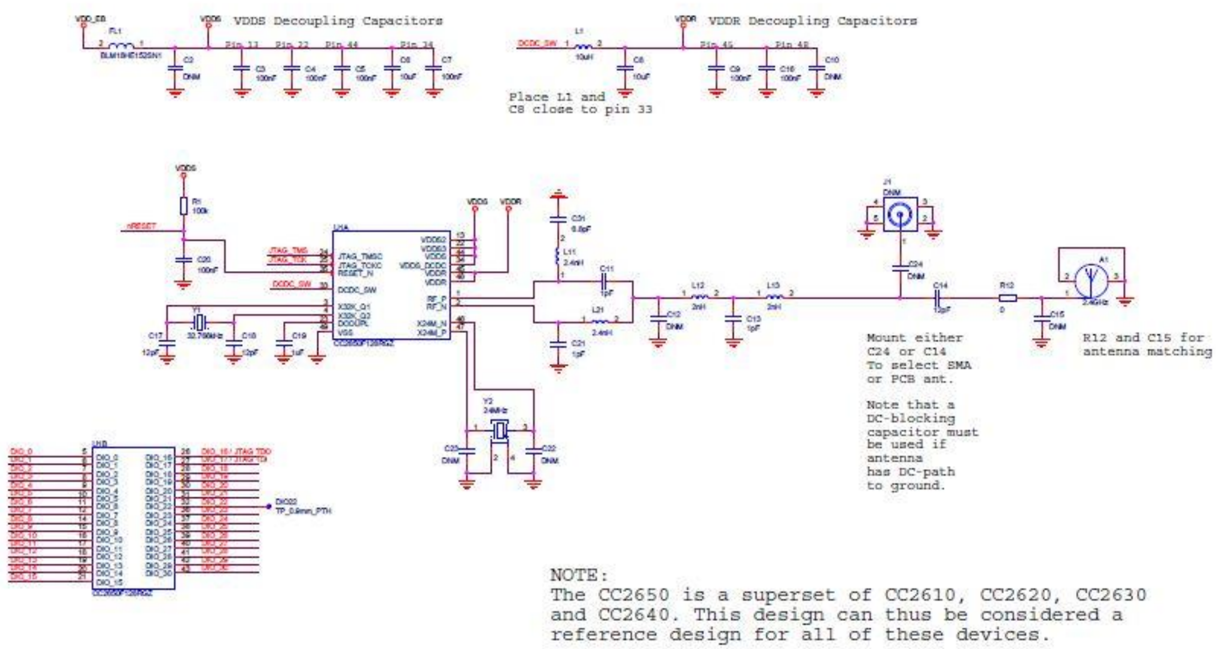

Figure 8: Reference Design Schematic

TI also supplied board layout files in the reference design, which were used to provide a template for the layout of the RF microstrip line as well as the layout of the clock crystals. The reference design layout is shown below in Figure 9.

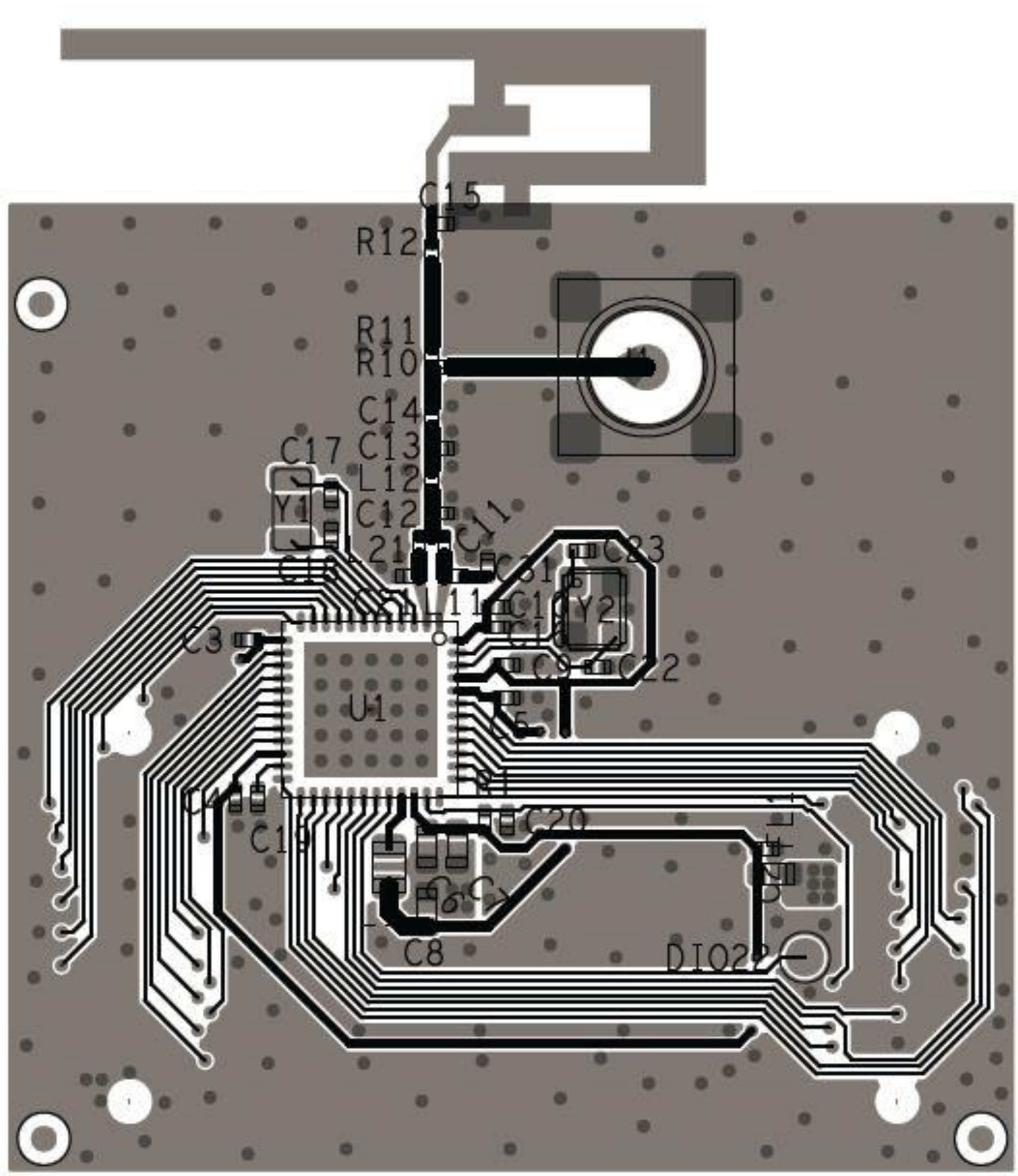

Figure 9: Reference Design Layout

The microstrip line runs from top side of the chip on the 2 rightmost pins towards the top of the board, and an effort was made to lay out the microstrip in the custom PCB nearly identically to help ensure good RF performance. The two clock crystals, Y1 and Y2, can also be seen connected to pins in the top right corner of the chip. Their layout was also mirrored in the custom PCB to help ensure good performance. However, because the reference design is a 2 layer PCB, and the custom PCB was designed to be a 4 layer board, the microstrip width had to be recalculated for the design. To perform these calculations, National Intstruments' microstrip calculator TX-LINE was used. The transmission line type used in the TI reference design was a coplanar wave guide with ground plane, so this same type of line was used in the custom PCB. The calculations to establish the appropriate dimensions for the microstrip transition line were performed using TX-LINE as shown in Figure 10 below.

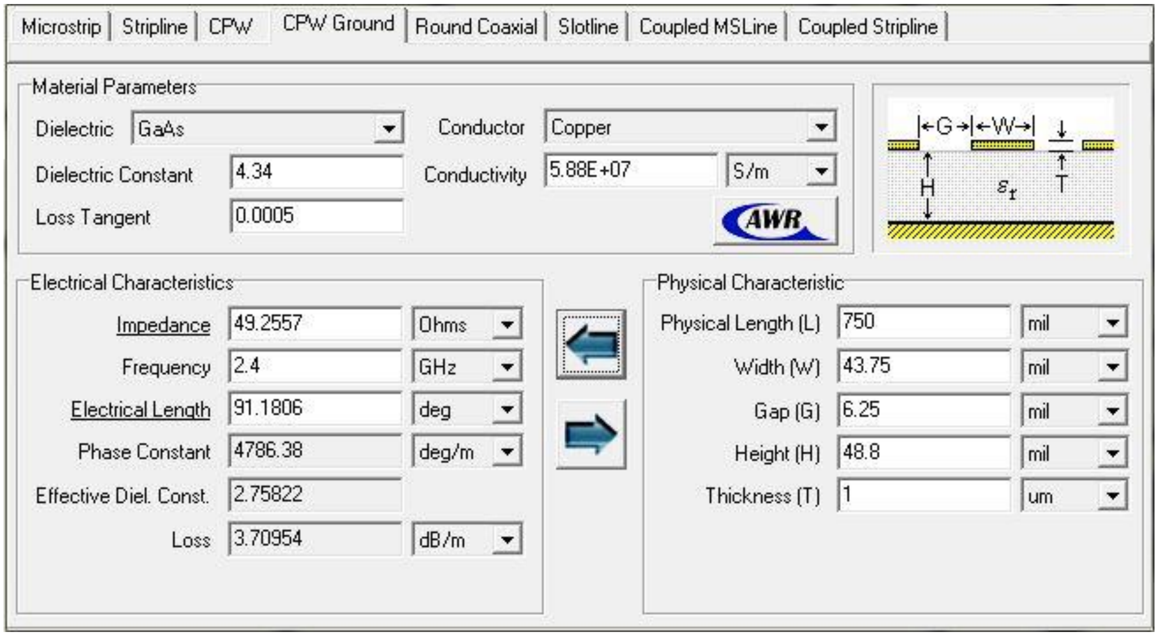

Figure 10: TX-LINE Microstrip Calculations

The small desired size of the PCB was also a design challenge, and resulted in the layout going through several iterations before being sent for manufacturing. Each redesigned resulted in successively smaller overall footprints, until total size began to be limited by the size of the ASIC itself, at which point it was determined little further progress would be made without reducing the size of the ASIC.

Once the PCB design had been sent to the manufacturer for a price quote, a further redesign was undertaken. The presence of blind vias in the design had resulted in a price quote that was determined to be out of the project's budget. To reduce the quote, all blind vias were replaced with through vias, requiring significant re-routing to be undertaken.

Design of Control Station Prototype

The control station was implemented using a Raspberry Pi with a BLE USB dongle. The goal for the control station was to replace the computer running the custom application from the ASIC vendor and the CC2650 attached to the computer, and to provide a convenient user interface that would provide for easy control of multiple implantable devices. This was important because the custom application only provided for control of one stimulator, and imposed limits on the format of the message being sent.

The gatttool linux command line tool was used to send BLE messages to the CC2650 on the custom PCB from the Raspberry Pi. Gatttool allowed for direct control of the USB dongle on the Raspberry Pi. The tool provides for transmission of various GATT messages, such as requesting a list of available characteristics, reading characteristic values, and writing values to characteristics. A python script was written that made system calls to gatttool. This script was capable of connecting to a device based on Bluetooth address, reading available characteristics, and sending a message by writing to those characteristics.

Results

Overall, this project demonstrated a successful proof of concept for a system capable of providing wirelessly controlled neuromodulation from implantable devices. The work has led to successful iterations towards a product from the sponsoring company, with improvements to both the implantable device and control station based on the work presented here.

Implantable Device

The message architecture designed for transmitting stimulation parameters over BLE was successful, proving the suitability of BLE for serving as the communication channel in an implantable neuromodulation device. Below in Figure 11 is an image showing the setup used to test this communication with the computer application running on a PC, the CC2650 development kit transmitting the BLE messages, and the custom PCB receiving the messages and generating stimulation waveforms.

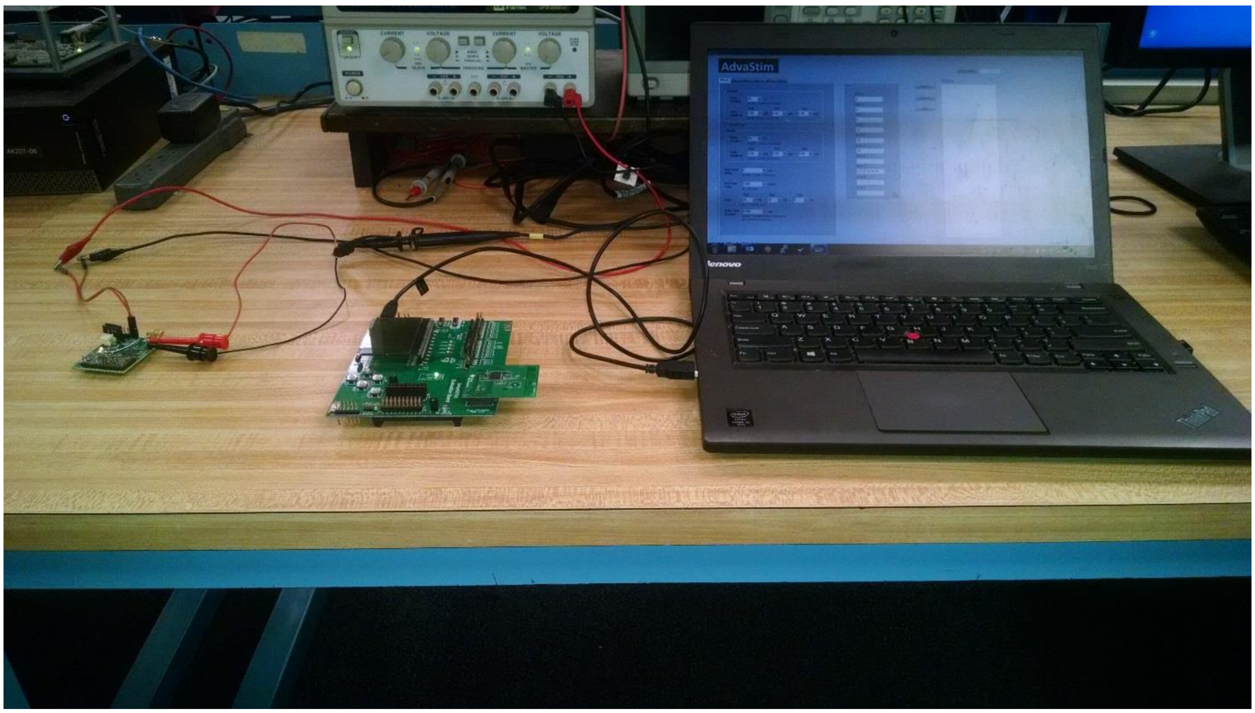

Figure 11: Custom PC Application Wireless Control

The custom PCB, although not small enough to serve as an implantable product, was successfully made reasonably compact given the quantity and size of components included, and was successful in implementing its core functions of wireless communication over BLE and generation of neuromodulation waveforms. The final design size was 40mm x 50mm. Included below are images of the layout for the top and bottom layers, as well as a picture of the PCB itself. Figure 12 shows the layout of the top side of the PCB, and Figure 13 shows the layout of the bottom. A photo of the top side of the assembled PCB is shown in Figure 14.

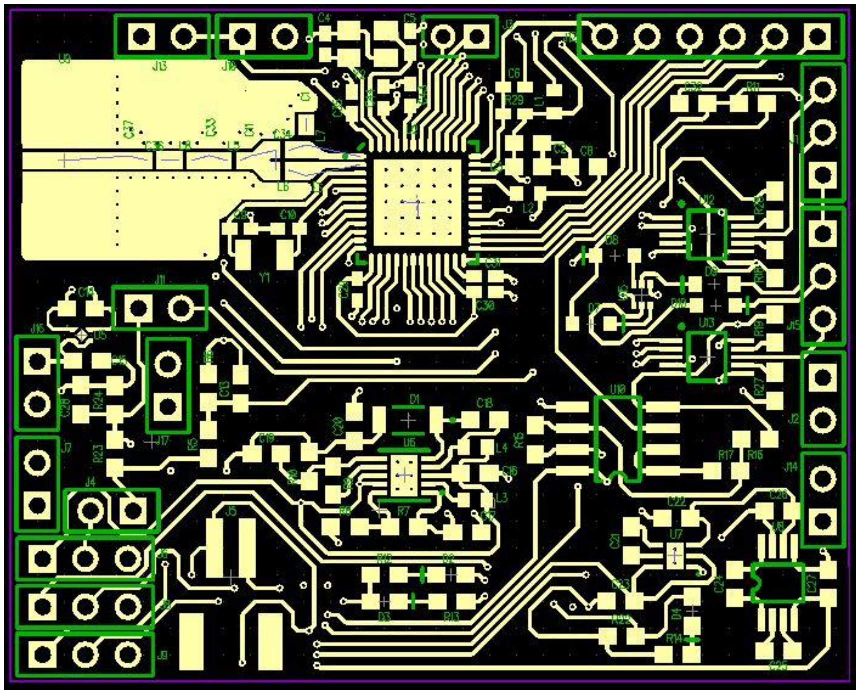

Figure 12: PCB Top Layout

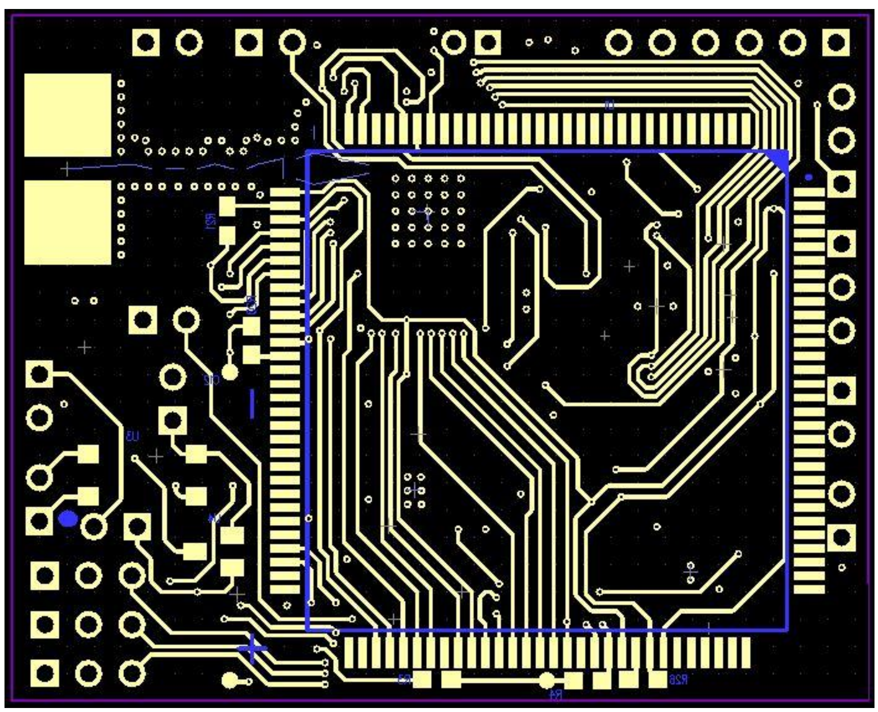

Figure 13: PCB Bottom Layout

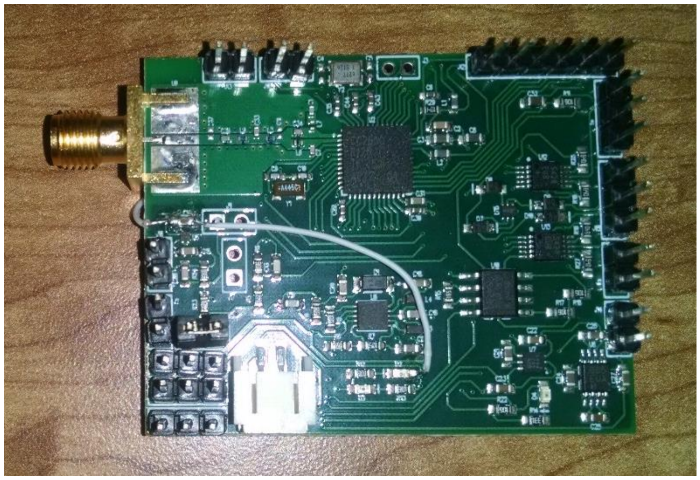

Figure 14: PCB Photo

After work for this project had concluded, Micro-Leads improved on the design of the PCB to move the device from prototype towards product. One important improvement made to the implantable device was to shrink the size. This was accomplished largely through a reduction in the size of the ASIC, in addition to refinement of wireless power circuitry and use of a chip antenna.

Control Station

The Raspberry Pi control station was shown to be capable of communicating with the implantable devices as desired. Shown below is the test setup used to demonstrate this functionality. The computer uses SSH to log in to the Raspberry Pi and run the python script to send messages to the custom PCB. Figure 15 below shows this test setup.

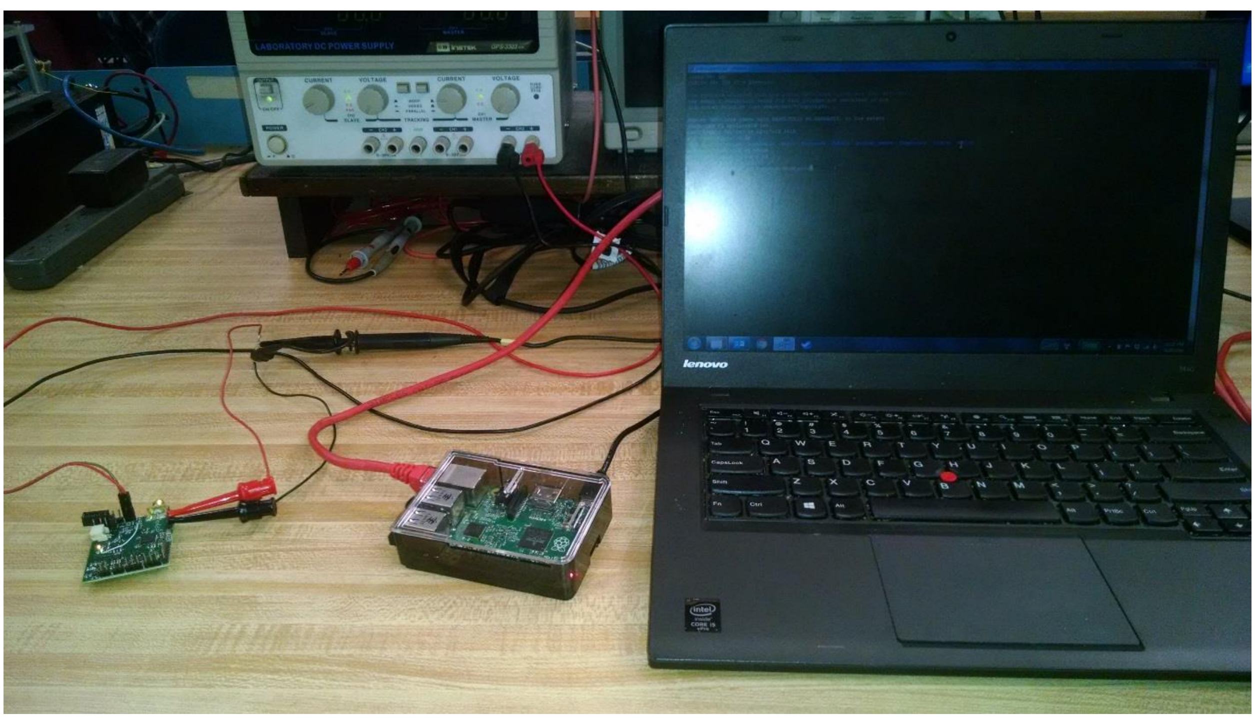

Figure 15: SSH Terminal Wireless Control

Another option for use of the Raspberry Pi was to connect a monitor, keyboard, and mouse, log into the device's operating system, and access the command line in that manner. Although this script accomplished the goal of demonstrating the ability of the Raspberry Pi to transmit messages to the implantable device, it fell short on the goal of providing a convenient user interface. Changing the device being controlled or the message being sent required editing the script in this implementation. These limitations were largely due to time limitations, and have since been rectified by Micro-Leads.

One of the key steps forward that was accomplished however was the ability to change the format of the message being generated by the computer. While before the BLE link had to operate within the framework of the single long serial message generated by the PC application that Micro-Leads already had, now the control signals could be generated in a way that better fit the BLE paradigm of shorter individual messages.

Micro-Leads built on the work accomplished during this project to create a very effective control station based on the Raspberry Pi. The simple python script written for the prototype control station was replaced with a web server hosted by the Raspberry Pi. The web server provided a much more user-friendly interface. Any computer on the same network as the Raspberry Pi can log into the web server and use an intuitive GUI to see nearby devices, read their status, and modify stimulation parameters. The communication protocol between the two devices was also rewritten to better reflect the BLE paradigm. The implantable device now implements a service with multiple different characteristics, a different one for each message type and stimulation channel. The control station now communicates using shorter messages, and message type is determined by which characteristic is written to as opposed to a field in the message.

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