

Abstract of “The Development of Transdermal Power Delivery and Freely-Moving Behavioral Applications Of Titanium Enclosed, Wireless, Neural Recording Implantable Devices” by Naubahar Agha, Ph.D., Brown University, May 2016.

This study chronicles the development and application of a fully-implantable, battery powered, wireless, neural recording device to facilitate freely-moving behavioral studies, as well as therapeutic applications including epilepsy monitoring and brain-machine interfacing (BMI). This work expands on the implantable wireless neural interface, designed by Borton et al. [*Journal of Neural Engineering*, **2**, 026010 (2013)], to transition it from experimental animal studies to human clinical use. The device life-span in an implanted setting was determined while also affirming its research potential with application specific studies. The device was successfully implanted and employed in behavioral experiments on multiple porcine as well as non-human primate animal models, for over 200 days each. The results showed that this active implantable device allows for a unique opportunity to study behavioral correlates of neural phenomena within unconstrained and freely-moving animal models of multiple species. Finally, a novel application of the Qi (pronounced “chee”) wireless charging standard is incorporated as the transcutaneous energy transmission systems (TETS) to charge the battery within the active implantable device. This technology is implemented into the device utilizing a, slightly modified, off-the-shelf Qi compatible charger. Application specific designing and optimization of the wireless power

transmission coil was performed. Our Qi inspired charging paradigm allows for our implantable device to be compatible with any Qi compatible wireless charger. Simulated implant conditions show that the internal heating of the device is compatible with the FDA regulated two degree Celsius rise from ambient conditions. In conclusion, the longevity of this device in an implanted setting has been validated, unique characteristics of the novel device were highlighted through specific research studies, and a consumer electronic wireless charging standard was integrated into the medical active implantable device territory.

The Development of Transdermal Power Delivery and Freely-Moving Behavioral
Applications Of Titanium Enclosed, Wireless, Neural Recording Implantable
Devices

by

Naubahar Agha

B.S., University of California, Riverside, 2008

A dissertation submitted in partial fulfillment of the
requirements for the Degree of Doctor of Philosophy
in the Department of Biomedical Engineering at Brown University

Providence, Rhode Island

May 2016

© Copyright 2016 by Naubahar Agha

This dissertation by Naubahar Agha is accepted in its present form by the Division of Biology and Medicine and the School of Engineering as satisfying the dissertation requirement for the degree of Doctor of Philosophy.

Date _____

Dr. Arto V. Nurmikko, Director

Recommended to the Graduate Council

Date _____

Dr. Jerry Daniels, Reader

Date _____

Dr. Edith Mathiowitz, Reader

Date _____

Dr. Anubhav Tripathi, Reader

Date _____

Dr. Ming Yin, Reader
Blackrock Microsystems

Approved by the Graduate Council

Date _____

Dr. Peter M. Weber
Dean of the Graduate School

Naubahar Agha

CV

Education

2009 – PRESENT **Doctor of Philosophy**

BIOMEDICAL ENGINEERING

Brown University

Providence, RI

2005 – 2008 **Bachelor of Science**

BIOENGINEERING

University of California

Riverside, CA

Posters

Annual Society for

Neuroscience Conference San Diego, CA – 2013

New Orleans, LA – 2012

Annual IEEE Engineering in

Medicine and Biology Conference San Diego, CA – 2013

Relevant Publications

D. Borton, M. Yin, J. Aceros, **N. Agha**, J. Minxha, J. Komar, W. Patterson, C. Bull, and A. Nurmikko. Developing implantable neuroprosthetics: A new model in pig. In Engineering in medicine and biology society, EMBC, 2011 annual international conference of the IEEE, pages 3024–3030. IEEE, 2011.

J. Wang, I. Ozden, M. Diagne, F. Wagner, D. Borton, B. Brush, **N. Agha**, R. Burwell, D. Sheinberg, I. Diester, et al. Approaches to optical neuromodulation from rodents to nonhuman primates by integrated optoelectronic devices. In Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE, pages 7525–7528. IEEE, 2011.

N. S. Agha, J. Komar, M. Yin, D. Borton, and A. Nurmikko. A fully wireless platform for correlating behavior and neural data from an implanted, neural recording device: demonstration in a freely moving swine model. In Neural Engineering (NER), 2013 6th International IEEE/EMBS Conference on, pages 989–992. IEEE, 2013.

M. Yin, D. A. Borton, J. Komar, **N. Agha**, Y. Lu, H. Li, J. Laurens, Y. Lang, Q. Li, C. Bull, et al. Wireless neurosensor for full-spectrum electrophysiology recordings

Research Interest

My principle research interests lie in the field of implantable devices with a strong preference toward brain-machine interfaces. I am interested in applying technological advancements such as new wireless telemetry methods, 3D printing, and small system on chip (SOC) applications in the commercial consumer market to the fast-growing field of neural implantable devices.

Work Experience

SEPT 2010 – DEC 2014

Teaching Assistant

Brown University

Served as a lab teaching assistant for a Bioinstrumentation course. Assisted with LabVIEW code generation and debugging, explaining basic electronics concepts, took preparedness quizzes, and provided general assistance to students.

SUMMER 2009

Summer Robotics Internship

Cal Poly San Luis Obispo

Performed research on vestibular stimulation as feedback and its effects on accuracy in flight simulation control. Developed feedback stimulation routines in MATLAB and compared flight paths with and without stimulation for path accuracy.

SUMMER 2008

Summer Research Program

University of Southern California

Conducted research in instrumentation in Dr. Gerald Loeb's lab at USC. Developed and instrumented a testing rig with multiple sensors in order to verify command actuation of a robotic prosthetic hand.

OCT 2006 – DEC 2007

Supplemental Instructor

Learning Center,

University of California, Riverside

Coordinated a class full of students working toward reviewing coursework material. Organized study sessions and practice/mock midterms and finals.

Awards

CSEMS Scholars Program

National Science Foundation Scholar

The California Alliance for Minority Participation in
Science, Engineering and Mathematics (CAMP-UCR)

Medical Scholars Program Research Stipend

Surgical Experience

Neural Recording Electronic Device Non-human Primates

Yorkshire Swine

Yucatan Minipig

Rats

Optogenetic Injections Non-human Primates

Animal Behavioral Training

Non-human Primates

Yucatan Minipigs

Electronic Design

PCB Level Miniaturized wireless charging board for
implantable devices

System Level Multiple Arduino based interactive projects
Multiple ZigBee based small, battery
powered wireless projects

Instrumentation Behavioral porcine feeding tray
Robotic prosthetic hand testing rig

Technical Experience

Optical Microscopy

Atomic Force Microscopy

Microwire Bonding

Polymer Encapsulation

Microsoldering

Printed Circuit Board Assembly

Computer Skills

Intermediate Knowledge ADOBE PHOTOSHOP,
Solidworks, C++

Advanced Knowledge JAVASCRIPT, HTML, L^AT_EX,
CadSoft Eagle, LabVIEW,
MATLAB

Doctoral Research Projects

Polymeric Encapsulation

I set up a Plasma-Enhanced Chemical Vapor Deposition device within a cleanroom environment for the purpose of depositing monolayer polymeric encapsulants on active electronic implantable devices. I also encapsulated many thin flexible polyimide based microelectronic circuit boards with PolyDiMethylSiloxane (PDMS) as well as Parylene in order to compare the two encapsulation methodologies.

Freely-Moving Behavioral Swine Study

I took part in multiple surgeries to implant small battery-powered, wireless, neural recording devices in pig models. I developed a battery-powered, wireless, fully instrumented swine feeding tray using commercially available Arduino and Zigbee devices. This device was used to conduct freely-moving behavioral experiments and

the behavioral data was wirelessly correlated with neural recordings conducted simultaneously.

Non-human Primate Sleep Study

I attached a wireless neural data transmitter (Cereplex-W) to an external pedestal on a freely-moving non-human primate for the purpose of recording neural data during natural behavior. The animal was then allowed to sleep in its home cage and data during the onset, duration and end of sleep was recorded from the motor cortex and analyzed.

Transfer of Intellectual Property

I compiled all relevant work done in application specific Integrated circuit (ASIC) design including testing boards and all design files and transferred them to an outside company for managing the manufacture of the ASICs. I determined what was needed by the company to move forward and collected the required data including contacting previous students who had worked on the designs.

Integration of a Wireless Charging Standard in an Implantable Device

I designed an extremely small but powerful wireless charging printed circuit board (PCB) in order to integrate it into small, battery-powered implantable devices. The circuit board has the capability of receiving wireless power from a compatible

coil and then charging an attached Lithium-Ion battery. This new circuit board, once integrated, allows the charging time of the implantable device to reduce from 4 hours down to under 30 minutes with a similar thermal footprint.

Acknowledgements

First and foremost, I would like to thank my family. My parents Sarah and Shahryar Agha, for always supporting and encouraging my curiosity. Thanks to their guidance, I fueled my passion for engineering and design with destructive ventures at a very young age. I could not have progressed to where I am today without them. My brother, Taimoor, and sister, Anusheh, who have been my harshest critics and my strongest supporters through all of my ups and downs.

On a professional level, I can't thank enough my PI, mentor, guide, and my financier: Dr. Arto Nurmikko. Professor Nurmikko has been a fantastic source of guidance and knowledge, his enthusiasm for the unknown or the novel with regards to technology or the brain never ceased to motivate me. His stories and references from travels across the world (such as Papua New Guinea) always brought brightness to early morning lab meetings. Dr. Nurmikko is one of the best scientists I have ever known, in the truest sense of the word.

I'd especially like to thank the rest of my committee: Dr. Anubhav Tripathi. His guidance, professional as well as personal, has been instrumental in helping me keep a

level head and continuing on to finish this program. Dr. Jerry Daniels, for letting me TA his class which has been an extremely rewarding experience and his suggestions have always been insightful. Dr. Edith Mathiowitz, her polymer science class was one of the most interesting ones I have taken here at Brown. Finally, Dr. Ming Yin, the most knowledgeable, humble, and hard-working electrical engineer i've ever met. His understanding, experience and work here at Brown have truly defined the "Ming Dynasty" within the Nurmikko Lab, and he has been a good and supportive friend. All the members of the Nurmikko Lab, as they have come and gone during my tenure here, have been incredibly friendly and provided a much needed reprieve during the daily grind of research. Past members such as Dr. Fabien Wagner, Benjamin Brush, Dr. Sunmee Park, Dr. Juan Aceros, Dr. Cuong Dang, Dr. Andrew Blaeser, Dr. Jing Wang, Dr. Kwangdong Roh, Juri Minxha and current members such as Dr. Joonhee Lee, Dr. Ilker Ozden, Farah Laiwalla, Travis May, Christopher Heelan, Yao Lu, Songtao Chen, Zeyang Yu, Marc Powell, Radu Darie, Nicole Dusang, Dmitrijs Celinskis, and Stefan Sigurdsson. Finally, last but not least I'd like to truly appreciate Dr. David Borton. Dave's mentorship has been extremely beneficial in the formative years of my graduate study. He was the best teacher anyone could ask for, always patient, always willing to lend a hand, and incredibly knowledgeable. Dave has been an indispensable mentor and a good friend throughout my time here at Brown. I would also like to thank Dr. James Harper, III, for teaching me the best way to take care of and manage animals. I could never have learned pig wrangling without

him. His care and knowledge about not only animal physiology but their behavior and mentality has been instrumental in my research as well as in training my own pets. Dr. Moses Goddard, whose calm and soothing teaching demeanor taught me the intricacies of neurosurgery without the hassle of medical school. Dr. Goddard is a wonderful, kind, and patient person which makes him an extremely effective and empathetic teacher, and a very skilled surgeon. A special thank you to the ACF veterinarian staff: Veronica Bouvier, Roxanne Burrill, Pamela Norberg, Ann Beauregard-Young, Dr. Lara Helwig, and Dr. Tiffany Borjeson. The wonderful and knowledgeable engineers who work at Brown including Christopher Bull, and William Patterson and many others.

The Brown community is extremely friendly and always willing to collaborate or assist others in their endeavors. I have met many such people in my time here and would like to acknowledge each of them for helping me along the way. People such as Dr. Carlos Vargas-Irwin, Dr. Jonas Zimmermann, Dr. David Sheinberg, Dr. John P. Donoghue, Dr. Leigh Hochberg, Dr. Danny Aghion, Dr. James Barrese, Dr. John Simeral, and David Rosler.

I would like to extend my thanks to all the supporting staff here at Brown who are the ones that keep the University functioning. Sandra Van Wagoner, Chantee Weah, Carol Folan, Jessica Bello, Beth Travers, and all of the animal care facility staff.

My good friends here in Rhode Island: Jacob Komar, who brought endless hours of “time wasting” or pop culture references to keep me from growing too old. Anton

Tokranov, who forced me to finally climb up over the walls holding me back, and also introduced me to the world of rock climbing. Octavian Biris, with whom I spent many nights playing video games and discussing the hardships of the graduate student life. I would also like to thank Mark Homer, Corey Triebwasser, Kelsea Laubenstein, Ali Biercevicz, Olivia Beane, James Niemeyer, Jorn Cheney, and Ravi Kumar.

The years I have spent at Brown in pursuit of my degree has brought me far away from all of my friends in California but I never lost touch with the ones that mattered. My closest friends in the world: Shawn Elwell and Leomar Patam. Shawn, with whom I spent hours on the phone complaining about my life's problems, or Leomar with whom I spent hours playing video games while complaining about my life's problems. They provided me with much needed sanity, comic relief, and above all: kinship. Without them, I wouldn't have had the state of mind to continue. My friends from UC Riverside such as Katie Peterson, Andrew Vu, Caitlin Schulz, Jacob Good, Gabriel Rodriguez, Sara Marie, Christopher Salam, Jeremy and Christie Busch, Stuart Le, Tung Trinh, David Slinger and Zach Gutterman.

Finally, last but certainly not least, i'd like to thank my beautiful fiancée: Anum. She has been my rock to keep me grounded and my guiding light to help me find the way. She's encouraged and supported me through my dark times and celebrated with me through my accomplishments. Behind every great man...

Dedication

This work is dedicated to my paternal grandfather, Agha Rishad Ahmed and to my maternal grandfather, my namesake, Khan Naubahar Yousafi.

Preface

“... with great power, there must also come – great responsibility!”

– Stan Lee, *Amazing Fantasy*, 1962

As able bodied people, we have a significant power. The power to do. We have the power to be able to manipulate and interact with the world around us, and to be able to communicate. A power that the disabled do not have. This gives us the responsibility of helping those less fortunate. We can help them achieve, provide them with opportunities they could never have, using our power. I choose to leverage this power in the form of interfacing technology with the human body for improving the quality of life of those less fortunate.

Interfacing technology with the human body has always been a dream for medical applications. With the help of Moore’s law, technological advancement has increased at breakneck speed. However, medical advancement has been relatively slow. If we could interface technology with the human body, the medical field could greatly benefit from the technological advancements in the last century.

Our work aims to exercise this power by applying technology to the medical field.

We aim to develop novel technological devices to interface with the body, so that they can allow the disabled to communicate with the external world. The purpose of this study, is to learn from the complex intricacies of the human brain. If we can develop technology to learn from the brain, the capabilities of the brain can further help technology, as well as many other fields, such as low power management, behavioral psychology, evolutionary biology, etc. Not only is the benefit to help people communicate, but also to help advance humanity, or society as a whole.

Imagine not being able to tell your loved ones that you love them, or having to use your eyes to tell someone you are hungry. Imagine being locked inside your body, unable to move your limbs, being stuck in a bed, physically restraint by your inability to communicate with your own arms and legs! Ultimately, giving someone back (or introducing them to) the ability to communicate with their loved ones and their surroundings is a gift with value most able-bodied persons can't even fathom.

We attempted at such a pursuit with an initial device internally called the Brain Implantable Chip (or BIC). This device is further discussed in A, but a short summary of the project is given here. The idea behind this device was a small, soft, flexible, implantable device which was still fully capable of broadcasting a very high amount of data from the brain to the outside world. This device lay dormant under the skin until it was provided power wirelessly from outside. It would then come to life, amplifying brain signals and sending them outside through the skin via a small infrared laser. The concept and execution was quite novel but the device suffered

from longevity issues. Implanting this device long term within a living organism was difficult because it was always subject to liquid and ionic penetration.

The next goal was to develop a device with the same concepts as the BIC but one that could last within an implanted environment. Thus, the titanium encased implantable device (focused on, in this work) was born. This device lasts for a half day of work with its battery, and absolutely surpassed our initial performance expectations. The reliability and performance of this device is beyond anything in the market today. Which is why this work aims to bring this device up to the standards of human clinical use. Human clinical use means traceability of all components, reliability of performance, and mitigation of risk. All of these concepts are achievable but require time and effort. It is in pursuit of this human grade implantable device, that we carry on the development and improvement of this device. Because, ultimately, giving someone back (or introducing them to) the ability to communicate with their loved ones and their surroundings is a gift certainly worth the effort.

Contents

List of Tables	xxvii
List of Figures	xxx
1 Introduction	1
1.1 The Pacemaker's Impact on the Implantable Device Market History and Adoption	3
1.2 The Cochlear Implant's Impact on the Implantable Device Market His- tory and Adoption	5
1.3 Implantable Neural Devices	8
1.3.1 Advancements in Implantable Neural Devices in the Research Phase	9
1.4 Requirements of Developing a Neural Recording Device	9
1.5 The Development of a Fully Implantable, Wireless, Broadband, Neural Recording Device	12
1.5.1 The Outer Packaging of the Implantable Device	12

1.5.2	The Internal Components of the Implantable Device	14
1.6	Wireless Charging in Implantable Devices	17
1.6.1	Transcutaneous Energy Transmission Systems (TETS) Appli- cation in Current Implantable Devices	19
1.7	Argument for Implementation of the Qi Charging Standard in Im- plantable Devices	21
1.7.1	History of the Wireless Power Consortium and the Qi Standard	23
1.8	Why Hasn't Qi Wireless Charging Been Implemented Into Implantable Devices?	24
1.8.1	The Proposal to Implement Qi Wireless Charging into Our Im- plantable Device	24
1.8.2	Benefits of Incorporating the Qi Standard	25
1.9	Taking Our Implantable Device Forward, Toward Human Clinical Use	26
2	Behavioral Applications in Freely-Moving Porcine Animal Models	35
2.1	Benefits of a Porcine Model for Implantable Device Neural Recording Experiments	36
2.2	Challenges of a Porcine Model for Implantable Device Behavioral Ex- periments	37
2.3	Solutions to Challenges of Implementing the Swine Model	42
2.4	Background on Development of a Wireless Neural and Behavioral Record- ing Platform	43

2.5	Introduction to Wireless Freely-Moving Animal Behavior Experimentation	44
2.6	Methodology of Developing a Fully Wireless System for Behaviorally Correlated Neural Recordings	45
2.6.1	Wireless, Fully-Implantable, Neural Recording Device	45
2.6.2	Wireless Behavioral Data Recording Device	47
2.6.3	Data Collection, Synchronization, Storage, and Playback	49
2.7	Results of the Fully Wireless Behavior and Neural Recording System	51
2.8	Conclusions Gathered Through the Development of this System	54
2.9	Conclusions on Utilizing a Swine Animal Model in a Wireless Implantable Device Study	55
3	Behavioral Applications in Freely-Moving Non-Human Primate Animal Models	63
3.1	Background of The Necessity of Freely-Moving Behavioral Neuroscience	65
3.2	Introduction to Implantable Neural Recording Devices to Non-Human Primates	67
3.3	Methods of Implementing Implantable Neural Recording Devices into Non-Human Primates	69
3.3.1	The Choice of a Non-Human Primate for Implantable Device Study	70
3.3.2	Non-human Primate Surgical Procedure	70

3.3.3	Charging and Experimentation Protocol for the Implantable Device	73
3.4	Results of Freely-Moving Non-Human Primate Neural Studies with a Wireless Implant	75
3.5	Conclusions on Utilizing a Non-Human Primate Animal Model in a Wireless Implantable Device Study	79
3.5.1	Future Direction of the Neural Implantable Device in Non-Human Primates	80
4	Wireless Power Delivery Optimization	84
4.1	Background on Power Management: Wireless Power Delivery and Storage Within an Implantable Device	85
4.1.1	Wireless Inductive Power Delivery	85
4.1.2	Transmitting Coil Design Parameters	90
4.1.3	Power Storage	91
4.2	Introduction to the Qi Wireless Charging Standard	93
4.2.1	Qi Standard Specifications	94
4.3	Methods of Incorporating and Testing the Integration of Qi Wireless Charging into the Previously Designed Device	98
4.3.1	Integrated Receive Coil Design Specifications	98
4.3.2	Qi Compatible Receiving Circuitry	100
4.3.3	Ferrite Integration into the Qi Compatible Implantable Device	107

4.3.4	Coil Efficiency Determination via Power Delivery Metrics and Thermal Measurements	109
4.3.5	Determination of Device Thermal Profiles Within a Simulated Implant Environment via A Thermal Bath	113
4.3.6	Introducing Fluid Flow into the Thermal Bath Heat Testing Apparatus	117
4.4	Results of Qi Integration within the Implantable Device	119
4.4.1	Results of Ferrite Configuration on the Radio Frequency Transmission Power of the Device	119
4.4.2	Results of Ferrite Configuration on the Efficacy of Charging Via Thermal Buildup	122
4.4.3	Results of Varying Transmitting Coil Configurations	125
4.4.4	Results of Elevated External Temperature on the Thermal Charging Profile via Thermal Bath Testing	127
4.4.5	Results of Elevated External Temperature While Active Cooling via Modelled Vascular Heat Transport	132
4.4.6	Final Comparison of Air Cooling Versus Thermal Water Bath Testing As Well As Active Heat Transport Cooling	134
4.5	Conclusions Drawn from Integrating a Wireless Charging Industry Standard into an Experimental Implantable Device	135
4.5.1	Future Qi Integration Improvement Design Ideas	136

4.5.2	Future Implantable Device Redesign Ideas	137
5	Discussion	145
5.1	A Summary of the Results of this Study	145
5.2	The Potential Impact of this Study on Implantable Devices	146
5.3	Future Avenues of Pursuit for Human Clinical Trials	147
5.3.1	The Transition From Research Grade Tool to Human Clinical Therapeutic Device	147
A	A Soft, Flexible, Thin, Fully-Implanted, Wireless Brain-Implantable Chip	149
B	Sleep Studies Utilizing the External Version of our Implantable De- vice	154
B.1	Background on External Wireless Transmitting Device	154
B.2	Sleep Study Methodology	156
B.3	Sleep Study Results	157
B.4	Sleep Data Analysis	159

List of Tables

1.1	A review of the current status of implantable devices in research today. © IOP Publishing. Reproduced with permission. All rights reserved, from [7].	10
1.2	Measured and designed specifications of the implantable device de- veloped and tested within our lab. © 2013 IEEE. Reprinted with permission, from [40].	18

2.1	Table of animal models implanted with the titanium enclosed implantable device for an extended period of time. All devices explanted from these animal models were fully functional at the time of explant. The two swine (SU and SM) were Yorkshire swine whose scalp grew too thick for the wireless charging of the implant to work effectively. This made charging the device impossible and we were forced to explant. Upon explant, the devices were charged and were shown to be fully functional. Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to loss of usable signals being collected from the brain/device interface which is well documented[1]	56
3.1	Table of animal models implanted with the titanium enclosed implantable device for an extended period of time. All devices explanted from these animal models were fully functional at the time of explant (NHP = Non-human primate). Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to loss of usable signals being collected from the brain/device interface which is well documented.[1]	79
4.1	Table of general lithium ion battery properties[15]	91

4.2	Table of physical dimensions of a Qi compatible coil from design B1 in the Qi standard.[27]	96
4.3	Table of physical dimensions of the coil embedded within the implantable device.[2]	98
4.4	Table of implantable device coil characteristics affected by different ferrites	108
4.5	Table of inductance and quality factor values for the transmitting coils within the three revisions of the charger.	127
4.6	Table of chemical composition of Grade 2 titanium.[24, 5]	137
5.1	Table of animal models implanted with the titanium enclosed implantable device for an extended period of time, arranged by most to least number of days implanted. All devices explanted from these animal models were fully functional at the time of explant (NHP = Non-human primate). The two swine (SU and SM) were Yorkshire swine whose scalp grew too thick for the wireless charging of the implant to work effectively. This made charging the device impossible and we were forced to explant. Upon explant, the devices were charged and were shown to be fully functional. Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to the brain/device interface which is well documented.	146

List of Figures

1.1	The progression of pacemaker design from the first fully implanted pacemaker ever made in 1958 (a), until today (b).	4
1.2	A prototype of the original cochlear implant which was developed and implanted by William House and John Doyle.[1]	6
1.3	A cochlear implant developed by Cochlear UK (http://www.cochlear.com/). This new device shows a small titanium package with a coil extending out from the top, encased in silicone with a magnet in the center for alignment. The bottom of the titanium enclosure shows the two leads for cochlear stimulation. Image courtesy of Cochlear Americas, ©2015. [24]	7
1.4	The fully implantable, wireless, broadband, neural recording device developed by our lab. The silver wires are reference wires for the amplifier integrated circuit.	13
1.5	The custom designed ASICs on PCB-A of our implantable device, designed by Ming Yin and others in our lab.	15

1.6	The two PCBs inside the implantable device.	16
2.1	The average rate of growth of various swine breeds. Yorkshire swine as also known as Domestic swine, as seen in this graph. (Sinclair Bio Resources, LLC, http://www.sinclairbioresources.com/)[20] . . .	38
2.2	A young 20 month old female Yucatan minipig skull extracted and bleached for preservation. (Photos courtesy of Dr. Moses Goddard) .	39
2.3	A transverse transection into the top layer of a pig skull showing the network of frontal sinus cavities, which make implanting a neu- ral recording device difficult.[8]	41
2.4	Skull of a pig underneath the scalp, with the top layer removed. The rostrum of the animal is toward the right. The red arrow points to the craniotomy to expose the dura, the yellow arrow points to one of the many chambers of the frontal sinus which extends over the cranial vault.	42
2.5	The pig and the feeder remain within the enclosed pen, wirelessly trans- mitting neural data (green) and behavioral data (yellow).	46
2.6	Center left: A complete instrumented, wireless, swine enrichment feed- ing device. Top right: Close up of the embedded Reed switches and IR sensor (emitters are on the opposite side of the food well, not pictured). Bottom right: Door with embedded magnets.	48
2.7	Process flow of the design of the Arduino Uno Rev. 3 board and the application of the FPGA.	50

2.8	A screenshot of the custom GUI in MATLAB showing neural recorded data and behavioral data as temporally synchronized. The top left of the image shows averaged, extracted spikes, while the bottom left of the image shows spike raster data from a select few channels. The top right of the image shows a heatmap representation of spiking rate per channel while the bottom right shows behavioral data from the enrichment feeder.	51
2.9	Mean neural spikes recorded during one session from the implanted array of a mini-Yucatan swine. Blank channels were either too noisy to discern individual spikes, or there was no spike found on that channel during this recording session. The total time duration for each spike represented is approximately 3 milliseconds, the scale is roughly 350 microvolts.	52
3.1	Image of a non-human primate with the neural implantable device fully implanted underneath the scalp (above the skull). The implant shape is difficult to discern from the shape of the natural skull of the animal.	67
3.2	Image of a non-human primate with the neural implantable device exposed and the skin of the scalp pulled back (around the dental acrylic).	68

3.3	Still from a video of a non-human primate performing an unrestrained reaching behavior within its home cage while neural data is collected wirelessly. The top left shows spike averages over 2.5 milliseconds, spikes sorted via threshold crossing, overlayed during the entire recording session. The top right shows a running trace of approximately 10 seconds, realtime raw data stream being recorded directly from 4 different channels within the array. (Image is a still taken from a video composited by Jacob Komar)	76
3.4	Raw data from a 100 channel implantable device within a non-human primate motor cortex sorted by threshold crossing. Each channels hows a 2.3 millisecond time bin averaged waveform. The scale of the entire length of each graph is 360 microvolts.	77
3.5	Raw data from a 96 channel microelectrode array after 1000 days implanted within a human with tetraplegia. The graph shows the mean sorted waveforms (in blue) from an entire day of recordings with spike sorting. Channels with multiple units show the second unit in red. The number on the top right signifies the number of mean waveforms (or total number of days) the unit was recorded from. Gray units were electrodes with over 4 M Ω impedance, classified as nonfunctional. © IOP Publishing. Reproduced with permission. All rights reserved, from [7]	78

4.1	Schematic representation of an inductive, wireless power transmission system. Z = distance between coils, d = diameter of the coils, B = magnetic field induced between the coils, P_s = supplied power, P_i = induced power.	86
4.2	Relationship of distance (z) over diameter (D) with respect to power transfer efficiency.[22]	89
4.3	Components of a lithium ion battery cell with cathode and anode terminals separated by an electrolytic layer. The arrows exemplify electron flow during processes of charge and discharge of the battery. . .	92
4.4	Generic Qi compatible transmission board acquired from Adafruit (http://www.adafruit.com , part#: 2162) with tank capacitors highlighted in red. Multiple capacitors are connected in parallel to obtain the desired capacitance.	97
4.5	Wireless power delivery coil extracted from within a smartphone. The graph shows temperature change profiles as a function of time. These thermal tests were done in air, at an ambient baseline room temperature of 25 °C.	99
4.6	Communication exchange between the transmitter and receiver components, outlined within the Qi standard.[27]	101

4.7	Schematic incorporating assisting circuitry for the Texas Instruments integrated circuit for a Qi wireless power receiver and lithium ion battery charger.	102
4.8	Layout of the testing board for incorporating the Qi compatible receiving and lithium ion battery charging circuitry into the implantable device.	103
4.9	This sequence of images shows the process of fabrication of the board once it returned from the fabrication house. Observe, in (c) the shorted legs on the TI IC as well as some capacitors standing upright on single pads as opposed to connecting across pads. These were manually corrected and the shorts were also manually cleaned after the state shown here.	104
4.10	Purple printed circuit boards provided by OSH Park (https://oshpark.com/).	105
4.11	Simplified schematic representation of a single plane slice of a model of the magnetic B field through an ideal current coil (in red).	112
4.12	An image of the water bath system with the top removed on a benchtop with an implantable device connected for thermal testing inside. . . .	116

4.13	An image of the electronics within the water bath system. This top down view shows the custom designed Arduino shield for the purposes of interfacing the Arduino to an LCD display, relays for heat pad controls and a potentiometer for controlling the temperature set point. .	117
4.14	Two types of ferrite assemblies packed inside a titanium enclosure sealed with tape. Configuration (b), with the continuous ferrite performed better on the thermal tests.)	121
4.15	Two types of possible ferrite assembly configurations that were assembled and tested. In both images: green is the PCB, black is the ferrite, blue is the RF antenna, and red is the coil (orange in figure b are conductive pins to connect the raised RF antenna to the PCB). While both performed comparably in the RF transmission test, configuration (b) with the continuous ferrite performed better on the thermal efficiency tests.	122
4.16	Signal strength decay over distance from transmitter. Two devices were tested (A and B), each device transmits at two frequencies (Due to Frequency Shift Keying, or FSK). The signal strength of each frequency on each device is shown here.	123

4.17	Temperature profiles of the titanium enclosure of each device with a different type of ferrite configuration, from room temperature to steady state. Device B was significantly more efficient, as it reached maximum charge much sooner and the charger switched to a low power “trickle charge” mode.	124
4.18	Commercially available, machine wound, single layer, wireless power delivery coil embedded within a smartphone.	126
4.19	Heat generated on the surface of an implantable device using three different revisions of the external transmitting coil with the same charger. Revision 1 is a commercial smartphone coil, Revision 2 is the coil that is the same coil as the one inside the implantable device, Revision 3 is the Qi compatible coil from Wurth Electronics.	128
4.20	Schematic image from the top down showing the device placed within the hot water bath with thermocouples for temperature measurement and control.	129
4.21	Schematic axial view showing the device placed within the hot water bath with thermocouples for temperature measurement and control. .	129
4.22	Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature.	131
4.23	Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature.	132

4.24	Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature with flow incorporated to mimic active heat transport.	133
4.25	Comparison graph of thermal profiles of the titanium can during charging in air, in a simulated implanted (37 °C) body temperature bath, and finally in a 37 °C bath with flow incorporated to mimic active heat transport. The original device is without Qi integration, the other three include Qi compatible charging.	135
A.1	Magnified images of a 1.5 mm long electrode array. (a) A 10 x 10 Utah Microelectrode Array (MEA) (b) An electrode in extracellular space.	150
A.2	A systems-level view of the Brain-Implantable Chip	151
B.1	Spectral analysis of sleep recordings collected from a freely-moving non-human primate in its home cage. The animal fell asleep and awoke of its own volition over the course of a 12 hour night.	157
B.2	Spectral analysis of sleep recordings collected from a freely-moving non-human primate in its home cage. The recorded data was binned at 1 minute intervals with some awake activity occurring within the sleep bands due to a mental “drowsy” state.	158

1

Introduction

At the turn of the century, implantable devices emerged as an interesting application of technology to interface with and assist the human body. New technologies for the development of implantable devices began to emerge and enjoyed widespread adoption. Ultimately, it was the development of the high power density lithium ion battery, and wireless charging which allowed implantable devices to proliferate. Many companies and businesses adopted these new technologies to further drive innovation. Implantable devices proved to be a very interesting new avenue for companies to invest into. Lithium polymer battery technology and charging protocol standards have recently begun to encroach into the implantable devices categories. Over the course of the next few years, many new innovations will apply themselves to the medical field. Viable, sustainable, long-term batteries and materials for elongating implanted life are crucial for the development of implantable devices in the future. Eventually

a device with a long term, reliable wireless data delivery, as well as power management (whether internal or external) will bring ubiquity to the fledgling market of implantable devices. Year after year, new developments in researched technologies are developed, which can vastly benefit the medical implant field. Our implantable device aims to be the first step in combining commercially available technologies with years of experience in medical device design research. Unique experimental applications and the combination of new innovative technologies is what makes our implantable device a forward driving tool for research and ultimately, human clinical use.

Implantable devices, in 2015, have come a long way from the mid 1950's implementation of pipes carrying blood to a shelf mounted motor for cardiac assistance. While total artificial hearts (TAH) have a rough history, the fully implantable artificial pacemaker has seen significant improvements and applications in the medical space today.[14]

Interfacing the human body with technology is certainly not a new concept. Some of the most common implantable devices are titanium hip replacements, vascular stents, silicone breast implants, or intraocular lenses.[10] However, the advent and growth of active (or battery powered) fully implantable devices is relatively new. The major players in this field are intrauterine devices (IUD), cochlear implants, and cardiac pacemakers. The active neural recording fully implantable device (a device that interfaces directly with the brain or central nervous system) is a very new player in this field, only arriving within the last decade.[27] These devices are commercially

available nuerostimulators for the purposes of treatment for neural disorders such as Parkinson’s disease, essential tremor, and dystonia.

1.1 The Pacemaker’s Impact on the Implantable Device Market History and Adoption

Current implantable devices focus primarily on a single, simple action that the device can perform very well. These devices, such as cardiac pacemakers have been developed over many years of research as well as application. The first official application of an implantable pacemaker came in 1958, almost 70 years after the first attempt to revitalize a heart with a needle based electrical stimulator from outside of the skin.[26] The patient of this implant, Arne H. W. Larson, underwent over 25 operations to replace varying models and features of his pacemakers, however, he managed to outlive both the inventor of his original pacemaker, Dr. Rune Elmquist, as well as the cardiac surgeon who first implanted him, Dr. Ake Senning.[4] Arne Larsson died at the age of 86 due to melanoma skin cancer, completely unrelated to his cardiac pacemaker. The advancement in artificial cardiac pacemaker has grown leaps and bounds since 1958. Todays cardiac pacemakers are small, sleek, titanium encased, battery powered devices with a small silicone encased feedthrough which ends in one (or two) conductive leads. Fig. 1.1b shows three different variations of

pacemaker models produced by the company Medtronic. These pacemakers, developed by companies such as Medtronic (<http://www.medtronic.com>), are assisting over 3 million patients in the United States alone.[15] Medtronic has also developed smaller and more portable pacemakers which allow for implantation procedures which do not require surgery, therefore making them safer and easier to implement.



(a) The original pacemaker developed by engineer, Dr. Rune Elmquist, in conjunction with Siemens, for Arne Larsson. This version of the cardiac pacemaker was encapsulated in epoxy resin in a plastic cup, and failed within a few hours.[29]

(b) Three models of artificial pacemakers commercially available from the company Medtronic. These pacemakers weigh 1 ounce each, and are titanium encased electronics with a small medical grade battery inside. They feature a small silicone encased feedthrough to bring electrically conductive leads out of the titanium packaging to the patient's heart.[29]

Figure 1.1: The progression of pacemaker design from the first fully implanted pacemaker ever made in 1958 (a), until today (b).

The half century of research and development that went into pacemaker technology has opened up the pathway for more implantable devices to follow suit. Many

implantable devices have spawned from the lessons learned by the pacemaker industry. Titanium has emerged as a reliable and biocompatible encapsulating metal for these types of implantable devices. Silicone and resin feedthrough technology has developed further into a reliable implantable encapsulant. Implantable lithium ion batteries allowed the potential to recharge implantable devices.

1.2 The Cochlear Implant's Impact on the Implantable Device Market History and Adoption

Another implantable device that gained traction for its medical therapeutic benefits is the cochlear implant. While this device does not have the prevalence of cardiac pacemakers, there were approximately over 300,000 patients in the world, by 2012, that have cochlear implants.[32] The first recorded use of electrical stimulation within the ear to restore hearing was in 1957 by André Djourno and Charles Eyriès.[9, 18, 39] Since their work, it took approximately 4 years for William House and John Doyle to implant the first device.[1] Finally a complete study of the feasibility of cochlear implants was conducted by asking the patients in 1977.[6] Within those 20 years, the cochlear implant had become a reliable method of restoring simple auditory sensation back to those who had suffered trauma or had been born deaf.

Fig. 1.3 shows one of the most recent, and advanced cochlear implants available in the market today. The cochlear implant has a different application than the cardiac

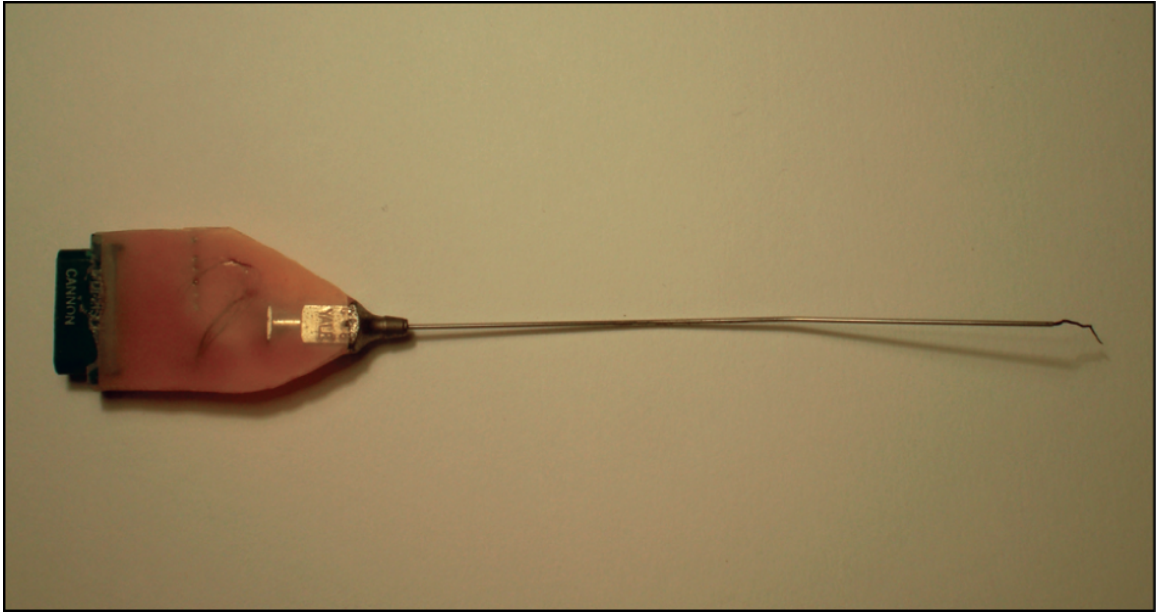


Figure 1.2: A prototype of the original cochlear implant which was developed and implanted by William House and John Doyle.[1]

pacemaker does. The cochlear implant, when powered on, needs to be continuously running as opposed to the cardiac pacemaker. The pacemaker sends short bursts of small electric potentials during the course of its life (battery lifetime). However, the cochlear implant needs to continuously stimulate the cochlea while it is enabled. This demands a longer term solution than a small battery that needs to provide short bursts of pulses.

The cochlear implant gets around the limitation of needing a large battery by outsourcing the power supply. The power supply for the cochlear implant rests outside of the body. This device delivers power transcutaneously via inductive coupling. Inductive coupling is explained in more detail in subsection 4.1.1, but a short summary consists of generating a magnetic field using an alternating current running through a



Figure 1.3: A cochlear implant developed by Cochlear UK (<http://www.cochlear.com/>).

This new device shows a small titanium package with a coil extending out from the top, encased in silicone with a magnet in the center for alignment. The bottom of the titanium enclosure shows the two leads for cochlear stimulation. Image courtesy of Cochlear Americas, ©2015. [24]

copper conductor arranged in a circle (a coil). This magnetic field transfers the energy within that copper conductor into any other coil that enters within the magnetic field. Thus, two concentric coils will transmit power between each other if one of them is delivered with the appropriate alternating current. Cochlear implants take advantage of this phenomenon by delivering wireless power across the skin of a patient. This allows the device inside to remain small, with no battery inside. Once the power delivery starts, the device turns on and begins stimulating the cochlea. The power delivery circuitry also involves sound processing in order to deliver the correct amount of power and stimulate the correct area in the cochlea.

1.3 Implantable Neural Devices

Utilizing implantable devices to interface with the brain, whether to record neural signals, or to stimulate (sometimes both) is a relatively new endeavor. Companies like Medtronic have used their experience in creating cardiac pacemakers to make very similar devices to stimulate deep areas of the brain for patients of brain dysfunctions such as epilepsy, dystonia, Parkinson’s disease and other psychiatric disorders.[19, 23] The Medtronic Activa Neurostimulators (<http://professional.medtronic.com/pt/neuro/dbs-md/prod/index.htm#tabs-1>) look very similar to their cardiac pacemakers, but offer longer leads to be inserted into deeper brain structures. The titanium enclosed device itself rests on the clavicle, or chest of the patient. These implantable neurostimulators come with a complimentary “Patient Programmer” handheld device. This handheld programmer uses wireless inductive links to transfer information between the device and the implant. For certain models of the implant, it also delivers power to charge the embedded battery inside. The small size and power requirements of the neurostimulator make the demands on the battery and charging circuit relatively low. The implantable device has two leads for neural stimulation which deliver stimulation at a low rate over time. This allows the rechargeable lithium ion battery inside to last a relatively long time.[28]

1.3.1 Advancements in Implantable Neural Devices in the Research Phase

While there are many implantable devices currently in research phase, the neural recording domain involves very few major devices in the advanced stage of development. Devices with high data rates, wireless telemetry, internal battery power, and long-term implant testing are very scarce. Table 1.1 shows recent advancements in implantable neural recording devices in research.

As neural implantable devices progress in the research field, very few have accomplished long-term animal model implantation trials. It is a difficult and expensive pathway which involves many years of research, animal model experimentation and consistent funding. There are many good concept level designs that have progressed to benchtop level testing [13, 38, 22]. Very few devices have progressed to animal model implanted testing such as the Hermes series of head-mounted devices.[11, 12, 30]

1.4 Requirements of Developing a Neural Recording Device

The bare minimum a neural implant should record, is local field potentials (LFPs). These local field potentials provide adequate data for general purpose brain machine interfacing (BMI).[17, 20, 35] The amount of data for cursor or single muscle movement control can also be determined by a small number of single unit neuron

Ref.	Type	Status	Noise (μV_{rms})	Res. (bits)	S/s (kSPs)	Ch.	Data (Mbps)	Power (mW)	Size (mm)
Harrison	ASIC	Bench	5	10	15	100	0.35	10	5.4x7.0xnr
Miranda	external device	3 mo. in NHP	5	12	30	32	24	142	38x38x51
Yin	external device	Rat	4.9	8	20	32	2.56	5.6	nrnxnrnr
Szuts	external device	1 h. in Rat	3.6	nr	20	64	10	645	nrnxnrnr
Sodagar	external device	Guinea pig	8.9	8	7.8	64	2	14.4	14x16xnr
Rizk	external device	Rat	nr	12	31	96	1	100	50x50x15
Rizk	external device	3 h. in Sheep	7	12	31	96	nr	2000	50x50x1
One Extra	implanted device	x mo. in Y	nr	nr	nr	nr	nr	nr	nrnxnrnr
One Extra	implanted device	x mo. in Y	nr	nr	nr	nr	nr	nr	nrnxnrnr
Our Device	implanted device	20 mo. in NHP	8.6	12	20	100	24	90.6	56x42x11
Our Device	implanted device	21 mo. in Swine	8.6	12	20	100	24	90.6	56x42x11

Table 1.1: A review of the current status of implantable devices in research today. © IOP Publishing. Reproduced with permission. All rights reserved, from [7].

recordings.[5, 34] This is true for devices that are rushing to interface patients of brain (developmental or accidental) trauma with machines to assist in interpretation of motor or cursor control. However, for a device to acquire as much data as possible, it would still be necessary to provide many possible avenues of data collection. The Utah MicroElectrode Array is a tool made to collect neural activity from many neurons simultaneously.[25] An array made of a silicon wafer etched into up to 100 shanks of a couple hundred micrometers thick, covered at the tip with platinum (to increase conductivity), then coated with non-conductive, biocompatible Parylene (poly p-xylylene polymer) for the remainder of the wafer. Each electrode from this array is then connected to a small gold wire which leads out of the array as a wire bundle. The Utah microelectrode array became known as a reliable method of collecting data from over 100 neurons simultaneously (as each electrode can record from multiple neurons).[21] This microelectrode array became the best method of collecting neural recordings from multiple single-unit neurons for the purposes of studying neural population dynamics.

With the advancement of neural recording technology, it became necessary to collect and record this massive amount of data being generated. Since the Utah array was capable of recording single action potentials from neurons as well as neural activity from multiple neurons across a larger area at lower frequency, it became a unique method to determine small local field potentials across a 4 millimeter space. Now that the Utah array could collect single unit potentials as well as local field potentials, it

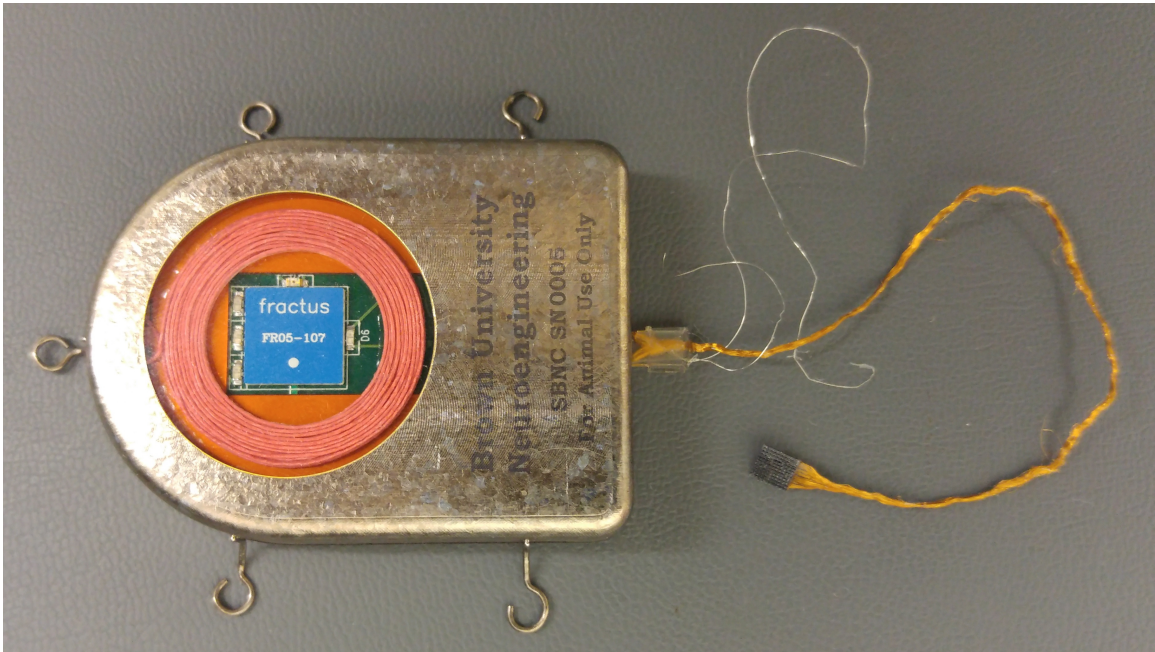
was necessary to take advantage of this tool for all types of behavioral neural studies. Comparing single unit recordings to local field potential studies across the cortex (using multiple Utah microelectrode arrays) became possible. Finally, the development of a neural recording implantable device to take advantage of the capabilities of a Utah microelectrode array became clear. This thesis focuses around the application and development of one such implantable device.

1.5 The Development of a Fully Implantable, Wireless, Broadband, Neural Recording Device

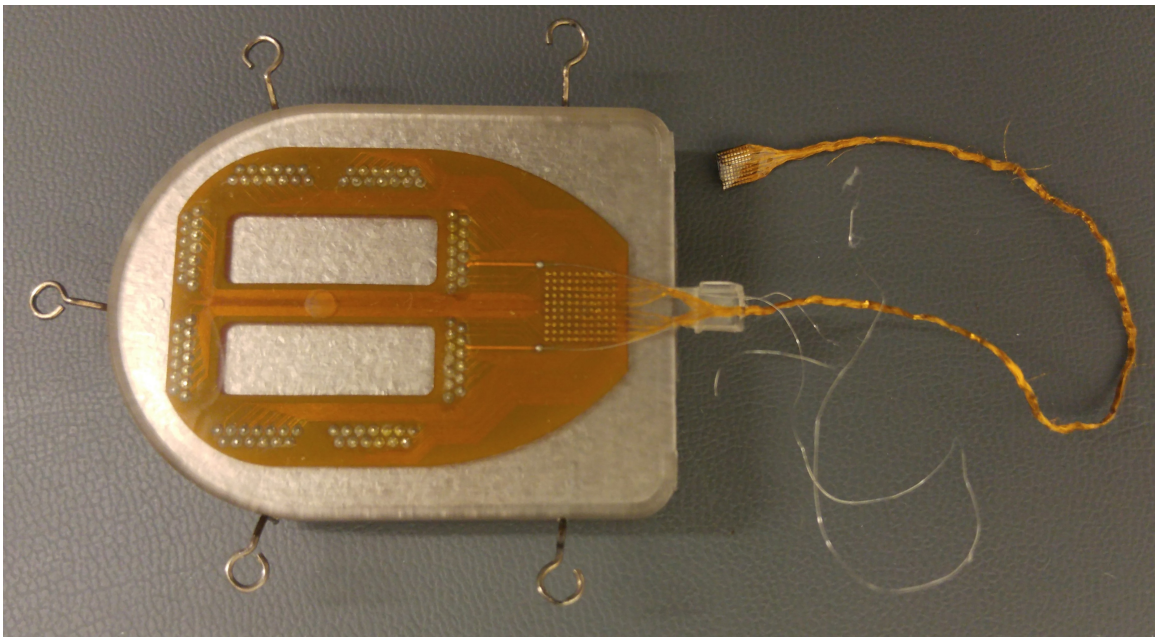
This section outlines the development of the device previously designed and published by our lab.[7, 40] At this point in the thesis, any reference to “the implantable device” will be referring to this neural implantable device developed in our lab.

1.5.1 The Outer Packaging of the Implantable Device

The device designed by our lab and fabricated by a multitude of commercial enterprises consists of processing of neural data collected directly from the cortex and wirelessly transmitting it out of the patient’s body. The device begins with a Utah microelectrode array which has a silicone coated gold wire bundle extending out from it. This gold wire bundle is bonded by Blackrock Microsystems (<http://www.blackrockmicro.com/>) to a Microconnex (<https://www.microconnex.com/>)



(a) The top of our implantable device, showing the sapphire window and a few of the internal electronics.



(b) The bottom of our implantable device, showing the flexible circuit which interfaces the Utah microelectrode array with the titanium enclosure.

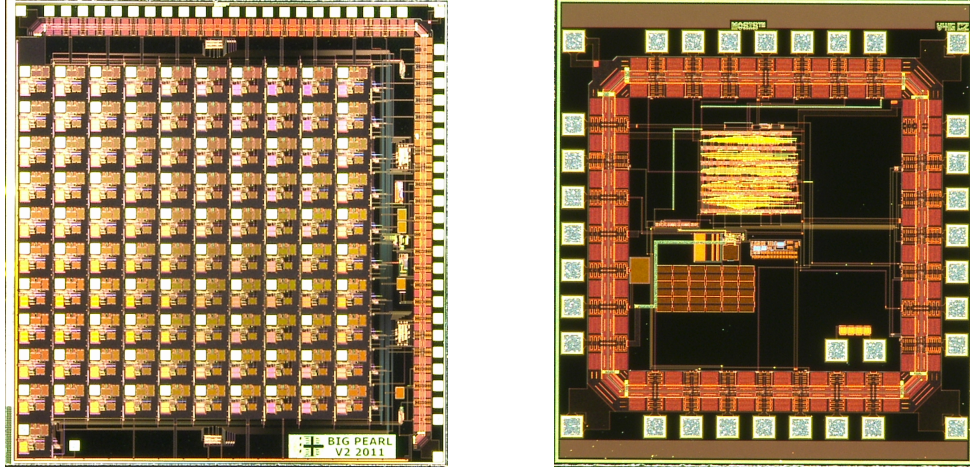
Figure 1.4: The fully implantable, wireless, broadband, neural recording device developed by our lab. The silver wires are reference wires for the amplifier integrated circuit.

built, Brown University designed flex circuit which is also encased in silicone. These 100 gold wires are independently bonded to pads on this flex circuit which breaks them out to a layout compatible for the TeknaSeal LLC. (<http://www.teknaseal.com/>) feedthroughs. These feedthroughs penetrate through a titanium enclosure, designed, built and sealed by Cirtec Medical Systems (<http://cirtecmed.com/>). The top of the titanium enclosure includes an open sapphire window to allow transmission of data and reception of wireless power, which was also braised by TeknaSeal. Fig. 1.4 shows the top and bottom of our implantable device. Two platinum wires also line the sides of the gold wire bundle. These wires are reference wires for the input of the amplifier chip. The following section will delve into the internals of the device developed in our lab.

1.5.2 The Internal Components of the Implantable Device

PCB-A: The Signal Amplification and Digitization Board

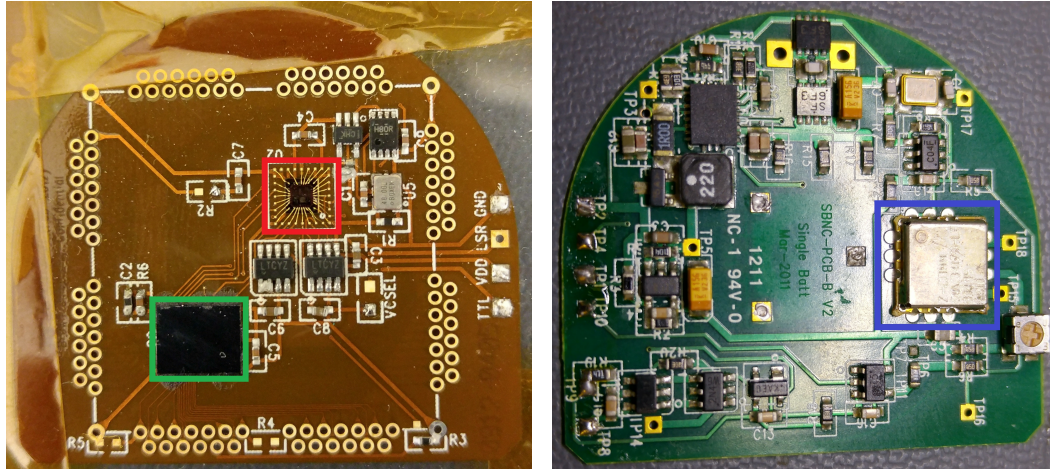
The internals of the device define a very powerful, low power, high throughput, high bandwidth, wireless data transmitting implantable device. The initial active electronic point of contact as the neural data is collected from the Utah microelectrode array, is a neural amplifier designed by Ming Yin.[42] This application specific integrated circuit (ASIC) is a custom designed chip (on AMI 0.5 micron technology) for preamplification of very low neural signals (sampled at 20 kiloSamples per second or kSps/Ch) at the relevant frequencies and multiplexing them. The preamplifiers work



(a) The analog amplifier ASIC, highlighted in green in Fig. 1.6a (b) The digital controller ASIC, highlighted in red in Fig. 1.6a

Figure 1.5: The custom designed ASICs on PCB-A of our implantable device, designed by Ming Yin and others in our lab.

across a wideband (0.1 Hz to approximately 7.8 kHz) and $3.2 \mu V_{rms}$ input referred noise. The preamplifier achieves a signal-to-noise ratio (SNR) of higher than 6dB for neural signals more than $100 \mu V_{pp}$. More detail for the amplifier design and circuitry can be found here: [2], pictured in Fig. 1.5a. The amplifier then multiplexes the 100 individual signals coming from the array and sends them out as two channels to on board commercial, off the shelf (COTS) analog to digital converters (ADCs). Once these signals are converted from analog to digital by the ADCs (at a 12 bit resolution), they are then sent to a digital controller chip, also designed by Ming Yin in conjunction with work done previously in our lab by Y.K. Song and others.[37] This data is then Manchester encoded by another COTS integrated circuit component. This entire PCB runs on a 24 MHz clock source. The data is then sent to our power/data transmission printed circuit board (PCB).



(a) PCB-A which amplifies, digitizes, multiplexes, and encodes the neural data. The red square shows the controller ASIC while the green square shows the amplifier ASIC.

(b) PCB-B which transmits the neural data on carrier frequencies, as well as receive wireless power and charges the attached lithium ion battery. The blue square shows the radio frequency ASIC.

Figure 1.6: The two PCBs inside the implantable device.

PCB-B: The Signal Packetization, Transmission and Power Management Board

The second PCB within the device manages the data transmission, as well as the power reception and delivery of the device. The data pathway continues as a digital, Manchester encoded, data stream (at 24 Megabits per second or Mbps, doubled to 48 due to Manchester encoding) on to a custom designed radio frequency transmission chip. This radio frequency ASIC outputs the data stream at 3.2 and 3.8 GHz carrier frequencies utilizing frequency shift keying (FSK). This data is finally broadcast utilizing a 1.5 dBi ultra wide band (UWB) COTS chip antenna (blue “fractus” labeled chip visible in Fig. 1.4a). The remaining area on this PCB is utilized by the power management circuitry. The remaining circuitry involves COTS power

management ICs from Texas Instruments (TI) for charging lithium ion batteries, as well as rectification circuitry to process power received by a custom designed coil. The wireless coil, designed in house and built by Cirtec, is explained in much more detail in Section 4.3.1. The attached battery is a Quallion (<http://www.quallion.com/sub-mm-implantable.asp>) supplied medical grade, implantable, rechargeable lithium ion battery at a capacity of 200 mAh. Finally, the backside of PCB-B houses a small infrared (IR) photodiode. The purpose of this photodiode is to enable or disable the data transmission activity of this device. This IR photodiode acts as a remote switch to turn on or off the device from outside. It sits inside the coil, next to the RF antenna and is visible through the sapphire window. The full specifications of our implantable device as designed and measured empirically are included in table 1.2.

Specification List of our Implantable Device

1.6 Wireless Charging in Implantable Devices

Wireless charging in implantable devices as seen on the rechargeable cardiac pacemaker, and wireless power delivery as soon on the cochlear implant are a relatively similar and common method of transferring power transdermally. Without puncturing, or creating an open pathway through the skin, wireless power transmission is the best way to power a device, or charge an internally implanted battery. However, the

Specification	Value
Number of Channels	100
Preamplifier gain	200 (46 dB)
Preamplifier bandwidth	0.1 Hz (tunable) to 7.8kHz
Preamplifier input referred noise	$2.83\mu V_{rms}$
Preamplifier ASIC size and power dissipation	5.2x4.9mm ² , 6 mW@3V
Controller ASIC size and power dissipation	2x2mm ² , 1 mW@3V
System resolution	12 bits for all channels
System sampling rate	2 MSps (20kSps/Ch)
Data encoding	Manchester (48Mbps)
RF FSK Tx frequency	3.2/3.8 GHz
RF FSK Tx power dissipation	50 mW
Inductive power carrier	150 kHz
Inductive power charging efficiency	57.8%@3mm
RF receiver sensitivity	-77.7dBm@48Mbps with 10^{-8} BER
Battery	200 mAh medical Li-ion rechargeable
Battery runtime	6.6 hrs
Total power dissipation	30.2 mA@ 3V (90.6 mW)
Titanium enclosure dimensions	56x42x11mm ³
Total system weight	44.5g

Table 1.2: Measured and designed specifications of the implantable device developed and tested within our lab. © 2013 IEEE. Reprinted with permission, from [40].

power draw of these commercially available devices is relatively small. They function in small bursts over a long period of time with small batteries. The challenge within our device was to provide consistent power for broadband, 100 channel data recording. Delivering 90 mW (or 30 mA) continuous power for a long runtime proves a challenge for a small implantable lithium ion battery.

The design of a transcutaneous energy transmission systems (TETS) must consist of a primary external coil (with its supporting electronics), which is closely coupled (via either inductive or resonant coupling) to a small, internal, implanted coil. A good system, for long term reliability, must be able to communicate with its charger.

Interaction between devices in order to verify alignment, power transmission, charging completion is necessary for a reproducible and reliable charging experience in a human-grade implantable device. A lot of research has been done in order to design a reliable TETS for the purpose of long-term implantable devices. Here we discuss the design of such systems.

1.6.1 Transcutaneous Energy Transmission Systems (TETS)

Application in Current Implantable Devices

In order to design a small, implantable device interface, which a patient can carry on their person, it is imperative to design a small, lightweight, cool running, battery powered charging system. In order to design such a system, the nuances of wireless power must be manipulated and a balance must be achieved between the distance power is transmitted, and the type of wireless charging available to a monolithic device enclosed in titanium. Wireless power delivery systems come in two primary types: magnetic resonance or magnetic inductance systems. There are distinct advantages and disadvantages to each. While the general principles behind each are the same (alternative currents sent in a conductive loop generate an alternating magnetic field, called flux, within the center of the loop), each have their unique characteristics. An inductive system works through tightly coupled coils which must remain close to each other, relative to their respective sizes. A resonant system works through loosely coupled coils which can remain a further distance away, but their respective

efficiency is much lower, and the coil sizes must be significantly larger. While it may seem that the range allowed by resonant systems is a benefit for implantable devices, efficiency and coil sizes are a major drawback to designing small, low power and low heat implantable systems. Work done by RamRakhyani et al have employed resonance systems in small, low power implantable applications. Their prototype system operates over a 700 kHz carrier frequency up to 20 millimeters away and shows efficiency of up to 80%.[33] However, this system requires a large transmitting coil and resonant coupling, inherently, is not stable when done across metallic housed components (such as a titanium enclosure).

Inductively coupled systems have also been prototyped and employed in implantable devices. However, most of these systems rely on low power transfer to avoid heating due to inefficiency. One such system, by Nag et al, can transmit 1.4 mW of power over 1 centimeter.[31] Their system can accomplish this because they do not utilize an implanted battery to charge, and their implantable system is relatively low power. Our system requires higher power, and enough power to charge the battery as well as run the device for an extended period of time. Systems designed to deploy over 100 μ A over 20 centimeters have also been developed, with a small implanted coil.[43] However, these coils have to be separated from the metallic housing, and must be coated in silicone. The external coil also needs to be relatively large, such as 15 centimeters in diameter. Ultimately, while penetration distance is high, the power delivery is still relatively low.

Alternative Methodology for Transcutaneous Energy Transmission Systems (TETS)

There are not very many alternatives to supplying power over a short distance, wirelessly, while making sure the object between the power transmission remains unharmed. One such concept is wireless transmission via magnetic inductance or resonance. An alternative is providing power via light. Taking advantage of the photovoltaic effect, it is possible to deliver power across short distances via light. Ahnood et al have managed to transmit 2.7 mW (at 400 millivolts) across 2 millimeters using diamond encased photovoltaics and a near infrared light source.[3] Unfortunately, for this method to work for high power implantable devices, the power needs to be significantly increased. The best way to increase the total power delivered is to increase the surface area of the photovoltaic cells, and increase the power of light transmitted. This increased light would need significantly more power and may harm the skin in the way as well. Current photovoltaic technology is not efficient enough to be employed in high power, high throughput implantable devices.

1.7 Argument for Implementation of the Qi Charging Standard in Implantable Devices

In order to employ wireless power delivery to implantable devices, a device needs to communicate power delivered, alignment of the implanted charger, and be able

to transmit a large amount of power across skin. All of these methodologies must be engineered and implemented within a small biocompatible package. Meanwhile, commercial products have implemented a similar method of power delivery for many years. The commercial smartphone market saw the wide adoption of inductive wireless charging when the, now defunct, Palm Inc. released their smartphone called the Palm Pre. The Palm Pre featured a proprietary wireless charging technology called “Touchstone”. Palm sold a touchstone dock accessory that was compatible with all their smartphones. The dock featured a hard ferromagnetic metal case with a coil inside. The inside of their smartphones featured an arrangement of magnets that aligned themselves to the metal of the charging dock, and a receiving coil that was compatible with the charger. This allowed their smartphones to mate with the charger, automatically align and begin wireless charging. The phones would provide an audible tone and show a notification on the screen to signify that the wireless charging had begun. At the time, the Palm smartphones would get warm to the touch while charging as the power supplied was just under 5 Watts. Over time, this charging was made efficient enough to allow for higher power transmission and lower heat generation.

1.7.1 History of the Wireless Power Consortium and the Qi Standard

Roughly around the same time (2008), a large coalition of commercial smartphone manufacturers got together to create a standard of wireless charging they could all follow. This consortium, known as the Wireless Power Consortium (WPC) could develop a method of standardized charging so that any charger would be compatible with any device (much like the Universal Serial Bus, or USB did for wires). The WPC developed the Qi standard of wireless power charging. The Qi standard was published and released as a specification in August 2008, and it took 3 years (until 2011) for the first Qi compatible smartphone was released.[8]

The Qi standard aimed to provide standardization for wireless power delivery in consumer electronics. The maximum power the Qi standard allowed at the time was 5 Watts (5 Volts, 1 Ampere). Today, over two hundred companies support the Qi standard and almost 900 products implement the standard. Large companies such as Samsung, Microsoft, Sony, etc. all support the Qi standard and provide products which integrate this method of wireless power. What that leads to, is market ubiquity and adoption of a general standard method of power delivery. This has led to perfection of the method of power delivery and more efficient manufacturing processes. Many commercial outlets now provide premade devices, integrated circuits, compatible coils, as well as premade solutions for implementing Qi wireless charging into new products. This market standardization led to the obvious inquiry.

1.8 Why Hasn't Qi Wireless Charging Been Implemented Into Implantable Devices?

Implantable devices are generally very small, have a low power requirement, and exist in difficult to reach areas (within a moving body). These challenges prove difficult for implementation of a wireless standard which was developed primarily for smartphones to sit on tables or docks. The inherent difference being, a smartphone has a fixed area to embed the receiving coil (a large, mostly flat, back area), while being mostly still while charging (on a dock or a flat surface). Implantable devices, however, tend to come in all different shapes and sizes. Generally, they are very small, tend to be implanted into areas not conducive to placing a large charging pad or surface on (due to the contours of the body), and are also generally encased in metallic enclosures (such as titanium) in order to be biocompatible. These challenges provide a difficult avenue for the implementation of a smartphone charging standard to address.

1.8.1 The Proposal to Implement Qi Wireless Charging into Our Implantable Device

To our knowledge, there have only been a few conceptual study done to implement the Qi standard into implantable devices, such as work done at Polytechnique Montreal and McGill University,[16] or work done to look at interference by Qi chargers on current non-compatible implantable devices.[36] This methodology is interesting as

it incorporates bluetooth communication between the implant and the charger as well. Our approach proposes something a little different, due to our device having a titanium enclosure and high power requirements.

We propose designing a custom small coil for the transmitting charger portion of any generic Qi compatible charger. The smaller coil will allow more efficient exchange between the transmitter and the receiver embedded within our implantable device. Due to the titanium in our implantable device, we can only have a small coil within. The outside coil should compliment the small coil inside the device, and should not leech power to the titanium enclosure on the outside of the coil. To implement the Qi standard, we propose setting up the appropriate electronics internal to our device, to make our device receptive to Qi compatible chargers. Finally, a smaller coil to replace the standard Qi charger coils (which are usually as large as our entire device) could allow any Qi compatible charger commercially available to be compatible with our device.

1.8.2 Benefits of Incorporating the Qi Standard

Once we integrate the Qi standard into our device, we will not have to design our TETS from scratch. We can automatically incorporate alignment assistance, standardized power delivery, large power transfer efficiency, and commercially available components into our device with minimal effort. This will allow our device to be compatible with the hundreds of different Qi compatible chargers available in the

market (after a small modification).

1.9 Taking Our Implantable Device Forward, Toward Human Clinical Use

The main goal of this work is to further our implantable device from a research tool into a fully human-ready therapeutic tool. This study aims to show this implantable device as a powerful research tool to unlock new pathways for behavioral neuroscientific study, as well as optimize the design and application of this device to be ready for human clinical use.

References

- [1] Mudry A and Mills M. The early history of the cochlear implant: A retrospective. *JAMA Otolaryngology–Head & Neck Surgery*, 139(5):446–453, 2013.
- [2] J. Aceros, Ming Yin, D.A. Borton, W.R. Patterson, and A.V. Nurmikko. A 32-channel fully implantable wireless neurosensor for simultaneous recording from two cortical regions. In *Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE*, pages 2300–2306, Aug 2011.
- [3] A. Ahnood, K.E. Fox, N.V. Apollo, A. Lohrmann, D.J. Garrett, D.A.X. Nayagam, T. Karle, A. Stacey, K.M. Abberton, W.A. Morrison, A. Blakers, and S. Praver. Diamond encapsulated photovoltaics for transdermal power delivery. *Biosensors and Bioelectronics*, pages –, 2015.
- [4] Lawrence K. Altman. Arne H. W. Larsson, 86; Had First Internal Pacemaker. <http://www.nytimes.com/2002/01/18/world/arne-h-w-larsson-86-had-first-internal-pacemaker.html>, January 2002. Accessed: November 5, 2015.
- [5] S. Ben Hamed, M. H. Schieber, and A. Pouget. Decoding M1 neurons during multiple finger movements. *J. Neurophysiol.*, 98(1):327–333, Jul 2007.
- [6] R. C. Bilger, F. O. Black, N. T. Hopkinson, and E. N. Myers. Implanted auditory prosthesis: an evaluation of subjects presently fitted with cochlear implants.

- Trans Sect Otolaryngol Am Acad Ophthalmol Otolaryngol*, 84(4 Pt 1):677–682, 1977.
- [7] D. A. Borton, M. Yin, J. Aceros, and A. Nurmikko. An implantable wireless neural interface for recording cortical circuit dynamics in moving primates. *J Neural Eng*, 10(2):026010, Apr 2013.
- [8] Wireless Power Consortium. Wireless Power Consortium: Our History. <http://www.wirelesspowerconsortium.com/about/>. Accessed: November 8, 2015.
- [9] A. DJOURNO and C. EYRIES. [Auditory prosthesis by means of a distant electrical stimulation of the sensory nerve with the use of an indwelt coiling]. *Presse Med*, 65(63):1417, Aug 1957.
- [10] FDA. Fda — Implants and Prosthetics. <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics>. Accessed: November 10, 2015.
- [11] Justin D Foster, Paul Nuyujukian, Oren Freifeld, Hua Gao, Ross Walker, Stephen I Ryu, Teresa H Meng, Boris Murmann, Michael J Black, and Krishna V Shenoy. A freely-moving monkey treadmill model. *Journal of Neural Engineering*, 11(4):046020, 2014.
- [12] Hua Gao, Ross M. Walker, Paul Nuyujukian, Kofi a a Makinwa, Krishna V. Shenoy, Boris Murmann, and Teresa H. Meng. HermesE: A 96-channel full data

- rate direct neural interface in 0.13 μm CMOS. *IEEE Journal of Solid-State Circuits*, 47(4):1043–1055, 2012.
- [13] P. M. George, A. W. Lyckman, D. A. LaVan, A. Hegde, Y. Leung, R. Avasare, C. Testa, P. M. Alexander, R. Langer, and M. Sur. Fabrication and biocompatibility of polypyrrole implants suitable for neural prosthetics. *Biomaterials*, 26(17):3511–3519, Jun 2005.
- [14] W. Greatbatch and C. F. Holmes. History of implantable devices. *IEEE Eng Med Biol Mag*, 10(3):38–41, 1991.
- [15] Arnold J. Greenspon, Jasmine D. Patel, Edmund Lau, Jorge A. Ochoa, Daniel R. Frisch, Reginald T. Ho, Behzad B. Pavri, and Steven M. Kurtz. Trends in permanent pacemaker implantation in the united states from 1993 to 2009increasing complexity of patients and procedures. *Journal of the American College of Cardiology*, 60(16):1540–1545, 2012.
- [16] S. Hached, A. Trigui, I. El Khalloufi, M. Sawan, O. Loutochin, and J. Corcos. A bluetooth-based low-energy qi-compliant battery charger for implantable medical devices. In *Bioelectronics and Bioinformatics (ISBB), 2014 IEEE International Symposium on*, pages 1–4, April 2014.
- [17] T. M. Hall, K. Nazarpour, and A. Jackson. Real-time estimation and biofeedback of single-neuron firing rates using local field potentials. *Nat Commun*, 5:5462, 2014.

- [18] W. F. House. Cochlear implants. *Ann. Otol. Rhinol. Laryngol.*, 85 suppl 27(3Pt2):1–93, 1976.
- [19] B. Howell, B. Huynh, and W. M. Grill. Design and in vivo evaluation of more efficient and selective deep brain stimulation electrodes. *J Neural Eng*, 12(4):046030, Aug 2015.
- [20] N. F. Ince, R. Gupta, S. Arica, A. H. Tewfik, J. Ashe, and G. Pellizzer. High accuracy decoding of movement target direction in non-human primates based on common spatial patterns of local field potentials. *PLoS ONE*, 5(12):e14384, 2010.
- [21] S. Kim, R. Bhandari, M. Klein, S. Negi, L. Rieth, P. Tathireddy, M. Toepper, H. Oppermann, and F. Solzbacher. Integrated wireless neural interface based on the Utah electrode array. *Biomed Microdevices*, 11(2):453–466, Apr 2009.
- [22] S. Kim, R. R. Harrison, and F. Solzbacher. Influence of system integration and packaging on its inductive power link for an integrated wireless neural interface. *IEEE Trans Biomed Eng*, 56(12):2927–2936, Dec 2009.
- [23] P. Limousin, J. D. Speelman, F. Gielen, and M. Janssens. Multicentre European study of thalamic stimulation in parkinsonian and essential tremor. *J. Neurol. Neurosurg. Psychiatr.*, 66(3):289–296, March 1999.
- [24] Cochlear Ltd. Nucleus Implant Portfolio.

- <http://www.cochlear.com/wps/wcm/connect/uk/home/discover/cochlear-implants/nucleus-6-for-adults/nucleus-implant-portfolio>, 2015. Accessed: November 5, 2015.
- [25] E. M. Maynard, C. T. Nordhausen, and R. A. Normann. The Utah intracortical Electrode Array: a recording structure for potential brain-computer interfaces. *Electroencephalogr Clin Neurophysiol*, 102(3):228–239, Mar 1997.
- [26] J. A. McWilliam. Electrical Stimulation of the Heart in Man. *Br Med J*, 1(1468):348–350, Feb 1889.
- [27] Medtronic. Medtronic — Deep Brain Stimulation for Movement Disorders. <http://professional.medtronic.com/pt/neuro/dbs-md/prod/activa-pc/index.htm>. Accessed: November 10, 2015.
- [28] Medtronic. *Patient Programmer: Medtronic DBS Therapy User manual*. Medtronic, 710 Medtronic Parkway, Minneapolis, MN 55432-5604, 2008.
- [29] Medtronic. Adapta Pacemakers for Bradycardia. <http://www.medtronic.com/patients/bradycardia/pacemaker/our-pacemakers/adapta/index.htm>, September 2015. Accessed: November 5, 2015.
- [30] H Miranda, V Gilja, C A Chestek, K V Shenoy, and T H Meng. HermesD: A

- High-Rate Long-Range Wireless Transmission System for Simultaneous Multi-channel Neural Recording Applications. *IEEE Transactions on Biomedical Circuits and Systems (TBCAS)*, 4(3):181–191, 2010.
- [31] S. Nag and D. Sharma. Wirelessly powered stimulator and recorder for neuronal interfaces. In *Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE*, pages 5612–5616, Aug 2011.
- [32] National Institute on Deafness and Other Communication Disorders. Cochlear Implants. <https://www.nidcd.nih.gov/health/hearing/pages/coch.aspx>, August 2014. Accessed: November 5, 2015.
- [33] A.K. RamRakhyani, S. Mirabbasi, and Mu Chiao. Design and optimization of resonance-based efficient wireless power delivery systems for biomedical implants. *Biomedical Circuits and Systems, IEEE Transactions on*, 5(1):48–63, Feb 2011.
- [34] A. Riehle and E. Vaadia. *Motor Cortex in Voluntary Movements: A Distributed System for Distributed Functions*. Frontiers in Neuroscience. CRC Press, 2004.
- [35] M. R. Scheid, R. D. Flint, Z. A. Wright, and M. W. Slutzky. Long-term, stable behavior of local field potentials during brain machine interface use. *Conf Proc IEEE Eng Med Biol Soc*, 2013:307–310, 2013.
- [36] T. Seckler, K. Jagielski, and D. Stunder. Assessment of Electromagnetic Interference with Active Cardiovascular Implantable Electronic Devices (CIEDs)

- Caused by the Qi A13 Design Wireless Charging Board. *Int J Environ Res Public Health*, 12(6):5886–5904, 2015.
- [37] Y.-K. Song, D.A. Borton, S. Park, W.R. Patterson, C.W. Bull, F. Laiwalla, J. Mislow, J.D. Simeral, J.P. Donoghue, and A.V. Nurmikko. Active microelectronic neurosensor arrays for implantable brain communication interfaces. *Neural Systems and Rehabilitation Engineering, IEEE Transactions on*, 17(4):339–345, Aug 2009.
- [38] T. Stieglitz. Considerations on surface and structural biocompatibility as prerequisite for long-term stability of neural prostheses. *J Nanosci Nanotechnol*, 4(5):496–503, May 2004.
- [39] S.B. Waltzman and J.T. Roland. *Cochlear Implants*. Thieme, 2011.
- [40] M. Yin, D. A. Borton, J. Aceros, W. R. Patterson, and A. V. Nurmikko. A 100-channel hermetically sealed implantable device for chronic wireless neurosensing applications. *IEEE Trans Biomed Circuits Syst*, 7(2):115–128, Apr 2013.
- [41] M. Yin and North Carolina State University. *A Multi-channel Wireless Implantable Neural Recording System*. North Carolina State University, 2009.
- [42] Ming Yin and M. Ghovanloo. A low-noise preamplifier with adjustable gain and bandwidth for biopotential recording applications. In *Circuits and Systems, 2007. ISCAS 2007. IEEE International Symposium on*, pages 321–324, May 2007.

- [43] Darrin J. Young, Peng Cong, Michael A. Suster, and Margot Damaser. Implantable wireless battery recharging system for bladder pressure chronic monitoring. *Lab Chip*, 15:4338–4347, 2015.

2

Behavioral Applications in Freely-Moving Porcine Animal Models

To leverage the extremely unique capability of a neural recording, implantable device with full broadband data wirelessly streaming, a freely-moving animal experiment was devised. Freely-moving animal models are an extremely difficult process to incorporate within a study. The conditions for an animal to move freely limit the methodology of data collection which in turn limits the behavior of the animal. However, this implantable device allowed us to give free range of motion to our animal models while maintaining up to a meter of distance with a receiving antenna. Common animal enclosures contain metal, which creates a problem for receiving radio

frequency signals beyond the metal. These types of challenges were overcome by mounting receiving antennas on the inside of the cages. The animals for these experiments did not get any behavioral training, or repeated sessions with an experimenter with positive reinforcement. These animals were left to their own instincts, their naturalistic behavior, and personal motivation. The goal of these experiments were two fold: 1) determine the reliability and longevity of a long-term, battery powered, fully implantable neural recording device and 2) Show the unique applications of a tool that allows for new types of experimentation and studies that were not possible before.

2.1 Benefits of a Porcine Model for Implantable Device Neural Recording Experiments

Neurological recordings require an animal with a concept of self and the capability to learn complex behavioral tasks. The usual animal models for these types of studies in animal laboratories in the United States is non-human primates, specifically Rhesus Macaques (*Macaca mulatta*). [11, 15] However, for the initial stages of studies for this implantable device, the emphasis was on physiological reactions to a foreign body, and the practical, beneficial use of such an implantable device in an unrestrained animal. With regards to non-human primates, there's a lot of regulatory rules that come into play. More specifically, non-human primates are carriers of the

Herpes B Virus and must be handled accordingly and carefully.[7] They also require proper care, maintenance, and the involvement of more personnel.[21] Therefore, our lab decided to pursue the porcine model. The initial concept was to use Yorkshire swine. Yorkshires are relatively easy to obtain and simple to maintain within a university/research environment,[19] and have been well studied.[18, 16] Yorkshire pigs were used for many soft, polymer implantable device studies done within the lab before the development of the titanium enclosed implantable device.[2] The benefits of using swine include ease of management, cost, personnel, and researcher health considerations. Swine are also known to have physiology (especially skin, and skin responses) very similar to humans (more so than monkeys).[12, 7] The Swine brain is also very well known,[10] and swine have been used for longevity of drug delivery and epidermal reactions to toxicity studies.[6, 9] Thus, Yorkshire swine were used for the initial studies with the titanium enclosed implantable device.

2.2 Challenges of a Porcine Model for Implantable Device Behavioral Experiments

Some challenges arose when applying this animal model to cranial implantable device studies. As can be seen in Fig 2.2, the porcine skull includes a relatively large frontal sinus which extends from the rostrum through the length of the elongated frontal bone to the coronal suture. The coronal suture is outlined in green in Fig 2.2a, while

the frontal sinus is outlined in red in Fig 2.2b.

The frontal sinus of the swine skull (as they grow older) are much more pronounced than what is observable in Fig. 2.2b. The frontal sinuses for the Yorkshire swine tended to extend further and also were quite a bit thicker (with more cavernous space inside) than the Yucatan minipig pictured in Fig. 2.2. The other challenge of working with Yorkshire swine was their growth rate. Fig. 2.1 shows the average growth rate of Yorkshire swine compared to other breeds.

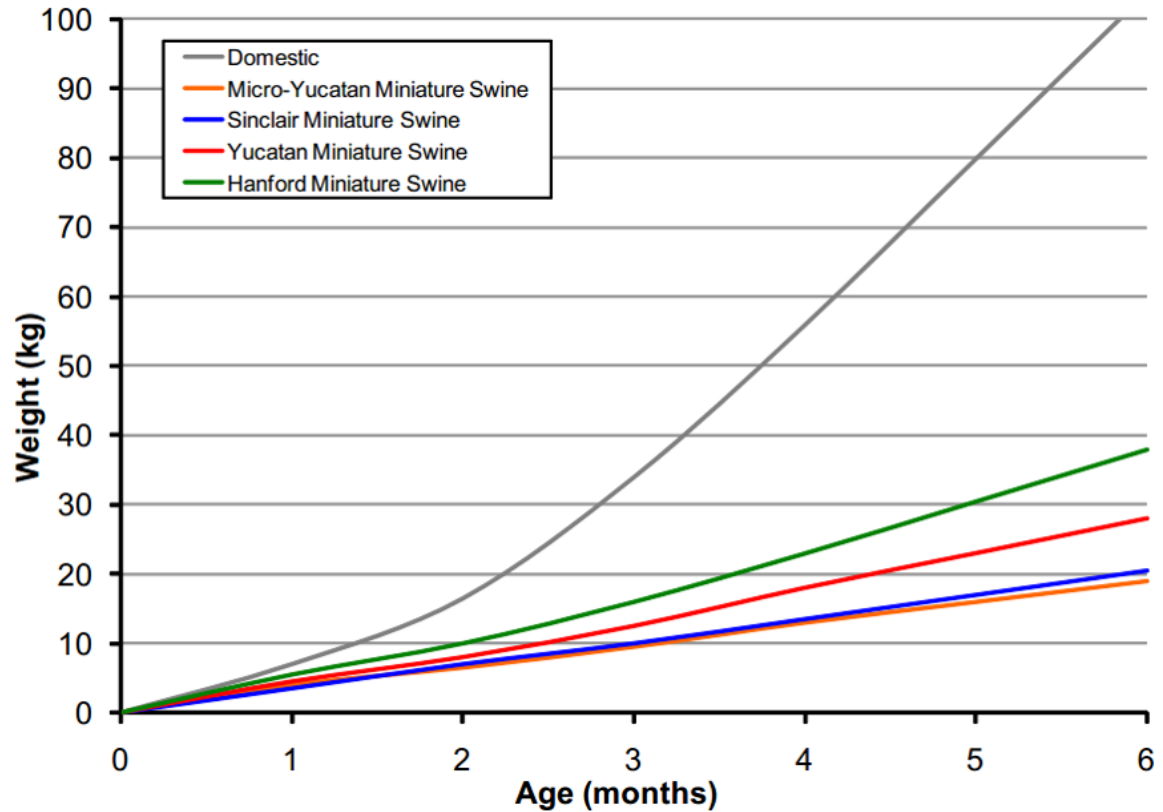
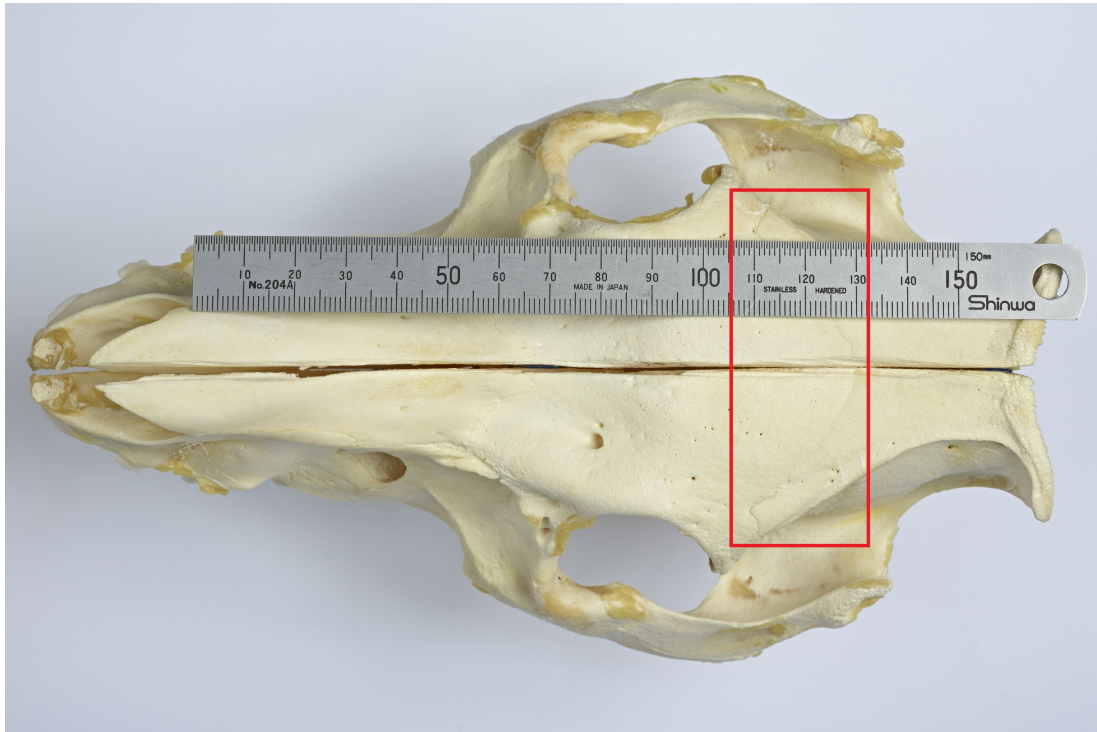
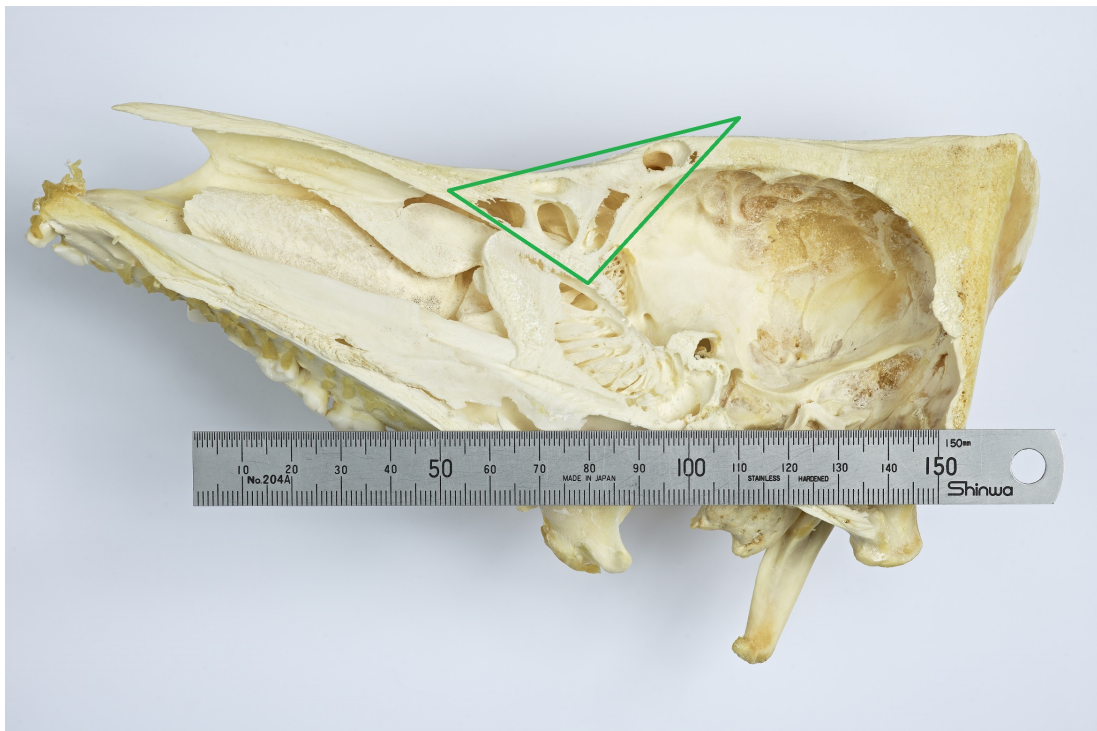


Figure 2.1: The average rate of growth of various swine breeds. Yorkshire swine as also known as Domestic swine, as seen in this graph. (Sinclair Bio Resources, LLC, <http://www.sinclairbioresources.com/>)[20]

One of the biggest challenges of utilizing a swine model in an implantable device



(a) The top of a young Yucatan minipig skull. The red outline shows the coronal suture.



(b) The cutaway side view of a young Yucatan minipig skull. The green outline shows the beginning expansion of the frontal sinus.

Figure 2.2: A young 20 month old female Yucatan minipig skull extracted and bleached for preservation. (Photos courtesy of Dr. Moses Goddard)

study (specifically a head mounted implant) is the unique physiology of the swine cranium. The extending deep, growing frontal sinus would create an open chamber above the cranial vault for the implantable device to sit in. This caused complications about sterile space during a surgical procedure. This also made the implantation procedure very difficult. Creating a craniotomy can be a long and sometimes difficult process. Due to the frontal sinus above the cranial vault, it was now necessary to essentially perform two craniotomies. The skull above the frontal sinus had to be bored through, and then the second layer of bone (as seen in Fig. 2.4) above the cranial vault had to be bored through. This extended the surgical procedure and caused trouble with maintaining a sterile field (opening a channel in from the non-sterile nose and into the sterile surgical field). The extremely fast growth of swine (especially Yorkshire/Domestic) also proved challenging for long term device longevity tests.

2.1 Yorkshire pigs grow very fast, and therefore, after implantation, continued to grow very large. The pigs were brought in at 20 months and were roughly 50 kilograms. Over the course of a few months, these swine had grown to be over 70 kilograms and still growing. The issue with these large animals was the displacement of the device. Most often, there was good osteointegration which lead to bone growth above the device (between the device and the skin). This caused the device to be covered in bone. The added thickness from the skin as well as the bone made it impossible to charge the implanted device. The distance introduced between the charger (outside) and the receiver (implanted) was far too great for power delivery.

Once the device was buried in bone, power transmission across the skin and through bone were impossible, thus the experiment had to be terminated.



Figure 2.3: A transverse transection into the top layer of a pig skull showing the network of frontal sinus cavities, which make implanting a neural recording device difficult.[8]

The other challenge resulting from the fast growth of the Yorkshire swine was the skin thickness. Since these animals are known for having a lot of body fat, this fat resulted in the thickness of the fat layer within the hypodermis (or subcutaneous tissue). The skin thickness of the Yorkshire swine increased well past 10 millimeters and the distance between power transmission coils was too far for efficient inductive coupling to occur. The extremely fast growth rate also made the animals difficult to manage, in terms of animal husbandry. They require more room, more food, and extra man power to deliver beneficial medicine or sedatives.

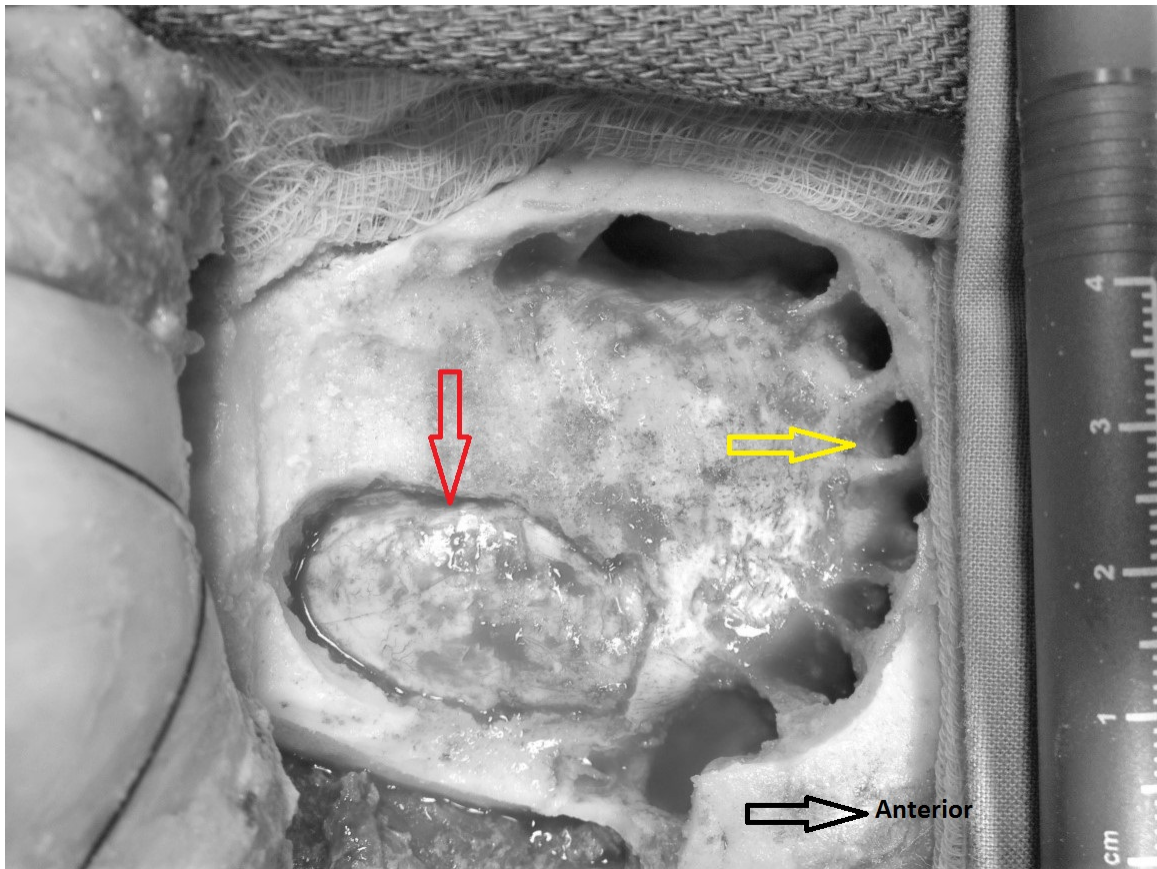


Figure 2.4: Skull of a pig underneath the scalp, with the top layer removed. The rostrum of the animal is toward the right. The red arrow points to the craniotomy to expose the dura, the yellow arrow points to one of the many chambers of the frontal sinus which extends over the cranial vault.

2.3 Solutions to Challenges of Implementing the Swine Model

The initial benefits of implementing the swine model were far too beneficial to bypass the swine model and revert to non-human primates. Therefore, in order to mitigate the disadvantages, the main problem that was addressed was swine growth rate.

Fig. 2.1 shows that there are other breeds of swine that do not grow as fast as the

Yorkshire. The challenge was to find one with a large enough skull to support a neural implantable device. Micropigs are small pets that are generally the size of large rabbits, or small dogs. They are much too small to be able to support a large titanium enclosed implantable device. So the best compromise between animal size and growth rate was achieved as the Yucatan Minipigs. Yucatans are known for being small sized swine, roughly the size of a large dog (around 50 kilograms). This balance of growth rate and animal size proved the best opportunity to try a large implantable device while maintaining the small size of the swine after an extended period of time.

2.4 Background on Development of a Wireless Neural and Behavioral Recording Platform

An entirely wireless neural and behavior recording platform has been developed for the purpose of studying cortical circuits during behavior of a freely moving animal with minimal observer intrusion. Our platform consists of (a) a 100-element micro-electrode, fully implantable, wireless, broadband neural recording device[3], and (b) a 2-channel, wireless, event tracking system, both of which simultaneously stream asynchronous data to a custom programmed FPGA (field-programmable gate array). All data is packetized and transmitted over Ethernet. The data are received by custom software (in MATLAB) which simultaneously animates neural data and behavioral data for the observer to draw correlations and witness patterns. This platform has

been implemented in a 10-month old female Yucatan mini-pig swine model (with the chronic, wireless, neural implant for over 9 months), extracting broadband neural data recorded simultaneously with time stamped behavioral recordings.

2.5 Introduction to Wireless Freely-Moving Animal Behavior Experimentation

Current technology utilized for microelectrode array or electrocorticography based electrophysiological neural recording setups from percutaneous implants include heavy cables connected to a rack of electronics, and a sophisticated restraint system (in the case of animal neural recordings). Such a total system can be divided into three major portions: (1) the neural recording device, (2) the method of data collection and aggregation (neural as well as behavioral), and (3) data storage and playback. Current procedures, while widely used, ask for an application of modern technological advances to upgrade the process flow, especially for mobile subjects. The neural recording device, such as a 100 channel microelectrode array (MEA) for non-human and human primates that is tethered to a percutaneous, stainless steel skull-mounted connector, has recently seen a push for wireless solutions[13, 5, 23]. However each of these methodologies have limitations since none are fully-implanted, broadband, or long-term tested in freely-moving animals. Data collection methodologies also remain limited in their capacity to be flexible or modular. These systems require bulky

electronics or custom proprietary solutions to be compatible with all use cases. Data storage and playback is an open-ended problem which currently begs for integration into a fully compliant, low-cost, compatible package. A complete platform built from the ground-up is introduced here which addresses each of these issues. This system is developed with modularity and portability, capable of being easily implemented in existing neural recording setups with relative ease. We have chosen a pig model, for economical and practical reasons, to test and exemplify the entire system concept which is ultimately aimed at primates.

2.6 Methodology of Developing a Fully Wireless System for Behaviorally Correlated Neural Recordings

2.6.1 Wireless, Fully-Implantable, Neural Recording Device

To address the process of developing a complete solution to the multiple problems afflicting current neural recording devices, a fully-implantable, wireless, neural recording device was developed and reported by our group[3]. This wireless 100-channel neural broadband interface mitigates risk of infection and externally mounted hardware[17], from percutaneous connectors. Our group has recently demonstrated this device as a chronic implant in the swine and non-human primate model. For the work reported



Figure 2.5: The pig and the feeder remain within the enclosed pen, wirelessly transmitting neural data (green) and behavioral data (yellow).

here, such a device was surgically implanted in a 10-month old female Yucatan mini-pig in the somatosensory association cortex. In order to charge the Li-ion battery in the hermetic subcutaneous implant, the swine (SY) is sedated for approximately 45 minutes with Dexmedetomidine while its blood oxygenation level and heart rate is observed with a pulse oxymeter. This allows charging of the device peacefully, without stressful restraint of an awake animal. The sedative is then reversed with an equal dosage of Atipamezole. Methods for charging the device without sedation such as non-stressful restraint are being pursued. The battery within the device lasts for approximately 8 hours on a single charge, thus allowing multiple 1 hour recording sessions per week. Robust multichannel recordings of spikes, field potentials and other low-frequency neural signal were recorded wirelessly and digitally on the 3.2 GHz RF carrier at approximately 48 Mbits/sec to a nearby receiver, while the animal was freely moving in its home pen (Fig. 2.5).

2.6.2 Wireless Behavioral Data Recording Device

The application of a neural recording tool requires the use of correlating specific behavior with neural data and thereby synchronized event tracking. In our work, the aim is to record from freely moving animals which are engaged in naturalistic yet stereotypical behavior such as foraging for food. Event tracking methodology today utilizes third party tools sending transistor-transistor logic (TTL) pulses to neural recording hardware in order to synchronize both types of data. A wireless, neural recording device especially argues for a wireless behavioral tracking method in order to keep the animal model freely-moving and untethered. While research is being conducted on visual and pattern recognition from video recordings, the real-time application and advanced computation required for such methodologies appears to be a limiting factor for their wide-spread application today[22]. Other types of vision tracking systems require an animal be shaved, or wear trackable position markers[25]. The approach proposed here consisted of a custom designed behavioral recording device. An enrichment feeding device designed by Fauna-Tek (<http://www.fauna-tek.net>), specifically for swine, was instrumented with Reed switches and IR sensors in order to determine how the animal interacts with the unit while retrieving food with its snout from various target wells. Fig. 2.6 shows the enrichment feeding device and its components.

Utilizing an open-source microcontroller (Arduino), the device polls the installed sensors at 20 kiloHertz and utilizes a maximum of 1 Watt to store the data and

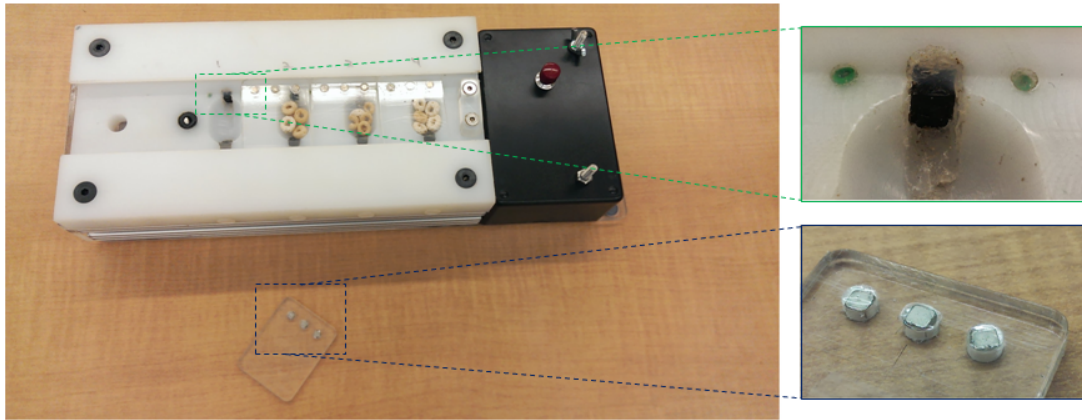


Figure 2.6: Center left: A complete instrumented, wireless, swine enrichment feeding device. Top right: Close up of the embedded Reed switches and IR sensor (emitters are on the opposite side of the food well, not pictured). Bottom right: Door with embedded magnets.

wirelessly transmit a timing pulse. The device is designed as a row of feeding wells with laterally sliding doors above each well which need to be slid in concert to access the food underneath. The sliding doors are embedded with magnets while the tray underneath has Reed switches installed to detect the presence of the magnetic field within the doors. Each well also has an IR emitter and detector pair embedded on opposite ends of the well to detect the presence of treats within the well. The current model of the device is a 4 well (8 sensor, 2 per well) device, but is scalable so that the next version of the device for minipigs will contain 11 wells (22 sensors). Each sensor is wired to a digital input pin on an Arduino Uno Rev. 3. The Arduino is equipped with a Wireless SD shield which provides microSD card read/write capabilities to the Arduino, as well as the ability to install an XBee S1 wireless communications board. The XBee S1 board broadcasts a wireless serial stream of data at 2.4 GigaHertz at a

rate of 250 kilobits per second to a compatible XBee S1 board utilizing the ZigBee (802.15.4) protocol. The Arduino has custom software that checks if the microSD card is inserted, all wells contain food, all the doors are closed and the locking pin is engaged, then waits for the animal to begin the experiment. Once the red button on top of the device (in Fig. 2.6) is depressed, the locking pin is disengaged and the animal is able to slide the doors open. As the animal interacts with the device, it records this activity and stores it on the inserted microSD card at a rate of 12.5 Hertz. It also simultaneously sends a timing pulse out wirelessly to synchronize this data with the neural data recorded externally. The process flow of the application of the device is exemplified in Fig. 2.7.

2.6.3 Data Collection, Synchronization, Storage, and Playback

A custom programmed FPGA (field-programmable gate array) from Orange Tree Technologies (<http://www.orangetreotech.com/>) was utilized to develop a method of receiving, packaging and synchronizing all neural and behavioral data together. The raw data are packaged in a custom format which is fully compatible with existing neural recording data formats such as neuroshare. This information is packaged into UDP packets and sent out over Ethernet. This approach provides flexibility for developing modular attachments for viewing, processing, or saving the received data without interrupting or introducing delay in the process flow. The process flow of the

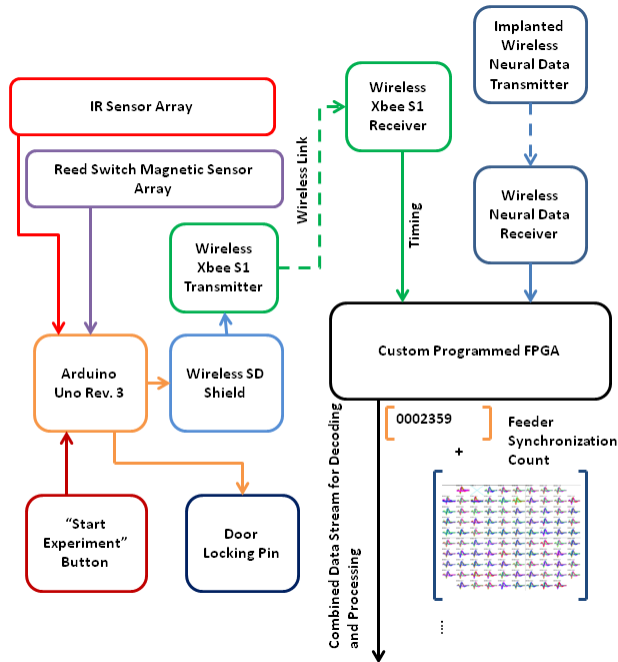


Figure 2.7: Process flow of the design of the Arduino Uno Rev. 3 board and the application of the FPGA.

programming of the FPGA is exemplified alongside the process flow of the Arduino in Fig. 2.7. These packets are received on a PC connected to the local Ethernet network. A script in MATLAB then takes the neural data and the behavioral events recorded on the microSD card and aligns them while storing them as a single MATLAB file. This single file has behavioral events time stamped and linked to the neural data for comparisons and correlation. A custom graphical user interface (GUI) was written in MATLAB to playback the recording obtained from each session. The GUI was built with modular visual segments in a window in order to view different processing methodologies on the neural data simultaneously. The user has the option of viewing raw data traces, extracted neural spikes, spike rasters, along with the capability of adding more visualization options in the future. The GUI also shows the recorded data from the instrumented enrichment feeding device. The GUI includes a progress

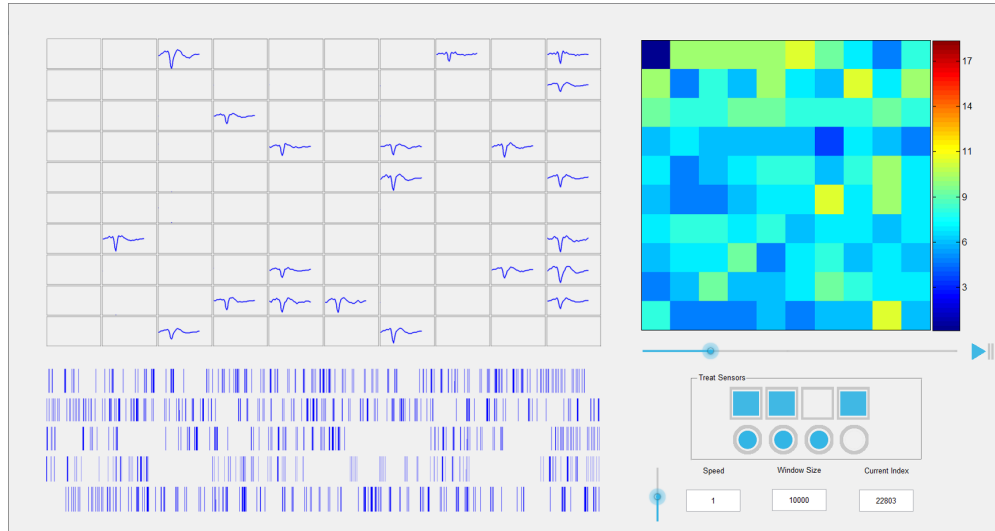


Figure 2.8: A screenshot of the custom GUI in MATLAB showing neural recorded data and behavioral data as temporally synchronized. The top left of the image shows averaged, extracted spikes, while the bottom left of the image shows spike raster data from a select few channels. The top right of the image shows a heatmap representation of spiking rate per channel while the bottom right shows behavioral data from the enrichment feeder.

slider which controls the playback (for both the neural data as well as the behavioral data) at variable speeds from much slower to twice as fast as real time. Fig. 2.8 exemplifies the capabilities of the GUI by showing a screenshot of the various parts of the window.

2.7 Results of the Fully Wireless Behavior and Neural Recording System

The neural recording device has been implanted in a swine model (animal SY) for over 9 months, providing broadband wireless neural data from the intracortical MEA,

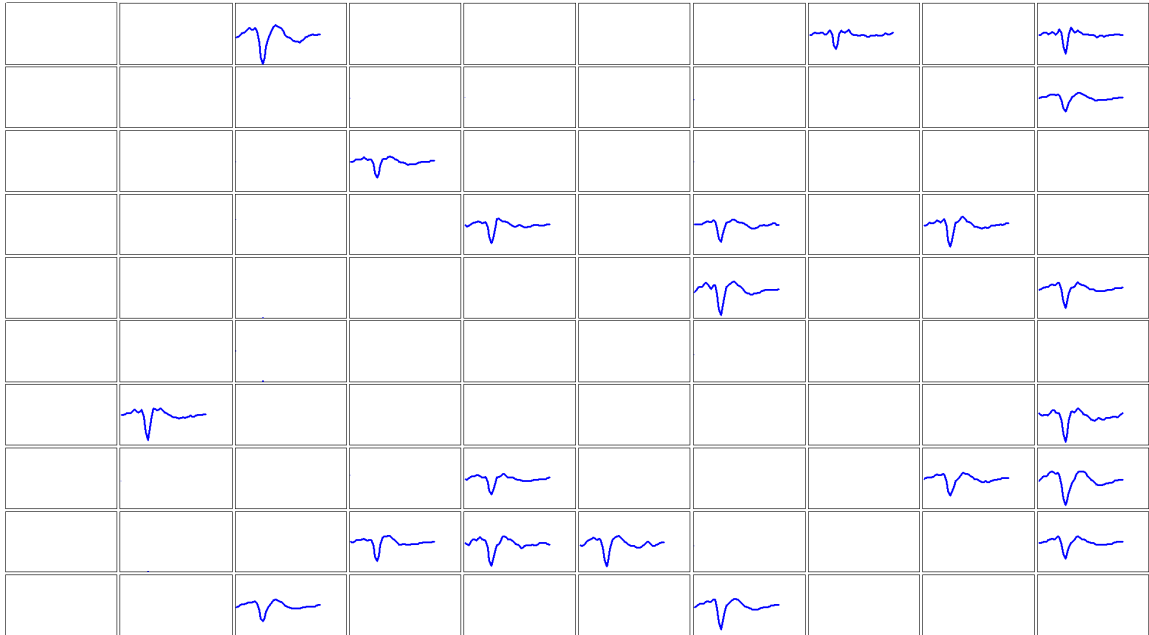


Figure 2.9: Mean neural spikes recorded during one session from the implanted array of a mini-Yucatan swine. Blank channels were either too noisy to discern individual spikes, or there was no spike found on that channel during this recording session. The total time duration for each spike represented is approximately 3 milliseconds, the scale is roughly 350 microvolts.

ranging from single unit spiking to local field potentials etc. Fig. 2.8 shows a screenshot of the custom GUI with neural data extracted from the swine model (SY). The top left of the figure shows threshold-extracted, average spikes per channel recorded 9 months after implantation. This recording is part of a larger set of recordings performed continuously over the course of 9 months. As exemplified by the figure, we have been able to record neural spikes as well as LFP data from, on average, 20% of our channels. This means that our neural recording device and behavioral setup can be implemented into current long-term neural recording systems in labs, and the

resulting data can be readily incorporated into previously implemented data flow processes. The device performs reliably and at present writing continues to record from SY, with broadband neural data being collected and neural spike data observed and extracted from many channels. The behavioral data from SY shows similar promise as decision-making trends are observed in SY's approach to the enrichment feeding tray, guided by the animal's acute sense of smell, and the subsequent procedure for emptying the tray. The feeding tray allows for the observation of SY's preferences and decisions as the tray is emptied (e.g. from right to left). Minimal amount of training was required for SY to be comfortable with accessing the food wells from the tray (approximately 3 months). SY required training to push the "red button" to begin the recording trial, and was able to perform the action after a few days of self-guided exploration. The trends shown by the recordings suggest that SY has a specific pattern of emptying the enrichment tray which involves beginning from one end of the tray and exposing each well one by one. Future experiments will attempt to guide SY to approach the tray from a different end, or to randomize the selection of successive wells. The data acquisition via an FPGA records a reliable, reproducible data stream which allows the user to save synchronized behavioral data with the neural data. The counter on the FPGA increments alongside the counter recorded on the microSD card within the enrichment feeding device. When the packaged data is extracted and aligned it shows observable trends within the time-stamped behavior. These trends will become more apparent as more data are recorded and sample sizes

increase over time. The GUI gives the user the ability to play through the trial with a slider showing the current time within each trial. This allows the experimenter to observe simultaneous neural data with behavioral data and to determine trends or correlations from the synchronized data. The GUI requires the observer to hit “play” or “pause” to control the trials recreation on screen. The GUI allows the user the ability to visually recreate the trials’ behavioral and neural data with different neural analysis techniques such as spike extraction (utilizing thresholding, template-matching, or hoops) and, in the future, dimensionality reduction techniques (such as Gaussian Process Factor Analysis or Principal Component Analysis). This capability allows simultaneous application of multiple analysis tools while observing the behavioral data to witness correlations which can then be empirically observed by exporting the data from the custom format (which includes raw data streams) to a standardized format for a neural analysis application of the users’ choice. We are currently exploring further the relationships between the behavioral data and neural data patterns, while transitioning the present proof-of-concept system to brain science studies.

2.8 Conclusions Gathered Through the Development of this System

In this work we report initial results from building a complete neural recording-behavioral tracking platform for freely moving subjects from the ground-up. The

platform was built with the idea of scalability in mind, so as to offer the ability to increase the number of recording channels, number and type of behavioral event tracking, as well as the types of data analytics utilized to visually represent the data recorded. Future versions of the platform can include more sophisticated behavioral event tracking (such as visual tracking), various types of biomarkers to compliment the neural data, and more data analysis techniques.

2.9 Conclusions on Utilizing a Swine Animal Model in a Wireless Implantable Device Study

Utilizing swine for a freely-moving animal experiment turned out to be a very fruitful experience. This type of neural implantable device significantly benefits from being developed and tested within a living organism, and having the “stress test” of being within a swine provides a unique and rigorous testing environment. Implantable devices need to examine a lot of variables before being ready for human clinical use and incorporating a swine study proved to be a way to speed up the collection of a lot of different types of data. The device longevity under question was very satisfactorily answered by the number of days the devices had been implanted. The benefits of using a swine animal model for this type of experiment were exemplified by the number of swine we were able to implant in quick succession. The results showed devices lasting over 250 days minimum within each animal, as can be seen in table 2.1.

Animal	Species	Days Implanted	Reason for Explantation
SY	Swine	613	Signal Degradation
SU	Swine	321	Scalp Thickness
SM	Swine	252	Scalp Thickness

Table 2.1: Table of animal models implanted with the titanium enclosed implantable device for an extended period of time. All devices explanted from these animal models were fully functional at the time of explant. The two swine (SU and SM) were Yorkshire swine whose scalp grew too thick for the wireless charging of the implant to work effectively. This made charging the device impossible and we were forced to explant. Upon explant, the devices were charged and were shown to be fully functional. Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to loss of usable signals being collected from the brain/device interface which is well documented[1]

The practical benefits of using many animal models for experiments and not having the restrictions generally associated with non-human primates, in this early stage, hastened the study to improve the implantable device. Yucatan minipigs proved to be a perfect application of the ease of experimental use of swine for a behavioral implant study. Once the swine experiments showed promise, the device progressed on to more active behavioral experiments with more complex behavioral tasks. The ability to perform more complex behavioral tasks and biomechanical similarity to humans paved the way for non-human primate studies with the implantable device.

References

- [1] James C Barrese, Naveen Rao, Kaivon Paroo, Corey Triebwasser, Carlos Vargas-Irwin, Lachlan Franquemont, and John P Donoghue. Failure mode analysis of silicon-based intracortical microelectrode arrays in non-human primates. *Journal of Neural Engineering*, 10(6):066014, 2013.
- [2] D. Borton, M. Yin, J. Aceros, N. Agha, J. Minxha, J. Komar, W. Patterson, C. Bull, and A. Nurmikko. Developing implantable neuroprosthetics: a new model in pig. *Conf Proc IEEE Eng Med Biol So*, pages 3024–3030, 2011.
- [3] David A Borton, Ming Yin, Juan Aceros, and Arto Nurmikko. An implantable wireless neural interface for recording cortical circuit dynamics in moving primates. *Journal of Neural Engineering*, 10(2):026010, 2013.
- [4] Christopher J C Burges. A Tutorial on Support Vector Machines for Pattern Recognition. *Data Mining and Knowledge Discovery*, 2(2):121–167, jun 1998.
- [5] C.A. Chestek, V. Gilja, P. Nuyujukian, R.J. Kier, F. Solzbacher, S.I. Ryu, R.R. Harrison, and K.V. Shenoy. Hermesc: Low-power wireless neural recording system for freely moving primates. *Neural Systems and Rehabilitation Engineering, IEEE Transactions on*, 17(4):330–338, Aug 2009.
- [6] T A Christensen, V M Pawlowski, H Lei, and J G Hildebrand. Multi-unit

recordings reveal context-dependent modulation of synchrony in odor-specific neural ensembles. *Nature neuroscience*, 3(9):927–931, sep 2000.

- [7] Committee for the Update of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, Division on Earth and Life Studies, and National Research Council. *Guide for the care and use of Laboratory Animals - 8th Edition*. National Research Council, 2010.
- [8] Wikimedia Commons. Opened frontal sinus of a pig skull. https://commons.wikimedia.org/wiki/File:Sinus_frontalis_pig.jpg, 2007. Accessed: November 4, 2015.
- [9] S L Craner and R H Ray. Somatosensory cortex of the neonatal pig: II. Topographic organization of the secondary somatosensory cortex (SII). *The Journal of comparative neurology*, 306(1):39–48, apr 1991.
- [10] Bernadette Félix, Marie Eva Léger, Denise Albe-Fessard, J. C. Marcilloux, O. Rampin, J. P. Laplace, a. Duclos, F. Fort, S. Gougis, M. Costa, and N. Duclos. Stereotaxic atlas of the pig brain. *Brain Research Bulletin*, 49(99):1–138, may 1999.
- [11] Justin D. Foster, Paul Nuyujukian, Oren Freifeld, Stephen I. Ryu, Michael J. Black, and Krishna V. Shenoy. A framework for relating neural activity to freely moving behavior. *Proceedings of the Annual International Conference of the*

IEEE Engineering in Medicine and Biology Society, EMBS, 2012:2736–2739, jan 2012.

- [12] M. A. Groenen, A. L. Archibald, H. Uenishi, C. K. Tuggle, Y. Takeuchi, M. F. Rothschild, C. Rogel-Gaillard, C. Park, D. Milan, H. J. Megens, S. Li, D. M. Larkin, H. Kim, L. A. Frantz, M. Caccamo, H. Ahn, B. L. Aken, A. Anselmo, C. Anthon, L. Auvil, B. Badaoui, C. W. Beattie, C. Bendixen, D. Berman, F. Blecha, J. Blomberg, L. Bolund, M. Bosse, S. Botti, Z. Bujie, M. Bystrom, B. Capitanu, D. Carvalho-Silva, P. Chardon, C. Chen, R. Cheng, S. H. Choi, W. Chow, R. C. Clark, C. Clee, R. P. Crooijmans, H. D. Dawson, P. Dehais, F. De Sapio, B. Dibbits, N. Drou, Z. Q. Du, K. Eversole, J. Fadista, S. Fairley, T. Faraut, G. J. Faulkner, K. E. Fowler, M. Fredholm, E. Fritz, J. G. Gilbert, E. Giuffra, J. Gorodkin, D. K. Griffin, J. L. Harrow, A. Hayward, K. Howe, Z. L. Hu, S. J. Humphray, T. Hunt, H. Hornshøj, J. T. Jeon, P. Jern, M. Jones, J. Jurka, H. Kanamori, R. Kapetanovic, J. Kim, J. H. Kim, K. W. Kim, T. H. Kim, G. Larson, K. Lee, K. T. Lee, R. Leggett, H. A. Lewin, Y. Li, W. Liu, J. E. Loveland, Y. Lu, J. K. Lunney, J. Ma, O. Madsen, K. Mann, L. Matthews, S. McLaren, T. Morozumi, M. P. Murtaugh, J. Narayan, D. T. Nguyen, P. Ni, S. J. Oh, S. Onteru, F. Panitz, E. W. Park, H. S. Park, G. Pascal, Y. Paudel, M. Perez-Enciso, R. Ramirez-Gonzalez, J. M. Reecy, S. Rodriguez-Zas, G. A. Rohrer, L. Rund, Y. Sang, K. Schachtschneider, J. G. Schraiber, J. Schwartz, L. Scobie, C. Scott, S. Searle, B. Servin, B. R. Southey, G. Sperber, P. Stadler,

- J. V. Sweedler, H. Tafer, B. Thomsen, R. Wali, J. Wang, J. Wang, S. White, X. Xu, M. Yerle, G. Zhang, J. Zhang, J. Zhang, S. Zhao, J. Rogers, C. Churcher, and L. B. Schook. Analyses of pig genomes provide insight into porcine demography and evolution. *Nature*, 491(7424):393–398, Nov 2012.
- [13] R.R. Harrison, P.T. Watkins, R.J. Kier, R.O. Lovejoy, D.J. Black, B. Greger, and F. Solzbacher. A low-power integrated circuit for a wireless 100-electrode neural recording system. *Solid-State Circuits, IEEE Journal of*, 42(1):123–133, Jan 2007.
- [14] S. K. Kelly, D. B. Shire, Jinghua Chen, P. Doyle, M. D. Gingerich, S. F. Cogan, W. A. Drohan, S. Behan, L. Theogarajan, J. L. Wyatt, and I. J. F. Rizzo. A Hermetic Wireless Subretinal Neurostimulator for Vision Prostheses. *IEEE Transactions on Biomedical Engineering*, 58(11):3197–3205, nov 2011.
- [15] N Ludvig, J M Botero, H M Tang, B Gohil, and J G Kral. Single-cell recording from the brain of freely moving monkeys. *J Neurosci Methods*, 106(2):179–187, apr 2001.
- [16] L M Malavasi. Physiological and behavioural effects of opioids in pigs subjected to abdominal surgery, 2005.
- [17] Angus J C McMorland and Meel Velliste. Baseplate for two-stage cranial mounting of bmi connectors. *Journal of Neural Engineering*, 10(3):034001, 2013.

- [18] S Saikali, P Meurice, P Sauleau, P A Eliat, P Bellaud, G Randuineau, M Vérin, and C H Malbert. A three-dimensional digital segmented and deformable brain atlas of the domestic pig. *Journal of Neuroscience Methods*, 192(1):102–109, sep 2010.
- [19] Toshiyuki Saito, Minako Uga, Daisuke Tsuzuki, Hidenori Yokota, Keiji Oguro, Tsuyoshi Yamamoto, Ippeita Dan, and Eiju Watanabe. Evoked potential mapping of the rostral region by frameless navigation system in Mexican hairless pig. *Journal of neuroscience methods*, 212(1):100–5, oct 2013.
- [20] LLC Sinclair Bio Resources. Sinclair Bio Resources literature. <http://www.sinclairbioresources.com/Literature/Literature.aspx>. Accessed: November 4, 2015.
- [21] Salah Sommakia, Heui C. Lee, Janak Gaire, and Kevin J. Otto. Materials approaches for modulating neural tissue responses to implanted microelectrodes through mechanical and biochemical means. *Current Opinion in Solid State and Materials Science*, 18(6):319 – 328, 2014. Neuroengineering Materials.
- [22] Andrew D. Straw, Kristin Branson, Titus R. Neumann, and Michael H. Dickinson. Multi-camera real-time three-dimensional tracking of multiple flying animals. *Journal of The Royal Society Interface*, 8(56):395–409, 2011.
- [23] Tobi A Szuts, Vitaliy Fadeyev, Sergei Kachiguine, Alexander Sher, Matthew V Grivich, Margarida Agrochão, Pawel Hottowy, Wladyslaw Dabrowski,

- Evgueniy V Lubenov, Athanassios G Siapas, et al. A wireless multi-channel neural amplifier for freely moving animals. *Nature neuroscience*, 14(2):263–269, 2011.
- [24] Fabio Valentini, Flavia Fassone, Andrea Pozzebon, Alessandra Gavazza, and George Lubas. Use of totally implantable vascular access port with mini-invasive Seldinger technique in 12 dogs undergoing chemotherapy. *Research in veterinary science*, 94(1):152–7, feb 2013.
- [25] Carlos E. Vargas-Irwin, Gregory Shakhnarovich, Payman Yadollahpour, John M. K. Mislow, Michael J. Black, and John P. Donoghue. Decoding complete reach and grasp actions from local primary motor cortex populations. *The Journal of Neuroscience*, 30(29):9659–9669, 2010.

3

Behavioral Applications in Freely-Moving Non-Human Primate Animal Models

While swine show a lot of promise for device longevity studies as well as physiological similarities to humans, ultimately, this implantable device is a neural recording tool. In order to prove its capabilities, the device must be implemented in a complex behavioral study similar to the type of therapeutic application it would encounter in human clinical use. The importance of utilizing this device in a non-human primate study became apparent. Non-human primate use for neuroscientific study is a complicated undertaking due to the moral and ethical questions it raises. These animals are relatively close to humans genetically and physiologically. Some subspecies are

also believed to be evolutionarily the closest species to the *Homo sapeins*. This brings a unique opportunity, as well as a challenge in the research world.

A Note on Using Non-Human Primates as an Animal Model for Experimentation

Obtaining an analog for the human form, physiology, behavior, and psychology is very difficult. However, short of experimenting with necessary procedures on humans, utilizing non-human primates is the next best thing. These experiments are, of course, handled with the utmost care. All protocols are approved by the Institutional Animal Care and Use Committee (IACUC), as well as the US Department of Agriculture (USDA). All guidelines defined by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) are followed, after obtaining their accreditation. The guidelines set within the guidebook printed by the Office of Laboratory Animal Welfare (OLAW) within the National Institutes of Health (NIH) are also strictly followed. The research sites (laboratories) as well as the animal housing facilities are regularly inspected and all protocols are checked for accuracy and consistency of regulations followed. All researchers working with these animals have to be regularly tested (for health) but also are given regular training for safety and regulation of animal control. All exchanges with the animal models is documented and every interaction is logged and has multiple levels of scrutiny (within the institution and beyond). The work done has to be justified within the tier of animal research

conducted, and the use of each specific animal has to be verified. The rules of utilizing animals in research is broken down into the 3 R's: 1. Replacement, 2. Reduction, 3. Refinement. If it can be, any work on an animal should be done on a replacement model be it bacterial, cellular, dummy etc. The reduction in the total number of animals used, the reduction in the processes, the reduction in complication, variables and loss of life should be attempted. Finally, the process should be refined so that there is as little as possible pain, discomfort or discomfort to the animal model.[8]

3.1 Background of The Necessity of Freely-Moving Behavioral Neuroscience

Classical neuroscience consists of well trained, well controlled experimental animal studies. These studies require the complete focus and participation of the experimental animals involved and usually demand months of training.[4] The animals are generally trained with positive reinforcement, giving juice or a treat for good or desired behavior, while unwanted behavior is ignored to discourage it. The classical clicker training method, or more generally, positive reinforcement is very effective in keeping all types of animals safe, happy, and motivated; be it in the laboratory or a pet at home.[6] However, it requires a lot of time and effort on the side of the researcher. The other major drawback of clicker training an animal, is the inherently shaping of its psychological behavior. Constraining an animal to study movement

in a classical neuroscientific study is a good method of focusing on the precise area of behavioral motor control. However, it is impossible to study naturalistic behavioral motion through such a paradigm. To study an animal's neural correlates to behavior, its interaction with its peers, or its environment in a naturalistic or instinctual way is impossible with the current technology. The entire concept of such a study seems outlandish or impractical with the idea of constrained or fixed neural recording experiments. However, recent advances in wireless telemetry have allowed various methodologies of transmitting the neural data stream so the animal model is no longer constrained.[2, 3, 4, 5, 9, 10]

The benefits of freely-moving animal experiments open up many advanced study possibilities that were not available before. The ideal goal, from a device development point of view, has always been to aim for a "Jane Goodall of Neuroscience". The concept behind this, is to study animals within their own natural habitat, performing their daily functions of their own volition. Allowing a researcher, a behavioral neuroscientist, the ability to read from the brain while an animal performs its naturalistic behavior, or communicates with its peers is revolutionary. This type of study has never been done before because it hasn't been possible before. The type of work unlocked by this implantable device allows for new ideas and new study possibilities to open up within the neuroscience community.

3.2 Introduction to Implantable Neural Recording Devices to Non-Human Primates

The use of non-human primates for neural recording implantation studies has been around for a few decades now.[4] However, as this work progressed, the limitations of the types of devices implemented in this study became clear. While these devices provide great benefit in terms of functionality and capability[5, 3, 9], the approach we took was in order to provide medium range, fully implantable systems that, when implemented, were relatively indistinguishable from a normal, healthy animal. As Fig. 3.1 shows, our primate with an implant only had a small raised section above its head for the implant, which eventually was met with the raising scalp muscles as they grew up around it.



Figure 3.1: Image of a non-human primate with the neural implantable device fully implanted underneath the scalp (above the skull). The implant shape is difficult to discern from the shape of the natural skull of the animal.

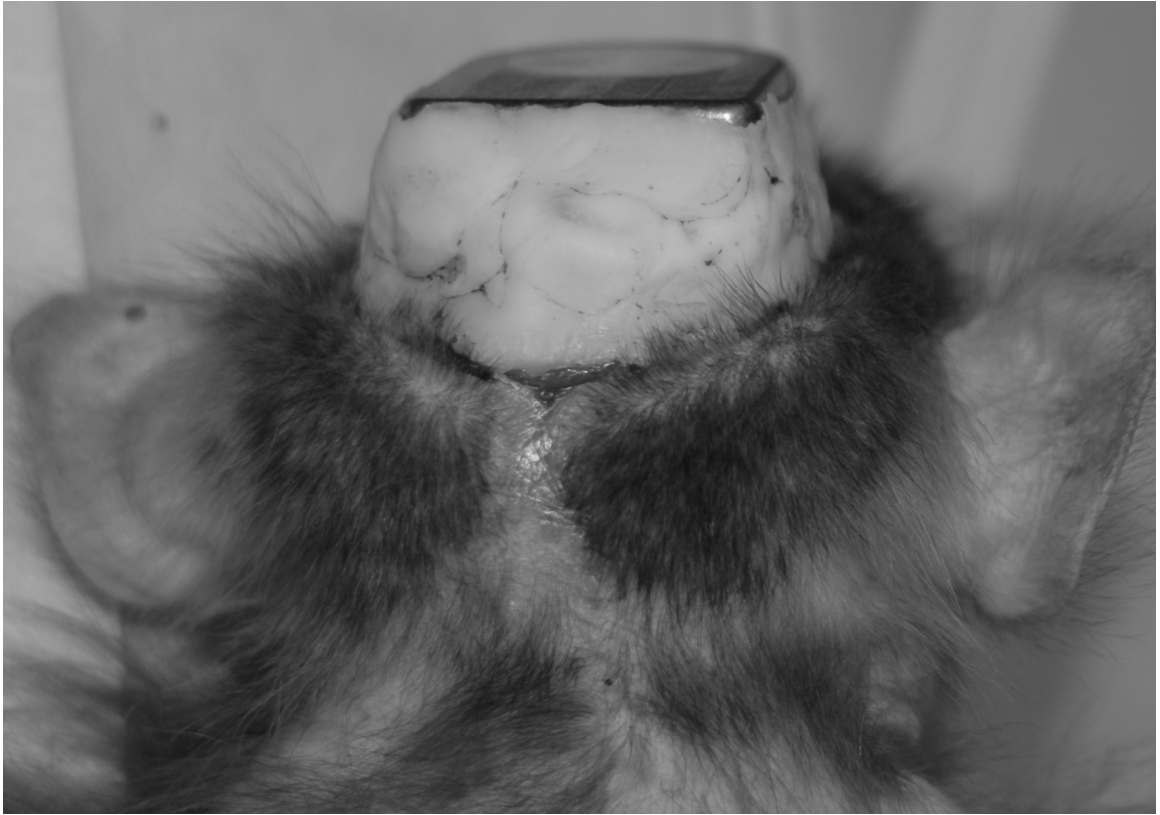


Figure 3.2: Image of a non-human primate with the neural implantable device exposed and the skin of the scalp pulled back (around the dental acrylic).

Within a few months time, the implant was indiscernible from the scalp muscles and hair around it. While this is a unique benefit of working with macaques, the implant itself is a relatively thin and small device, relative to its capabilities. This allowed the animal to freely move around and transmit its neural data to an accompanying computer wirelessly. Not shown in Fig. 3.1 is the wireless receiving antenna positioned just above the non-human primate to record the data being transmitted. While our current application of this technology consisted of discerning behavioral action from freely-moving naturalistic tendencies, the productive applications of this system can be greatly varied. The challenge in designing a freely-moving animal

experiment is the careful metrology of the behavior performed. A methodology of quantitatively determining what the animal is doing, how it is performing, or when it is performing. These behaviors must be measured and time synchronized with the incoming neural data in order to correlate behavior to neural computation. This is the basis of behavioral neuroscience, which will now be greatly improved due to the potential of recording freely-moving neural activity. This study will discuss the development ideas behind freely-moving behavioral activity to compliment the neural activity, and what the potential to learn from that is.

3.3 Methods of Implementing Implantable Neural Recording Devices into Non-Human Primates

Non-human primates have a unique and very important role in the study of neuroscience. The implementation of implantable devices for the study of non-human primate behavior allowed the study of various aspects of psychological and neural aspects of these animals. In our study, we implanted these devices into non-human primates in order to pave the way for human therapeutic applications, as well as opening the channels for new (neuro)scientific pursuit.

3.3.1 The Choice of a Non-Human Primate for Implantable Device Study

For this study, adult non-human primates were selected, in order to provide a larger bone surface area to fit our implantable device onto the skull. Older primates are generally over 30 kilograms, and offer larger skull area for implantable devices. Since the footprint of the device is roughly 4.2 centimeters by 5.6 centimeters, it would be beneficial for the study to have a large enough head (skull) to accomodate this size. This is why mature, relatively large non-human primates were chosen.

3.3.2 Non-human Primate Surgical Procedure

Each non-human primate surgery was handled the same way to reproduce the results. Two of the three surgeries maintained an open head wound above the implant (in order to not stretch the skin) and kept the device exposed and the skin retracted from above the implant. The following procedure defines the protocol of the primate surgeries conducted.

Primates were sedated with ketamine (0.15 milligrams/kilogram) from their home cages. They were then transported to a surgical preparatory suite where they were intubated and delivered isoflurane at MAC levels (approximately 1.2 - 1.4%). At this stage, the animal was transferred to the operating room. Once the animal is in the

operating room, the surgeon will go and “scrub in” to prepare for the sterile procedure. The sterile surgeon then prepares the surgical site utilizing sterilizing agents (antibiotics) such as Povidone-iodine (Betadine). The remaining area (non-sterile) is then covered with sterile surgical sheets. Thereby, only the sterile surgical site is exposed, covering the remaining body/parts of the area with a sterile sheet.

The implantation procedure included at least two surgeons: a main surgeon (usually a practiced Neurosurgeon, neurosurgery resident associated with the lab or a collaborator) and one or more secondary surgeons (graduate students trained in surgical procedures). With the help and supervision of the Brown Animal Care Facility (ACF) veterinary technicians, the vitals of the animals were observed and logged during the entire procedure. The procedure involved making a U shaped incision in the skin to flap it over, allowing for a vascularization path for the skin. There was then a craniotomy made above the cortical area of interest (usually the motor cortex, MI). The array from the device was then inserted into the top of the cortex utilizing a special pneumatic inserter. This was a small tool for the purposes of lightly tapping the array of electrodes the correct distance (1.5 millimeters) into the cortex. This was done with a physical spacer that allowed the “hammer tip” of the device to only move a total of 1.5 millimeters. This was then hammered by a piston inside the device, which was driven by a gust of compressed air at a preset pressure and velocity. Once the array was placed inside, the tether of 100 gold independently insulated wires wrapped in silicone were then looped around the craniotomy in a trough. The

titanium can of the device (the terminus of the gold wire bundle) was then placed above the craniotomy, closing up the gap physically. There was a small shallow bed carved into the bone using a handheld surgical drill in order to allow the device to sit comfortably flat on the rounded, curved surface of the skull. The metallic feet of the titanium enclosure were then screwed into the skull using 2 or 3 millimeter small titanium surgical screws. the remaining gaps around the device were then filled with dental acrylic (polymethyl methacrylate, PMMA). The PMMA allowed the contours of the device to have a smoother transition down to the bone and give the “bulge” created by the device on top of the skull a smoother curvature. The idea behind the PMMA was also to give the skin something below it to fill the gap, otherwise the skin would be tenting across the device leaving open gaps between the skin and the skull, allowing for ingress of foreign material and waste tissue to collect. This could potentially lead to infections and immune or inflammatory reactions by the body, which would be exacerbated by the presence of the titanium can.

Once the dental acrylic was in place, the surgical procedure bifurcated for the different surgeries. For two of the three non-human primate surgeries, the skin was allowed to relax around the sides of the dental acrylic and antibiotics were administered to help the immune system fight the open wound and foreign body present. For the fully implanted case, the skin was extended and sutured closed around the device. In all cases, the animal was then brought back into its home cage and allowed to recuperate and given food and water until it was ready to sustain itself. Up to three

days of direct post-operational care was given to each animal. Post-operational care consisted of constant supervision by the veterinary technicians as well as consistent check ups by the animal care facility staff and researchers involved in the procedures.

3.3.3 Charging and Experimentation Protocol for the Implantable Device

The daily protocol of conducting experiments with the implanted non-human primates consisted of sedating the animals with a small intramuscular dose of ketamine and laying them down on a table. Then the devices on (or in) the non-human primates' heads were charged. The charging protocol involved a home-made 4 Watt amplifier that took an approximately 220 millivolt, 130 kilohertz sine wave from a signal generator. This amplified signal was then bifurcated to be sent to an oscilloscope to be observed and also to a handmade coil for the output of the charging power. The coil was then visually aligned with the clear sapphire window on the implantable device (to be concentric with the coil internal to the implantable device). At this point, the frequency on the signal generator was adjusted (usually at a step of 1 kilohertz) in order to obtain the resonant frequency of the two coupled coils. The oscilloscope was observed due to the reduction of the amplitude in the power delivered to the coil at the resonant frequency of the system (roughly 150 kilohertz). This would cause the minimum point in the waveform due to the maximum reflection from the secondary when maximum efficiency is achieved at the resonant frequency. When this frequency

was found, the charger was manually held on top of the implanted device to allow for charging while the animal was sedated. Due to the inefficiencies in the original coil design and implementation (as well as the presence of the titanium enclosure), the charging protocol was found to heat up the implanted device. The charger itself was also observed to get uncomfortably hot. This required the use of active water cooling via a wet towelette which was kept cool with pouring fresh water over it during the entire charging session. The addition of water cooling, as well as temperature measurement allowed safe and continuous charging of the implanted device.

These charging sessions usually lasted between 45 minutes to an hour in order to sum up to roughly a 4 hour charging time during a week. Then after 4 total hours of charging were collected on to the device, the animal was returned to its cage and allowed to recover from the sedation. While the animal was outside its cage, the inside of the cage was fitted with receiving antennas (sometimes left outside). The antennas were connected to a custom built receiver hardware system which received the data stream collected by the antennae. This data stream was then processed and sent to a computer for visual inspection as well as storage to a computer using software and hardware designed by Blackrock Microsystems, LLC (<http://www.blackrockmicro.com/>).

3.4 Results of Freely-Moving Non-Human Primate Neural Studies with a Wireless Implant

The implantation procedure in a non-human primate taught us a lot about potential application to humans of this implantable device. The curvature of the skull of a non-human primate relative to a human's skull is significantly sharper. The small size of the non-human primate skull makes a comparison of size affecting the patient very difficult. However, the one point that can be learned, which was also corroborated by neurosurgeons, is that the size of this device would be perfectly acceptable if implanted into a human being.

Fig 3.3 shows a freely-moving feeding session where the non-human primate sat in its cage and was fed treats through the door. The animal is calmly sitting in its cage, has not been trained for any behavior or been introduced to any undue stress or behavioral conditioning. However, the recording of its neural data and arm reaching movement can be observed from this image. The image is a still taken from a video recording of the behavioral experiment. The experiment involved a freely-moving non-human primate which was presented treats through a door (on top of which a receiving antenna was placed). The primate approached the treat of its own volition, and reached for the treat without any given cue. The primate then reached for the treat, obtained it and retreated back into its cage to eat the treat. All of this was time synchronized on video as well as the neural data stream (as seen on the top

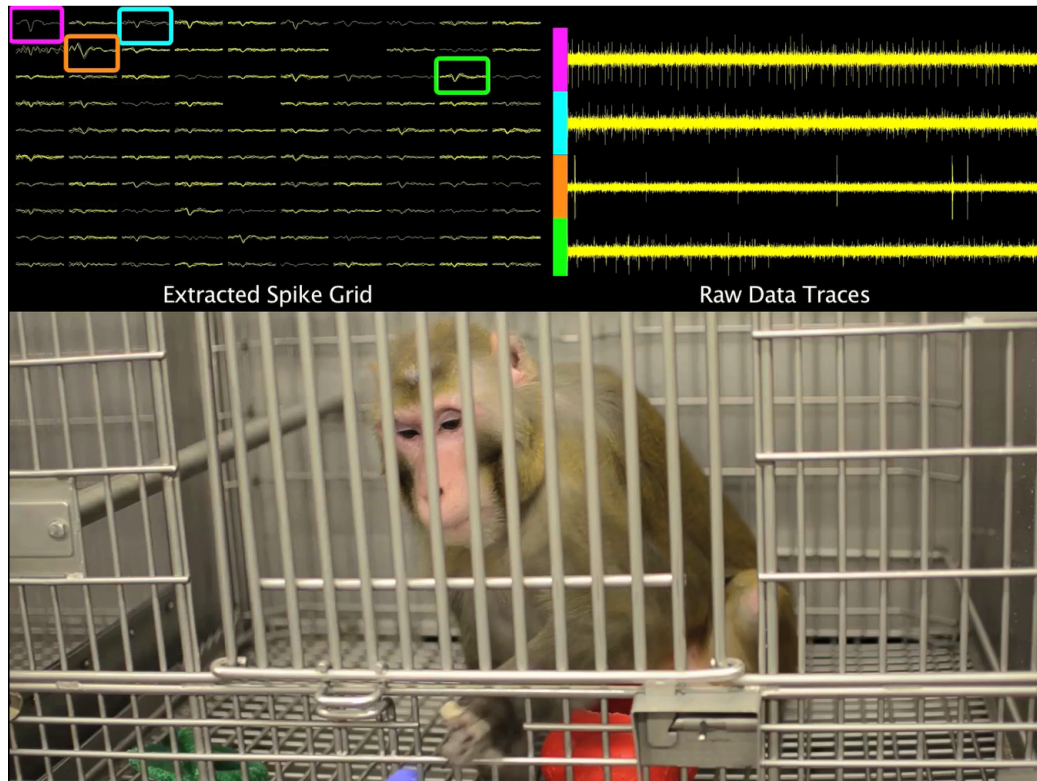


Figure 3.3: Still from a video of a non-human primate performing an unrestrained reaching behavior within its home cage while neural data is collected wirelessly. The top left shows spike averages over 2.5 milliseconds, spikes sorted via threshold crossing, overlayed during the entire recording session. The top right shows a running trace of approximately 10 seconds, realtime raw data stream being recorded directly from 4 different channels within the array. (Image is a still taken from a video composited by Jacob Komar)

section of Fig. 3.3).

Fig 3.4 shows the data collected and recorded from the 100 channel implant within the non-human primate. This is data recorded during activity by the non-human primate which was not learned or trained. The animal was simply behaving in a naturalistic way, reaching for treats being provided by a researcher while it was entirely unrestrained. For comparison's sake Fig 3.5 shows data collected from a tetraplegic human. This human had the same type of electrode array implanted as the arrays

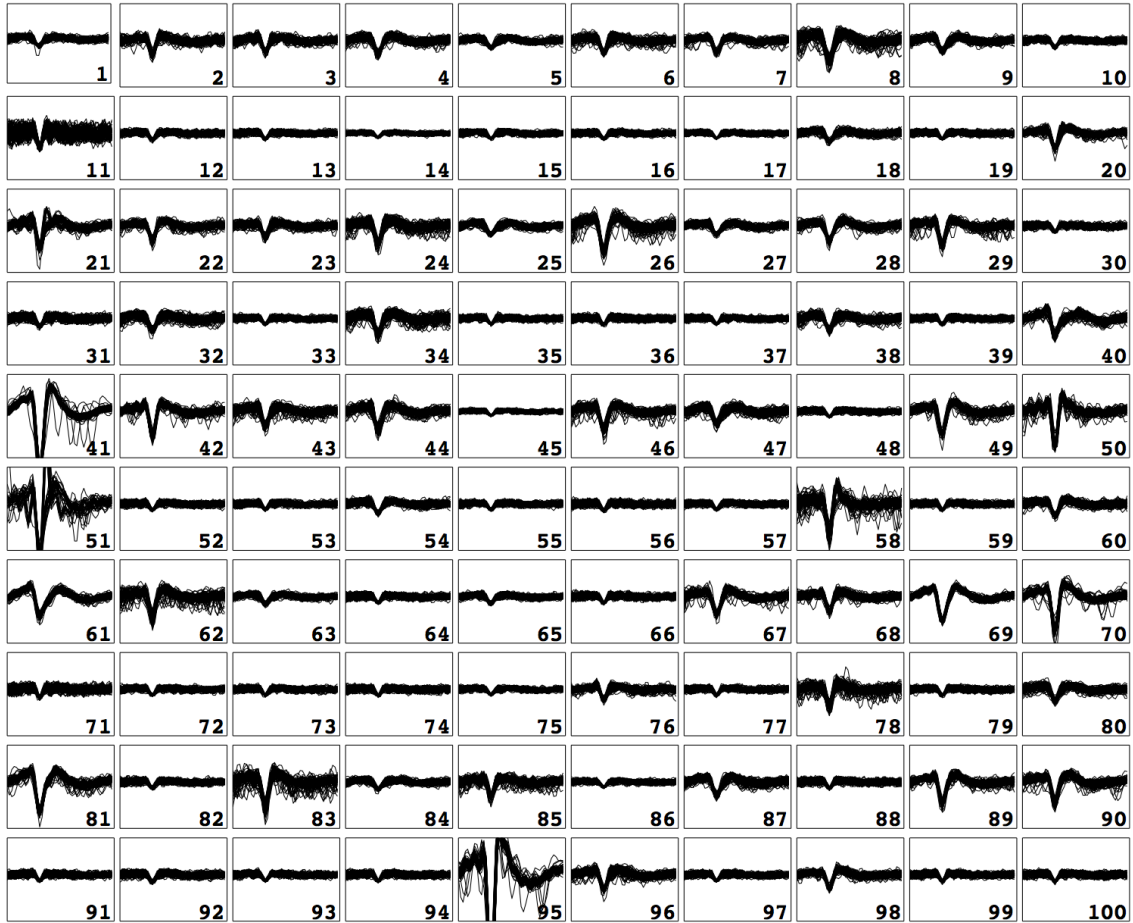


Figure 3.4: Raw data from a 100 channel implantable device within a non-human primate motor cortex sorted by threshold crossing. Each channels hows a 2.3 millisecond time bin averaged waveform. The scale of the entire length of each graph is 360 microvolts.

attached to our implantable device. Their array recorded data from the motor cortex of the human patient in order to obtain cursor trajectory via neural control.

Comparing Fig. 3.4 to Fig 3.5 shows a similarity in the type of signals and the quality of the recorded neural activity. The activity recorded from a human is capable of producing enough information to relay an intent to move on a two dimensional plane with a cursor. Therefore, it is easy to determine that the data recorded from

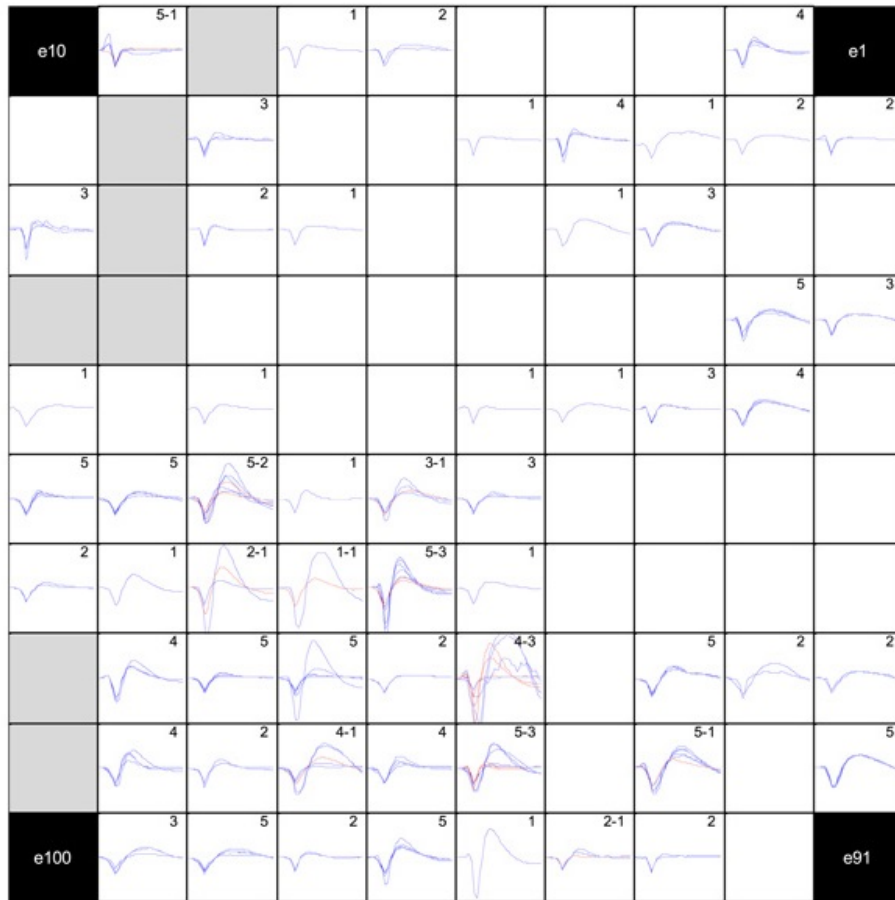


Figure 3.5: Raw data from a 96 channel microelectrode array after 1000 days implanted within a human with tetraplegia. The graph shows the mean sorted waveforms (in blue) from an entire day of recordings with spike sorting. Channels with multiple units show the second unit in red. The number on the top right signifies the number of mean waveforms (or total number of days) the unit was recorded from. Gray units were electrodes with over 4 M Ω impedance, classified as nonfunctional. © IOP Publishing. Reproduced with permission. All rights reserved, from [7]

the implantable device from a non-human primate should be enough to control a simple machine (i.e. a food/treat dispensing tool). Planning an experiment which utilizes non-human primate intellect to enable them to assist daily living, or allow them to affect their surroundings would be the next step for behavioral data collection with this device.

3.5 Conclusions on Utilizing a Non-Human Primate Animal Model in a Wireless Implantable Device Study

We have done many experiments with non-human primate animal models lasting over at least 500 days each, as can be seen in table 3.1. The table shows the length of time three of our implantable devices have spent within living animals. Animal WN had the longest implant period (of 594 days) and was the only one of the three where the device was fully implanted and the skin closed on top. The other two (JA and JN) had implants with skin opened above them for safety and practical reasons.

Animal	Species	Days Implanted	Reason for Explantation
WN	NHP	594	Signal Degradation
JA	NHP	561	Signal Degradation
JN	NHP	519	Signal Degradation

Table 3.1: Table of animal models implanted with the titanium enclosed implantable device for an extended period of time. All devices explanted from these animal models were fully functional at the time of explant (NHP = Non-human primate). Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to loss of usable signals being collected from the brain/device interface which is well documented.[1]

Ultimately, the device performed very well in an implanted setting for a long term application. Using the device for an extended period of time for a behavioral experiment would prove to be very beneficial as it would allow for neural correlates of behavior that is not easily represented by a restrained, unnatural behavior.

3.5.1 Future Direction of the Neural Implantable Device in Non-Human Primates

The implementation of this device into non-human primates was very fruitful. Future applications of this device in a non-human primate animal model would require a large (or geriatric) non-human primate with the invention of a behavioral recording apparatus. Similar to the porcine behavioral recording device, a non-human primate model would require a device which the primate can interact with, of its own volition. A device such as this would be synchronized with the wireless data streaming out of the implanted device. This would then provide the basis to perform neural analysis on the data extracted, and would allow correlations between the neural and behavioral data recorded.

By implementing a charger into the resting or sleeping area of a non-human primate, or training it to rest its head in an apparatus (with a charger embedded inside) would give the experiment (and the animal model) some novel autonomy in being able to reproduce and continue its own experiments. This would give the researchers the capability to being the experiment anytime they wished (starting it with the push of a button of an infrared laser). This would keep the battery charged without the need of sedating the animal, and provide the least amount of stress and discomfort to the animal. However, the design of such a “charging station” in order to provide efficient alignment and repeatable mechanical placement could prove tricky for a researcher. This would have to be a collaboration with engineers and animal care specialists in

order to design and implement such a concept.

Future designs could also benefit from a small curve to the device, in order to follow the contour of the skull underneath. This would allow the device to sit comfortably underneath the skin instead of protruding from the edges. However, curving two independant pieces of titanium, the printed circuit boards inside, the battery, as well as the sapphire window would prove to be a challenge to fit everything together. This is a step which must be taken when the industry and manufacturing procedures have matured to allow for such mechanical flexibility in the processes to develop such materials.

References

- [1] James C Barrese, Naveen Rao, Kaivon Paroo, Corey Triebwasser, Carlos Vargas-Irwin, Lachlan Franquemont, and John P Donoghue. Failure mode analysis of silicon-based intracortical microelectrode arrays in non-human primates. *Journal of Neural Engineering*, 10(6):066014, 2013.
- [2] Justin D. Foster, Paul Nuyujukian, Oren Freifeld, Stephen I. Ryu, Michael J. Black, and Krishna V. Shenoy. A framework for relating neural activity to freely moving behavior. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, 2012:2736–2739, jan 2012.
- [3] Hua Gao, Ross M. Walker, Paul Nuyujukian, Kofi a a Makinwa, Krishna V. Shenoy, Boris Murmann, and Teresa H. Meng. HermesE: A 96-channel full data rate direct neural interface in 0.13 μm CMOS. *IEEE Journal of Solid-State Circuits*, 47(4):1043–1055, 2012.
- [4] N Ludvig, J M Botero, H M Tang, B Gohil, and J G Kral. Single-cell recording from the brain of freely moving monkeys. *J Neurosci Methods*, 106(2):179–187, apr 2001.
- [5] H Miranda, V Gilja, C A Chestek, K V Shenoy, and T H Meng. HermesD: A

- High-Rate Long-Range Wireless Transmission System for Simultaneous Multi-channel Neural Recording Applications. *IEEE Transactions on Biomedical Circuits and Systems (TBCAS)*, 4(3):181–191, 2010.
- [6] K. Pryor. *Don't Shoot the Dog!: The New Art of Teaching and Training*. Ringpress Books Limited, 2002.
- [7] J D Simeral, S-P Kim, M J Black, J P Donoghue, and L R Hochberg. Neural control of cursor trajectory and click by a human with tetraplegia 1000 days after implant of an intracortical microelectrode array. *Journal of Neural Engineering*, 8(2):025027, 2011.
- [8] N.H. Steneck. *ORI: Introduction to the Responsible Conduct of Research*. Clinical Research Resources, 2007.
- [9] Nachum Ulanovsky and Cynthia F Moss. Hippocampal cellular and network activity in freely moving echolocating bats. *Nature Neuroscience*, 10(2):224–233, feb 2007.
- [10] Ming Yin, David a Borton, Juan Aceros, William R Patterson, and Arto V Nurmikko. A 100-channel hermetically sealed implantable device for chronic wireless neurosensing applications. *IEEE transactions on biomedical circuits and systems*, 7(2):115–28, 2013.

4

Wireless Power Delivery Optimization

The one challenge we experienced, after implanting our devices into multiple animal models was inefficient charging. Due to the lack of visual alignment guides and the thickness of skin (in the porcine model), it was difficult to physically align the two charging coils for efficient charging. It also became apparent that the power being delivered externally was not all being absorbed by the internal coil. The inefficiency of the charger led to power being drawn into the skin as well as the titanium enclosure of our implantable device. The inefficient charging caused significant heat buildup within the system, which had to be active cooled with running cold water or cooled, compressed air. The need for making our wireless charging system more efficient became clear. In order to make wireless charging more efficient, There are

a few variables that can be manipulated. The biggest variable for inductive wireless charging is distance between the primary and secondary coils. This variable, however, is fixed in context of an implantable device under the skin. The only way to shorten the distance from coil to coil is to keep your encapsulating material around the coil as thin as possible. However, this material must maintain all other characteristics of a good implantable device encapsulating material i.e.: hydrophobicity, impermeability, non-electrically conductive, and impact resistant. The skin thickness is the only thing that truly defines the distance between the two coils, and that is something outside of the designer's control. Other variables such as coil size, coil “ Q ” value or quality factor, and coil inductance are more approachable in the design of an implantable device. These are the ones that will be focused on for the design and implementation of a wireless power delivery system in this chapter.

4.1 Background on Power Management: Wireless Power Delivery and Storage Within an Implantable Device

4.1.1 Wireless Inductive Power Delivery

In order to design a reliable wireless power delivery system, there needs to be a standardization in charging paradigms. Different implantable devices incorporate varying

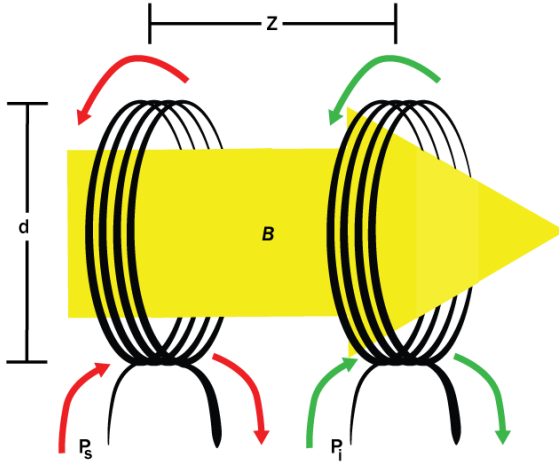


Figure 4.1: Schematic representation of an inductive, wireless power transmission system. Z = distance between coils, d = diameter of the coils, B = magnetic field induced between the coils, P_s = supplied power, P_i = induced power.

methods of wireless charging, but the most prevalent to date is inductive coupling, which has been studied and analyzed for decades as a safe and reliable method of transdermal power delivery.[9, 17] Inductive charging requires two concentric coils, made of wound conductive but individually insulated wire, in very close proximity. Power in the form of an alternating current is ran through one coil which generates a magnetic field within the center of the coil, this coil is called the primary coil. The magnetic field generated within the center of this coil is perpendicular to the axis of this coil. If another coil is brought to have its center within this magnetic field, a current is induced within the windings of the secondary coil and it receives the transmitted power. Fig 4.1 shows a schematic of what the basic components of inductive wireless power delivery incorporate. As Fig 4.1 shows, the system (in its simplest form) consists of two conductive wires coiled into a pair of concentric rings. The diameter of these rings varies with distance of effectiveness. In other words, the variables d and Z in Fig 4.1 are related as shown in equations 4.1 and 4.2. To begin, we must first establish a metric to determine the quality of a wire wound coil. This

quality factor is known as the “Q” of a coil. This Q value is determined by characteristics of the coil, as shown in equation 4.1. As can be seen by the equation for the Q factor, the inductance of the entire coil and the resistance of the wires couples with the resonant frequency desired for the coil ($\omega = 2\pi f$) to determine its ultimate quality factor.

$$Q = \frac{\omega L}{R} \quad (4.1)$$

Where:

ω : frequency (rads)

L: inductance (μH)

R: resistance (Ω)

The other factor that ultimately determines coil transmission efficiency is the coupling factor or “k” between the two coils. This coupling factor is known to determine the amount of flux penetrating the receiving coil (surrounded by green in Fig. 4.1) relative to the entire flux (B in Fig. 4.1) actually generated by the transmitting coil (surrounded by red in Fig. 4.1). This k factor approaches 1 as the two coils are very well coupled and approaches 0 when they are decoupled. Both the Q factor and the k factors determine the “optimum loss factor” (λ_{opt}). The optimum loss factor is determined by equation 4.2.

$$\lambda_{opt} = \frac{2}{(kQ)^2} * \left(1 + \sqrt{1 + (kQ)^2}\right) \quad (4.2)$$

Where:

λ_{opt} : optimum loss factor

k: coupling factor

Q: quality factor

The coupling factor (k) is how well the magnetic flux from the primary coil is transferred to the secondary coil. This value ranges from 0 (none of the energy through the flux is transferred) to 1 (all of the energy via the flux is transferred). This value is determined by distance between coils as well as size and shape of the coils relative to each other. The k value can be analytically determined via eqn. 4.3.

$$k = \frac{L_{12}}{\sqrt{L_{11} * L_{22}}} \quad (4.3)$$

Where:

k: coupling factor

L_{12} : coupling inductance

L_{11} : self inductance of the primary coil

L_{22} : self inductance of the secondary coil

While there are analytical methods to obtain the k factor of two coils using each of their inductances (L_{11}, L_{22}) as well as their mutual inductance (L_{12}) using equations

derived from Maxwell's work ([12]), for this study these were obtained utilizing the empirical method of a commercial LRC meter.

The optimum loss factor from eqn. 4.2 can be used to determine the total efficiency of the coil to coil power transfer. When simulated with a coil of $Q = 1000$ (an ideal coil), the relationship between efficiency achieved as a function of the ratio of distance between coils and coil diameter. Fig 4.2 shows the relationship of coil diameter to distance ratio with respect to efficiency of the power transfer.[22]

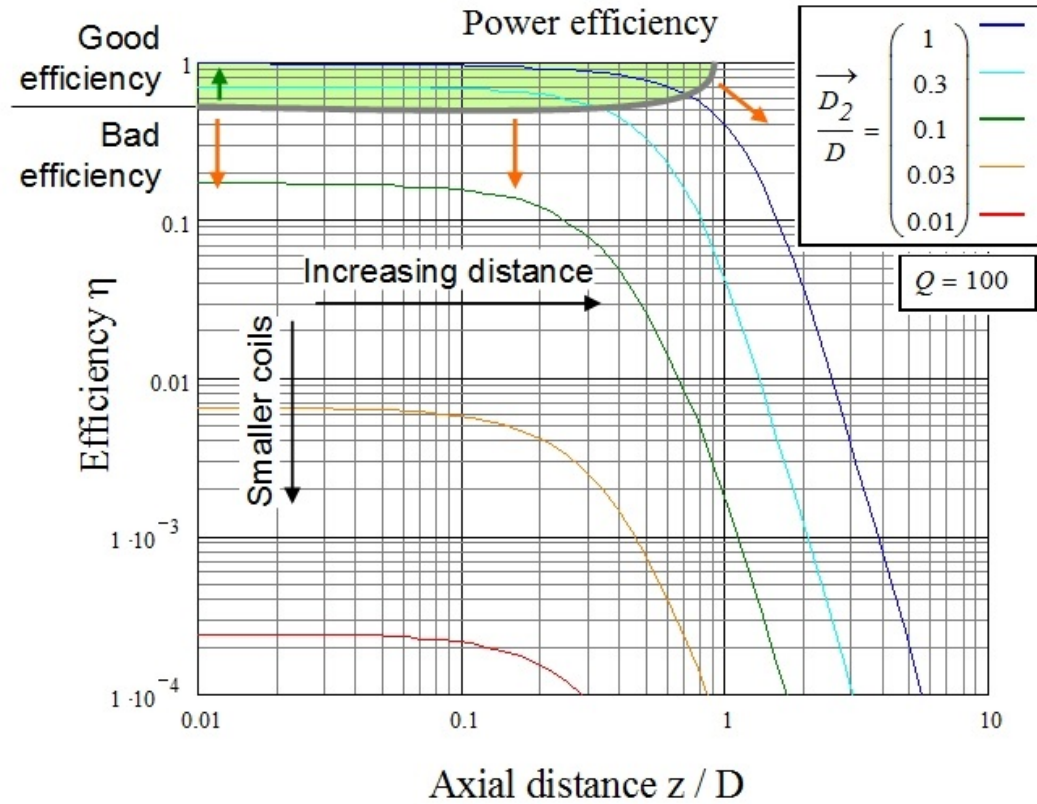


Figure 4.2: Relationship of distance (z) over diameter (D) with respect to power transfer efficiency.[22]

It is quite apparent from Fig. 4.2 that the coils should be as close together as

possible, but also that their radii should be relatively large. This would allow for better efficiency. The larger the coil and the closer together they are, the more efficient the power transfer between them.[23]

4.1.2 Transmitting Coil Design Parameters

To design the optimal coil for transmitting power into the receiving side, the inductance and frequency of the transmitting coil must be matched to the receiving side. These characteristics of a radio frequency coil can be determined using equation 4.4, which defines the resonant frequency of an LC circuit. In order to use a coil as a wireless power transmitter, it is modeled as a simple LC circuit resonating at a specific frequency F .

$$F = \frac{1}{2\pi\sqrt{LC}} \quad (4.4)$$

Where:

F : frequency (Hz)

L : inductance (H)

C : tank circuit capacitance (F)

Equation 4.4 can be used to design coils based on certain design constraints such as inductance or frequency. It is also used to manipulate the tank circuit to make similar electronics compatible with completely different coils.

4.1.3 Power Storage

We've seen characteristics and limitations of power delivery, but what about power storage? The best methodology of power storage in the market today is Lithium Ion batteries. They are the most power dense, longest lasting, rechargeable, and have the highest power retention of all available battery chemistries in the market today.[15] Lithium Ion batteries are built with two chambers, the cathode and the anode, separated by an electrolyte layer to provide a medium for the transfer of charges (as ions in solution). Figure 4.3 shows an internal view of a lithium ion battery cell.

Battery Characteristic	Value
Nominal Voltage	3.6 V
Specific Energy Density	125-196 Wh/kg
Energy Density	554 Wh/L
Temperature Range	-20°C to 60°C
Self Discharge	less than 5% per month
Cycle Life	1000 - 1,000,000 cycles

Table 4.1: Table of general lithium ion battery properties[15]

The area that affords the most room for advancement in lithium ion cells is from the variation in electrolytic material between the two terminals. The advancements in the field of battery technology have produced specialized polymers to cater to the specific needs of the electrolyte in this application. These materials have led to the development of the lithium polymer (or LiPo) battery. Unfortunately, these batteries are still too new and constantly under development and therefore have not arrived

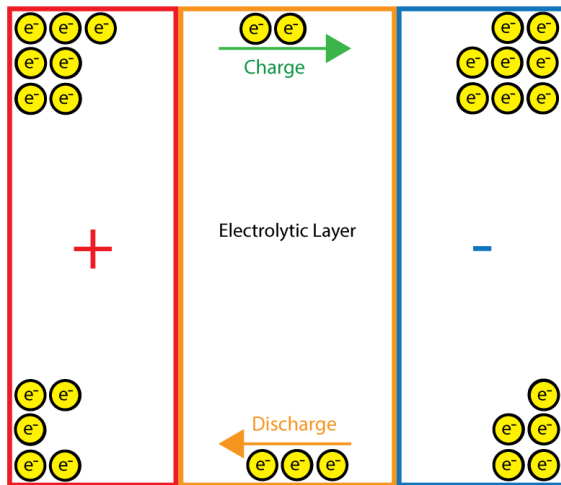


Figure 4.3: Components of a lithium ion battery cell with cathode and anode terminals separated by an electrolytic layer. The arrows exemplify electron flow during processes of charge and discharge of the battery.

at the medical device or biological implantation safety level as of this writing. The lithium ion cell works by storing charge (in the form of lithium ions) within its negative terminal (or anode, blue in Fig. 4.3). When a load is connected between the anode and cathode, this charge is depleted in the form of a voltage potential which allows electrons to transfer from the anode to the load and back to the cathode. As the electrons flow through the electronic load, the lithium ions flow across the electrolyte and attach to the positive terminal side (or cathode, red in 4.3). When recharged, the electrons being introduced into the system pull the lithium ions back toward the negative electrode, and thus the voltage potential within the cell is restored.[8] What this means from a power storage point of view is that an implantable device has the best opportunity to store large amounts of power if it were to embed a lithium ion battery within. This lithium ion battery must be charged inductively via coils to transfer power transdermally. The power transfer mechanism has a lot of variables which need to be decided upon. There's a lot of variation in inductively coupled power

delivery mechanisms, so it would be best to decide on the most optimum method. The alternative to researching the most optimum method, is to integrate a previously developed, well researched, and heavily invested technology currently available in the consumer market. The following section describes, in detail, one such methodology.

4.2 Introduction to the Qi Wireless Charging Standard

The Wireless Power Consortium (WPC) was formed in December 18, 2008 under the auspices of developing a standard method of charging small consumer electronic devices wirelessly. The standard they settles upon is referred to as the Qi (pronounced “chee”) inductive wireless power. The Qi standard allows for multiple different manufacturers to produce many different types and configurations of chargers, while they all remain compatible with any power receiving device.

The main benefit of the Qi standard came from the decision to choose a single frequency and standard size of coil. As shown from equations 4.1 and 4.2, limiting these two factors start narrowing down the options of coils and configurations available that can retain compatibility. The Wireless Power Consortium then resorted to choosing a limited subsets of allowable coil configurations in order to make sure coupling of the different coils remained consistent and reliable. This also allowed the manufacturers a bit of variability in designing and implementing their coils, while making sure

they remain within the standard and stay compatible. Thus the Qi Wireless Power Specification was born.

The following subsections summarize the standards outlined by the WPC[27], as the document defines the Qi standard and its specifications.

4.2.1 Qi Standard Specifications

The Qi standard dictates a power transmission frequency between 100 - 115 kHz. This is important because, as observed in equation 4.1, in order to maintain a good Q value (coil quality factor), we are limited to minimum values of coil inductance and resistance. As long as the values fall within the allowable coil dimensions within the Qi specification, they should be compatible with all the available Qi chargers.

Approaching the design from the point of view of the implantable device developed in our lab, we have a 3 centimeter diameter sapphire window on the top of the device, so the coil and its accompanying ferrite must fall within this limit. The physical limitation of the coil limits the inductance value of the coil as determined by the inductance equation 4.5. Inductive wireless power delivery has been studied for decades and established as a reliable method for powering low-power, relatively small, electronics. From the time of Maxwell[12], in 1873, there has been a lot of study on the different ways to determine inductance within a wire wound coil and how to design coils based on magnetic field requirements. Wheeler[26], in 1928, performed an empirical study to determine the inductance of coils via the number of windings

and the physical dimensions of the coil made of conductive copper wire. Wheeler's empirical study produced a "simple inductance formula" which is still used to design radio frequency (RF) coils today: the multi-layer coil equation 4.5.[26]

$$N^2 = \frac{L(3a + 9b + 10c)}{0.2(a)^2} \quad (4.5)$$

Where:

N: number of turns

L: inductance (μH)

a: coil total diameter (mm)

b: number of layers

c: radius of coil from open center (mm)

Therefore, using equation 4.5, we can design a coil based on our physical constraints and determine its number of turns required which correspond to a specific inductance. However, the benefit of adopting the Qi standard is that if we can find a commercially available Qi compatible coil that falls within the physical constraints of our device, it should already have the corresponding inductance value.

Qi Coil Specifications

To determine a compatible Qi coil, we must first obtain the physical dimensions that fall under the Qi standard which can fit within our constraints. The closest coil appeared to come from the Qi standard primary coil power transmitter design B1.

The table from the Qi standard is included here as table 4.2. This table shows the physical dimensions of the coil that the Qi standard dictates for one of the smallest coils allowed within the standard.

Parameter	Value
Outer diameter	28.5 ± 0.7 mm
Inner diameter	10.5 ± 0.3 mm
Layer thickness	0.6 ± 0.1 mm
Number of turns	16
Inductance	$8.1 \mu\text{H}$

Table 4.2: Table of physical dimensions of a Qi compatible coil from design B1 in the Qi standard.[27]

A compatible coil was found in the Digikey (<http://www.digikey.com>) online catalog. The found coil was a Wurth Electronics Inc coil (part#: 760308101103). This coil fit almost all of the Qi standard requirements and also had the outer diameter to fit just within the sapphire window of our implantable device. The coil has an inductance of $6.6 \mu\text{H}$, [28] which will come into importance as we determine the design of the accompanying circuitry. As observed, this value is a bit lower than the inductance level required by the Qi standard (table 4.2), however empirical tests show this variation does not hinder the performance of the coil within the specification.

Qi Coil Compatibility with Chargers

In order to make sure the Digikey coil was compatible with chargers, it is necessary to determine what type of tank circuit it would require. The frequency of interest

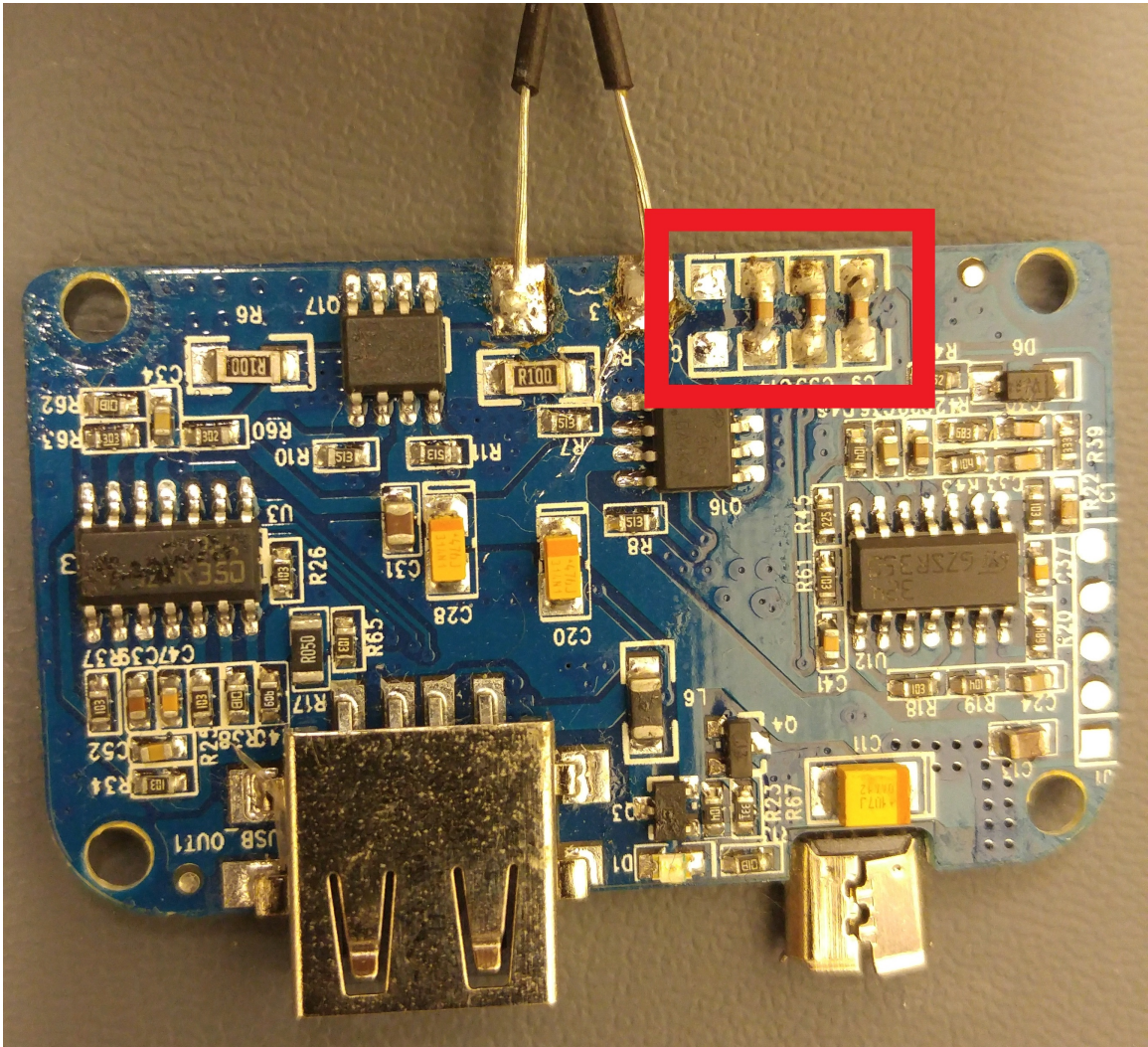


Figure 4.4: Generic Qi compatible transmission board acquired from Adafruit (<http://www.adafruit.com>, part#: 2162) with tank capacitors highlighted in red. Multiple capacitors are connected in parallel to obtain the desired capacitance.

would be the Qi compatible charging frequency of 115 kiloHertz. The inductance of the Digikey coil is $6.6 \mu\text{H}$, [28]. Applying these values into equation 4.4 we obtain a capacitance of $0.16 \mu\text{F}$. This capacitor are located directly attached to a single terminal on the coil as a series LC circuit. Figure 4.4 shows an image of the commercially available Qi charging transmitter board used for the following experiments.

This board was obtained from Adafruit (<http://www.adafruit.com>, part#: 2162).

4.3 Methods of Incorporating and Testing the Integration of Qi Wireless Charging into the Previously Designed Device

4.3.1 Integrated Receive Coil Design Specifications

The internal receiving (secondary) coil of the implantable device has been designed in regards to its application within a titanium device. The coil dimensions and specifications have been determined previously, and are included in table 4.3.

Parameter	Value
Outer diameter	27 mm
Inner diameter	20 mm
Layer thickness	1 mm
Number of turns	27
Inductance	30 μ H

Table 4.3: Table of physical dimensions of the coil embedded within the implantable device.[2]

This coil is the receiving (or secondary) coil, and its design requirements are much looser. In order to be Qi compatible, Section 4.3.2 of the Qi standard states that the receiving coil must provide under 0.8 Amps when the centers of the coils are aligned.[27] Empirical results showed that our device received less than 0.8 Amps when connected to an external Qi compatible charger.

Multiple coil designs were utilized in testing the implementation of Qi within the receiving implantable device. The metric for looking at successful integration was heat generation (more heat generated, the more inefficient the coil coupling, as shown in equation 4.5). Figure 4.5 shows heat generation using three different coils within the receiving implant. The receiving side showed that the previously designed coil was the best option for integration of a coil with receiving Qi circuitry within the implant itself.

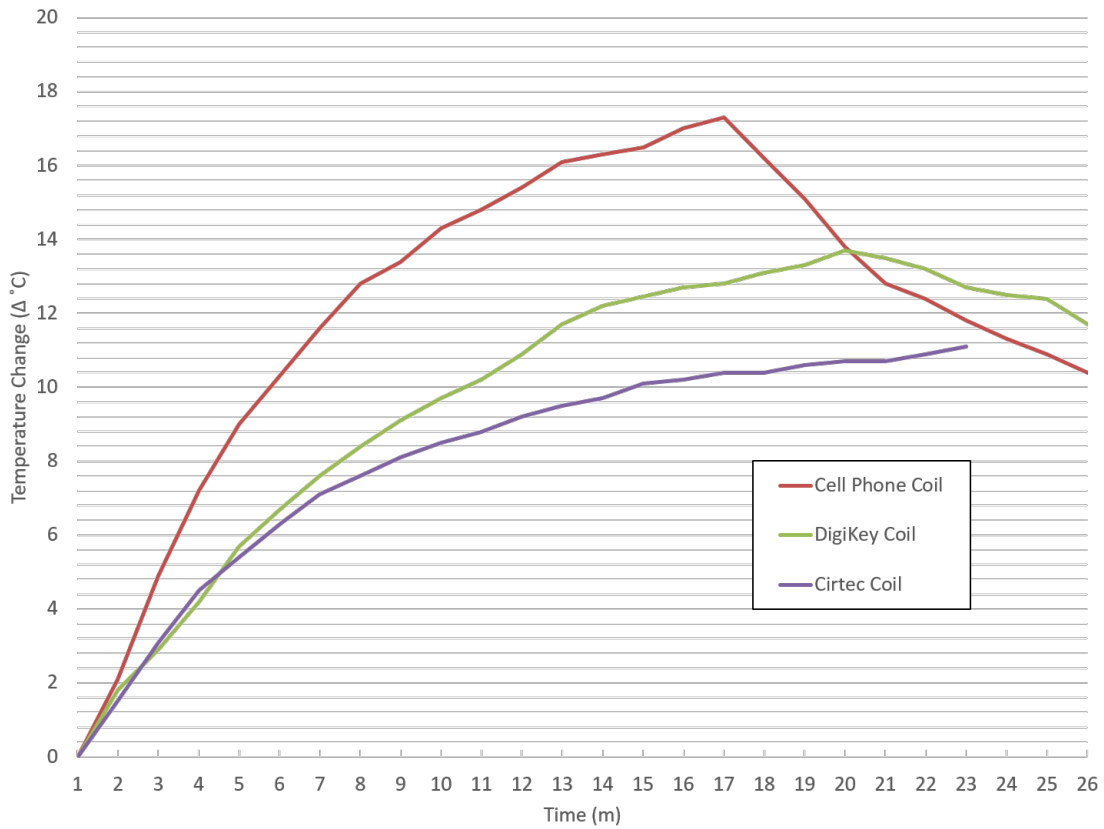


Figure 4.5: Wireless power delivery coil extracted from within a smartphone. The graph shows temperature change profiles as a function of time. These thermal tests were done in air, at an ambient baseline room temperature of 25 °C.

4.3.2 Qi Compatible Receiving Circuitry

In order to make a device Qi compatible, it needs to communicate with a charger utilizing the Qi protocol. The Qi standard includes a small information exchange between the transmitter and receiver. In short, the transmitter is constantly searching for a compatible receiver. When it finds something that acknowledges it, it affirms Qi compatibility and the receiver responds with a desired charging rate and whether that is currently being met or not. The transmitter then attempts to approach the desired charging rate by slowly increasing its transmission power. When the receiver obtains the desired charging rate, it continuously acknowledges receipt of this power. Once this power is achieved, the receiver acknowledges that charging does not need to continue, and the charger switches to “trickle charging” mode, or low power mode to keep the receiver topped up.[27] This information and communication exchange has been outlined within the Qi standard and exemplified by the image obtained within the standard here as Fig. 4.6.

Qi Receiver Board Design

The best way to integrate this into a previously designed circuit is to include custom designed integrated circuits which incorporate Qi communication protocols. These integrated circuits would require an electrical engineer with a specialization in application specific integrated circuit (ASIC) design. Fortunately, due to the ubiquity of Qi chargers and devices in the consumer electronic device space, these ASICs are

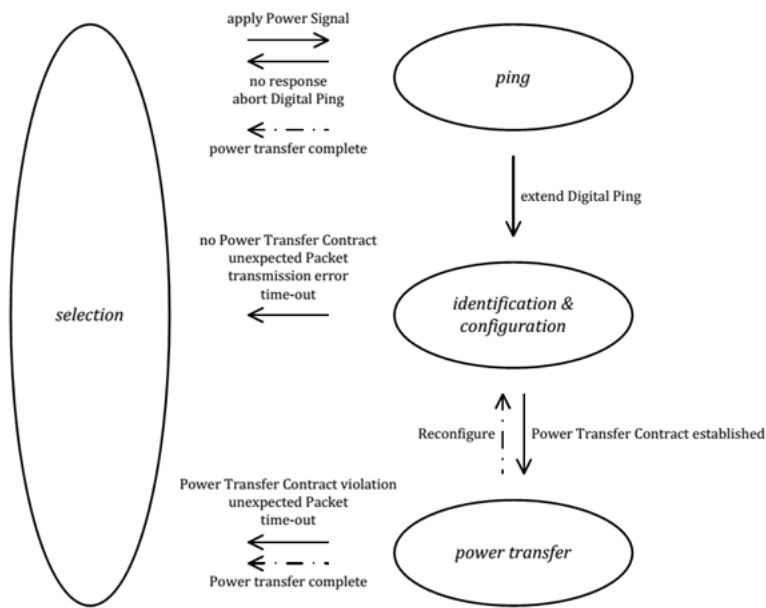


Figure 4.6: Communication exchange between the transmitter and receiver components, outlined within the Qi standard.[27]

commercially available from a few major integrated circuit manufacturers. Texas Instruments (<http://www.ti.com/>) was chosen for its large variety of integrated circuit designs for Qi compatibility. One such chip available from Texas Instruments is the BQ51013B (<http://www.ti.com/product/bq51013b>). This chip is an extremely useful integrated circuit, as it combines the functionality of a Qi compatible circuit receiver as well as a lithium ion charger circuit. With this single integrated circuit implemented, a device could receive a charge wirelessly via Qi inductive coupling and simultaneously charge an attached lithium ion battery.[19] This integrated circuit was incorporated into a schematic design of its supporting circuitry to produce a circuit that receives wireless power from a Qi compatible coil and then outputs the power to a pair of terminals for the attachment of a lithium ion battery. Figure 4.7 shows an image of the schematic designed to accommodate this integrated circuit.

After designing the schematic, it became important to integrate this into the power harvesting circuit of the current implantable device. This integration required an extremely small footprint, since the current device design was very compact and could not afford expansion in any dimension. In order to test the implementation of the integrated circuit into a schematic, the need arose to develop a small testing board before the integration into the current printed circuit board of the implantable device could begin. This board needed to obtain the smallest possible footprint to be able to fit inside the titanium enclosure of the implantable device while still allowing

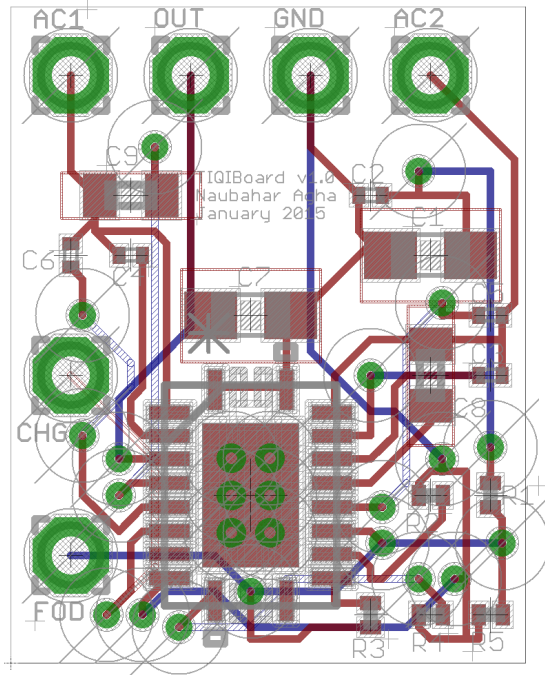
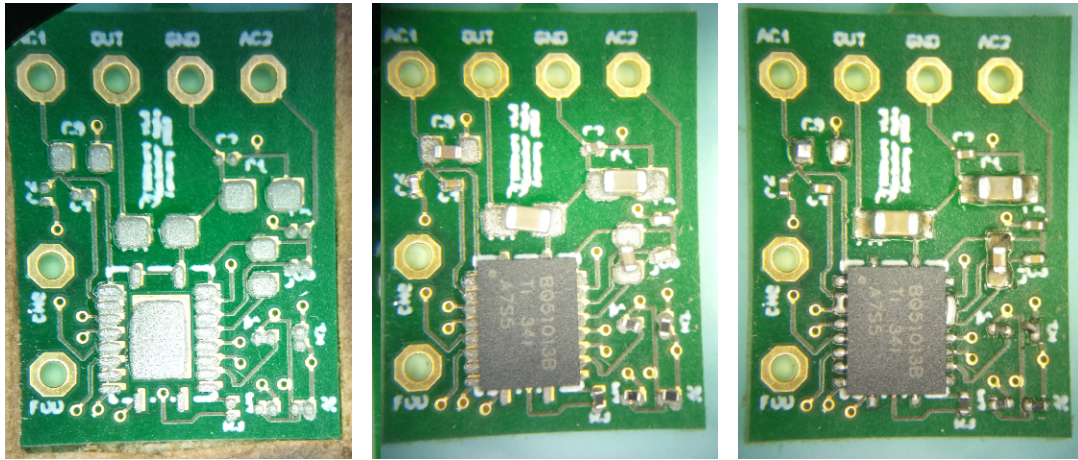


Figure 4.8: Layout of the testing board for incorporating the Qi compatible receiving and lithium ion battery charging circuitry into the implantable device.

the device's enclosure to close. A lot of time and care went into organizing the layout of this board to minimize the total footprint, while still allowing attachment points for the input terminals for the receiving coil as well as output terminals for the attachment of the lithium ion battery. The final designed layout of the testing board which corresponds to figure 4.7 is included here as figure 4.8.

The final dimensions of the designed and laid out board were 10.9 millimeters by 13.89 mm. Although this layout was not done by a professional electrical engineer, an extremely small footprint for the entire board was achieved and printed out by a fabrication shop in Germany called Beta LAYOUT (<http://www.pcb-pool.com/ppus/index.html>).



(a) The board with solder paste on each of the conductive surface mount device pads. (b) The board populated with components before being reflow soldered. (c) The board after being run through the reflow oven.

Figure 4.9: This sequence of images shows the process of fabrication of the board once it returned from the fabrication house. Observe, in (c) the shorted legs on the TI IC as well as some capacitors standing upright on single pads as opposed to connecting across pads. These were manually corrected and the shorts were also manually cleaned after the state shown here.

Qi Receiver Board Fabrication Process

The fabrication process of these boards are shown shown in figure 4.9. An Essemtec Reflow Systems (<http://www.essemtec-usa.com/>) reflow oven was used at a custom manual setting of preheat temperature of 190 °C, soak temperature of 199 °C, and reflow temperature of 255 °C. The bed of the reflow oven was traveling at a rate of 200 millimeters/minute. These boards were hand populated and electrically tested for verification after running through the reflow oven. The boards were photographed during fabrication, population and finally after coming out of the reflow oven. Unfortunately, this board provided some complications as the conductive pads around the

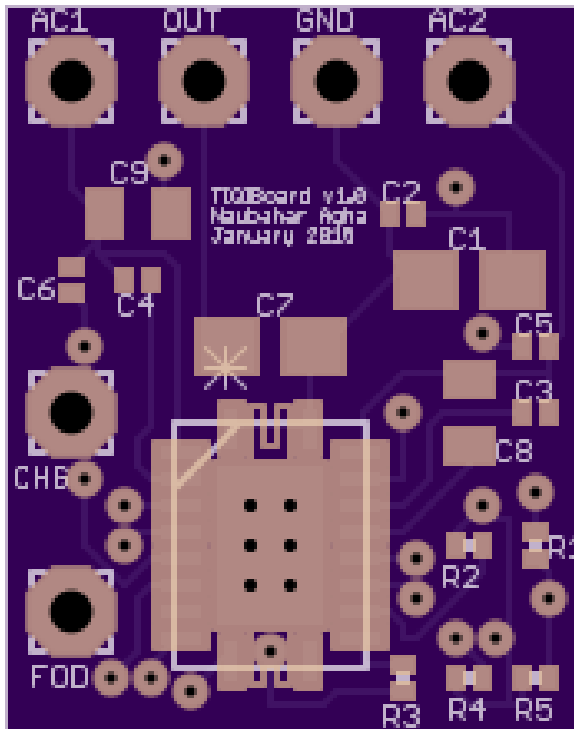


Figure 4.10: Purple printed circuit boards provided by OSH Park (<https://oshpark.com/>).

vias as well as some surface mount component pads showed delamination too often from the FR4 substrate.

Due to the complications with these boards, another printed circuit board manufacturing house was chosen for its price and proximity to the lab. This manufacturing house, known as OSH Park (<https://oshpark.com/>) and commonly used for hobbyist electronics, had a fast turnaround time and provided purple PCBs at the correct specifications. An autogenerated image from OSH Park is included here as figure 4.10.

Qi Receiver Board Integration

Once the Qi receiver board was fabricated and verified to be functional, the board was placed within the titanium can. Due to the constraint and very specific designs of the implantable device, it was impossible to fit a board of any finite thickness, and dimensions (although relatively very small) of roughly 11 millimeters by 14 millimeters. The only option for testing this board within the device appeared as using a smaller battery. The currently designed battery is a Quallion (<http://www.quallion.com/index.asp>) 200 milliAmpere hour medical grade battery.[2] This battery was removed to be replaced by a smaller, thinner 155 milliAmpere hour battery for the sake of testing. This smaller battery allowed the Qi receiver board to fit within the same space as the battery compartment within the device, which ultimately allowed the titanium can to close with the board inside.

Once the board was closed, the coil inside the implantable device was rewired to bypass the receiving circuitry currently implemented within the device. This coil was wired directly to the AC1 and AC2 terminals of the Qi receiver board (fig 4.10). The OUT and GND terminals from the board were then connected to the 155 milliAmpere hour battery now within the implantable device. This assembly was packed into the implantable device and the device was placed on top of a Qi compatible charger to observe power reception. The final step in developing the full system was to integrate the ferrite mentioned by the Qi standards[27] into the system.

4.3.3 Ferrite Integration into the Qi Compatible Implantable Device

The Qi standard dictates the necessity of including a ferrite backing to each coil. This necessity comes from the electromagnetic properties of the ferrite material and its use in focusing the magnetic flux around it. Ferrite is an electrically nonconductive but magnetically conductive (or ferromagnetic) material. They are most commonly used to make magnets or shielding from magnetic fields.[13] Nowadays, ferrites can be found on the back of small radio frequency antennas or coils in order to divert, direct, or focus their generated magnetic flux. They come in ceramic or soft flexible polymer flavors, in varying thicknesses and malleabilities. Usually consisting of resin, or ceramic materials with embedded nanobeads. Soft ferrites usually consist of Manganese-Zinc ($\text{Mn}_x\text{Zn}_{(1-x)}\text{Fe}_2\text{O}_4$) for lower frequency applications (below 5 MHz) or Nickel-Zinc ($\text{Ni}_x\text{Zn}_{(1-x)}\text{Fe}_2\text{O}_4$) for higher frequency applications.[21] Harder ferrites usually consist of Barium or Cobalt and are generally used to make permanent ferrite magnets.

The choice for our ferrite came down to referring to the list of ferrite manufacturers provided in the Qi standard. The challenge with choosing the right ferrite was to determine which one would be thin enough to fit within the physical confines of the implantable device, yet thick enough to be effective. A multitude of ferrites from varying sources were tested to determine the best and most effective component. This was determined by measuring the Q , quality factor, of the coil attached to it. Since, due

to their ferromagnetic nature, ferrites directly affect any radio frequency coil they are near by altering their inductance. This change in inductance is immediately reflected on the Q value of the coil, as shown in equation 4.1. Various ferrites were attached to our implantable device's internal coil and the inductances and Q values were measured at 100kHz by an Agilent Technologies (<http://www.agilent.com/home>) LCR Meter (4263B). The meter was calibrated by measuring the inductance and Q value of a commercially known coil. Once the coils values agreed with its documentations, the implantable device's internal coil's characteristics were measured. The results of measuring varying ferrite attachments to the device's coil are shown in table 4.4.

Ferrite	Series Inductance (μH)	Q (@100kHz)
No Ferrite	29.513	18.2
20 μm Ferrite Disk	37.300	24.2
Digikey (DN41996-ND)	38.009	24.5
45 μm Ferrite Disk	38.845	24.4
120 μm Ferrite Disk	39.308	25.2
220 μm Ferrite Disk	40.276	26.6
Commercial μmetal Strip	47.615	29.2
Commercial Ferrite Sticker	48.920	33.5

Table 4.4: Table of implantable device coil characteristics affected by different ferrites

The no ferrite control measurement (29.513 (μH)) verified the design specifications of the integrated coil at 30 μH (table 4.3) within a 10% error margin. Table 4.4 is arranged by increasing inductances (and, in turn, rising Q values). The ideal coil would have a very high Q value while maintaining its designed inductance. Therefore, the goal of this test was to find the ferrite which would yield the highest Q value

while staying as close to the original inductance as possible. The two commercial materials (μ metal strip and ferrite sticker) had the highest Q values but also the highest inductances. They drove the characteristics of the embedded coil beyond its acceptable parameter range. They were also of unknown material and composition as they were extracted from various commercial products instead of ordered by themselves, therefore they were difficult to reproduce. The ferrite disks of varying thicknesses had decent specifications, however they were solid, brittle, and difficult to implement cleanly on top of a printed circuit board with a surface morphology of multiple components with varying heights. This left the Digikey product (DN41996-ND) which is a soft polymer rubber ferrite which was 0.6 millimeters thin from API Delevan Inc (<http://www.delevan.com/web/Contact/distributors.html>, part#: FFAM06 1*1T1). This material seemed to be the perfect combination of pliable enough to fit on the printed circuit board, the right thickness to fit inside the implantable device, and good enough electromagnetic characteristics to allow the embedded coil to function as a Qi compatible receiver coil.

4.3.4 Coil Efficiency Determination via Power Delivery Metrics and Thermal Measurements

In order to verify the designs and determine whether the coil had good transfer efficiency of power, two metrics were established: electrically observe power being delivered on the receiving end (by the battery) and thermally determine heat being

dissipated by the titanium can (energy loss in wireless power transmission).

Power Delivered to the Battery of the Implantable Device

The best way to determine the power being delivered to the battery is to measure the current passing through the output lead of the Qi receiver board to the battery. This would give a real world absolute value to the amount of power being wirelessly delivered, and actually reaching the battery within the implantable device. This was done using an Agilent Technologies (<http://www.agilent.com/home>) 34401A Digital Multimeter hooked in series with the battery. The Agilent mutlimeter determined the amount of current flowing to the battery while an occasional measurement of the voltage provided the total power delivery using equation 4.6.

$$P = VI \quad (4.6)$$

Where:

P: power (W)

V: voltage (V)

I: current (A)

The power obtained flowing into the battery was compared to the total power being drawn by the transmitter board from the wall. The adapters attached to the wall to supply power to the transmitter board had a maximum of either 1 or 1.5 Amps at 5 Volts. Therefore, the maximum power we could ever supply to the transmitter

board (using equation 4.6) was 7.5 W.

However, once the device was finished and assembled, it would need to be sealed shut to mimic real world application (being implanted within a living organism). The metric of measuring current flow to the battery terminal would not be possible. Therefore, the secondary metric of measuring the temperature of the titanium enclosure was developed.

Thermal Profile of the Titanium Can During Wireless Charging

Inductive wireless power delivery is very dependent on the alignment of the primary, transmitter, and the secondary, receiver, coil. As exemplified across the x-axis of Fig. 4.2, the further away, or the more misaligned the coils are, the faster their efficiency drops. Coils that are not close together or concentric are referred to as “loosely coupled”. These loosely coupled coils require a significant stronger magnetic field to be able to transmit the same amount of power. The same principle applies when coils are different sizes relative to each other. A smaller secondary coil will be loosely coupled with a larger primary coil as opposed to a secondary coil closer in size to the primary. Another complication is the addition of material (especially conductive metals) between the two coils. Any ferromagnetic material would affect the magnetic flux being used to transfer the energy between the two coils. Figure 4.11 shows the flow of magnetic field around a coil. When this magnetic field meets a metal then it gets distorted and the flow of energy, as with anything following the laws of physics,

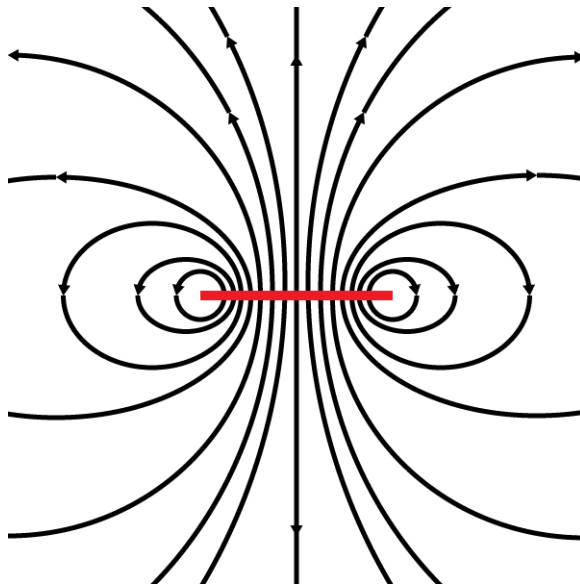


Figure 4.11: Simplified schematic representation of a single plane slice of a model of the magnetic B field through an ideal current coil (in red).

follows the path of least resistance.[12]

The presence of the titanium in between the two coils and the distortion of the magnetic B field that it causes, resorts to taking the majority of the energy from the B field. Since there is nowhere for this energy to go (the titanium enclosure does not consume any energy), this energy is radiated out as heat. Therefore, there's a complicated yet direct relationship between the inefficiencies of power transfer between the coils and the heat build up (temperature) of the titanium enclosure.

The initial thermal profiling was done using a handheld Fluke (<http://en-us.fluke.com/products/thermometers/fluke-51-ii-thermometer.html>) 52 II Dual Input Digital Thermometer. This was connected to a Fluke 80PK-1 Bead Probe thermocouple (or its equivalent), which was then taped to the outside titanium can of the device using Kapton tape. This measurement was corroborated with an Omega

(http://www.omega.com/pptst/HH21_22_23.html) Model HH22 Exceptional Accuracy Digital Microprocessor Thermometer connected with a similar thermocouple. The external charger was held 2 millimeters away (because of the average human scalp thickness of roughly 2 - 4 millimeters)[14, 18, 6] from the device body by two glass microscope slides (exactly 1 mm thick, each). The charger was connected to a 1 Amp (5 Volt) wall adapter which provides power at the coil end of 2.5 Watts (500 milliAmperes, 5 Volts). Temperature was taken once per minute until the calculated maximum charge time required for the device (roughly 30 - 40 minutes).

Once integrated, the titanium enclosure was sealed using HYSOL® FP4549 Flip Chip Encapsulant (<http://www.henkel-adhesives.com/brands-5497.htm?nodeid=8797571154062>). After verification of functionality, the bottom of the device was then coated with PDMS (polydimethylsiloxane, MED-4211) from NuSil Technology (<http://nusil.com/en/LifeSciences>).

4.3.5 Determination of Device Thermal Profiles Within a Simulated Implant Environment via A Thermal Bath

While the thermal profile of the device was a significant improvement from previous implementations, it was still not accurate within an implanted setting. A living organism has active heat transport capabilities (utilizing blood as a heat transport

mechanism).[11, 3, 25] This active heat transport allows the body to maintain homeostasis at 37 °C. This heat transport effect is very beneficial to a device that produces localized heating. The question with the thermal profile of our device remained whether the heat that was being generated (by the inefficiencies of coupling inductive coils near titanium) could be mitigated by active heat transport within a body.

In order to model an elevated temperature setting, a thermal bath testing apparatus was designed and developed for extended thermal testing. This thermal bath was built using a roughly 130 millimeter cubed acrylic chamber. The acrylic walls were 5 millimeters thick each, in order to provide some thermal insulation from the environment. The top and bottom were isolated by thermally insulating foam. Electric heating pads from Adafruit (<https://www.adafruit.com/products/1481>, 10 x 5 cm, part#: 1481) were attached to three of the four sides. These thermal pads were driven by a 12 Volt power supply gated by relays dividing up to roughly 1.2 Amperes per pad. The relays were driven by an Arduino Uno R3 (<https://www.arduino.cc/en/Main/ArduinoBoardUno>), on top of a custom designed Arduino shield specifically built for this thermal bath. The Arduino shield consisted of digital outputs programmed to control an LCD display, a potentiometer to dial the desired water bath temperature (usually set to 37 °C to simulate the human body internal environment), LEDs to signify power being delivered via the relays which were gating the 12 Volt power supply to the heating pads. An XBee Arduino shield from Sparkfun Electronics (<https://www.sparkfun.com/products/12847>, Sparkfun XBee Shield,

part#: WRL-12847) was attached on top of the custom Arduino shield to provide the capability to stream recorded data wirelessly to a receiving device. Finally three thermocouples from Adafruit (<https://www.adafruit.com/products/270>, Type-K Glass Braid, part#: 270) were attached to amplifiers (<https://www.adafruit.com/products/269>, MAX31855, part#: 269). One of the thermocouples was utilized as the water bath temperature control, and would be dedicated to measuring the water bath temperature. If the water bath temperature ever fell one degree Celsius below the set point, the custom code in the Arduino would enable the relays in order to provide power to the heating pads and bring the water temperature back up to the set point. The other two thermocouples were attached to the outside surface of the titanium enclosure of the device in order to monitor and verify the device temperature during charging. Data from the current setpoint, the water temperature, and temperature from the device were streamed in real time through the XBee board (<https://www.sparkfun.com/products/8665>, XBee 1 mW Wire Antenna - Series 1, part#: WRL-08665). A corresponding receiving XBee Board was mounted on a XBee to USB board (<https://www.sparkfun.com/products/11373>, XBee Explorer Regulated, part#: WRL-11373) which was then attached to a PC. Custom software was written to read serial data from the incoming stream and configure it into a usable data of time and temperature values. Lost packets were ignored as the timing of the Arduino/XBee was sufficiently high enough (roughly 1.43 Hz sampling rate, significantly faster than the previous 1 sample per minute manual recording). Fig

4.12 shows the water bath testing apparatus with the electronics enclosed in a black commercial project box. Fig 4.13 shows the electronics within the testing apparatus (Arduino, custom shield, wiring harnesses, and components) all connected, and hidden inside the project box when fully assembled.

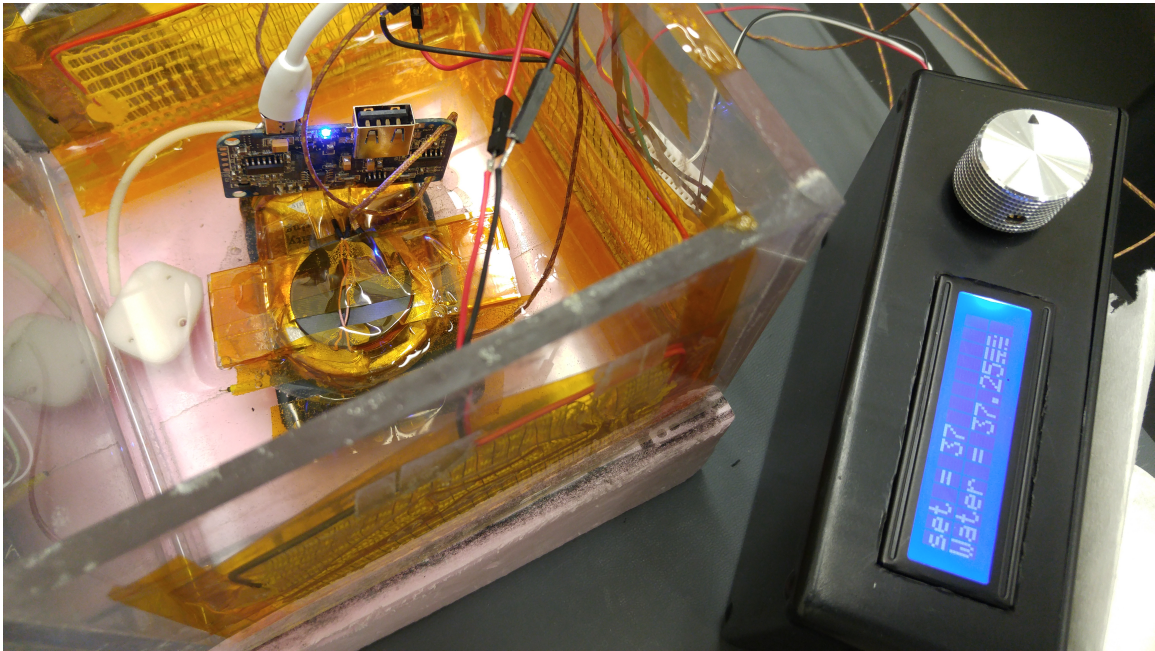


Figure 4.12: An image of the water bath system with the top removed on a benchtop with an implantable device connected for thermal testing inside.

Ultimately, the goal of collecting this metric would be to remain within the FDA (United States Food and Drug Administration) mandated limit of change in temperature of the outside surface of an implantable device (which is two degrees change from ambient temperature).[7]

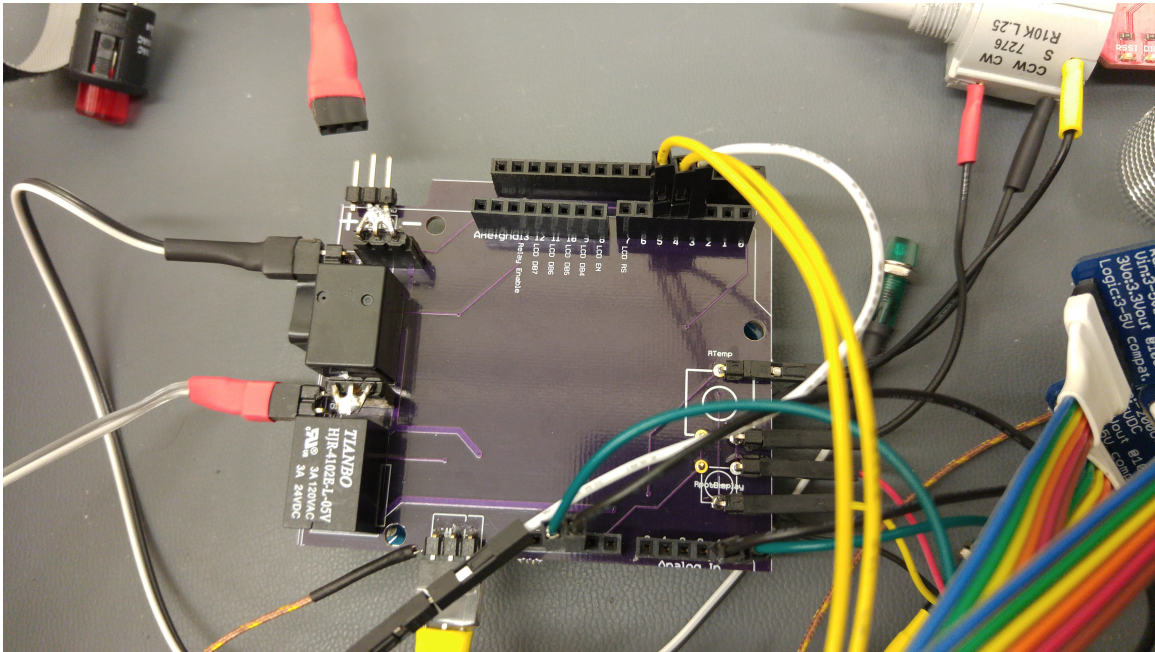


Figure 4.13: An image of the electronics within the water bath system. This top down view shows the custom designed Arduino shield for the purposes of interfacing the Arduino to an LCD display, relays for heat pad controls and a potentiometer for controlling the temperature set point.

4.3.6 Introducing Fluid Flow into the Thermal Bath Heat Testing Apparatus

In order to more closely mimic body active heat transfer, fluid flow was introduced into the thermal bath testing apparatus. This introduced the prospect of more evenly distributing locally generated heat, just like the active transport of heat due to blood perfusion of tissue in a living mammalian organism. This process was introduced by transferring the device and its testing accouterments into a circular glass beaker. This beaker was then placed on a heating pad which also incorporates a magnetic stirrer. Then a small magnetic stirrer was placed within the center of the bath. The

device and testing rig was placed near the edge of the circular bath (approximately 1 centimeter from the edge). Water was then filled into this circular bath until the device was submerged 1 millimeter under water level (approximately 1 centimeter). This gave roughly two channels of 1 cm^2 cross sectional area on either side of the device. The magnetic stirrer was set to turn at 400 rotations per minute (RPM). In order to get a very rough estimate of fluid flow around the device, each channel was estimated as a blood vessel with a flow rate of $40 \frac{\text{cm}}{\text{s}}$ with a cross sectional area of 5 cm^2 . [20, 10] This gives a rough volumetric flow rate of $200 \frac{\text{cm}^3}{\text{s}}$ which converts to 0.2 l/s . To calculate our modeled flow rate, we determined our magnetic stirrer speed at 400 RPM, which translates to $6.66 \frac{\text{rotations}}{\text{s}}$. Of course, the volumetric flow rate varies with respect to distance from the center (point of magnetic stir bar), however, we can safely estimate as close to the stir bar as possible. The flow rate at the stir bar position is estimated at roughly $50 \frac{\text{cm}}{\text{s}}$ by Halász et al.[4] So, $50 \frac{\text{cm}}{\text{s}}$ turned 6.66 times equals roughly $333 \frac{\text{cm}}{\text{s}}$. If we apply this flow rate to our model vasculature with a surface area of 1 cm^2 , we get $333 \frac{\text{cm}^3}{\text{s}}$ as our volumetric flow rate, which converts to $0.33 \frac{\text{L}}{\text{s}}$. This flow rate is a bit higher than the biological flow rate of $0.2 \frac{\text{L}}{\text{s}}$, however this is only at one side surface of the implantable device. Unlike the entire volume or top surface being subjected to the body's vascular active heat dissipation. Therefore, this higher flow rate across a smaller surface area can suffice for a rough estimate of active cooling by vasculature within a living organism. While this small model may be inaccurate for precise vascular blood flow modeling within an implanted body

system, it still gives an approximate overview of the scale at which we can observe heat transfer within the system.

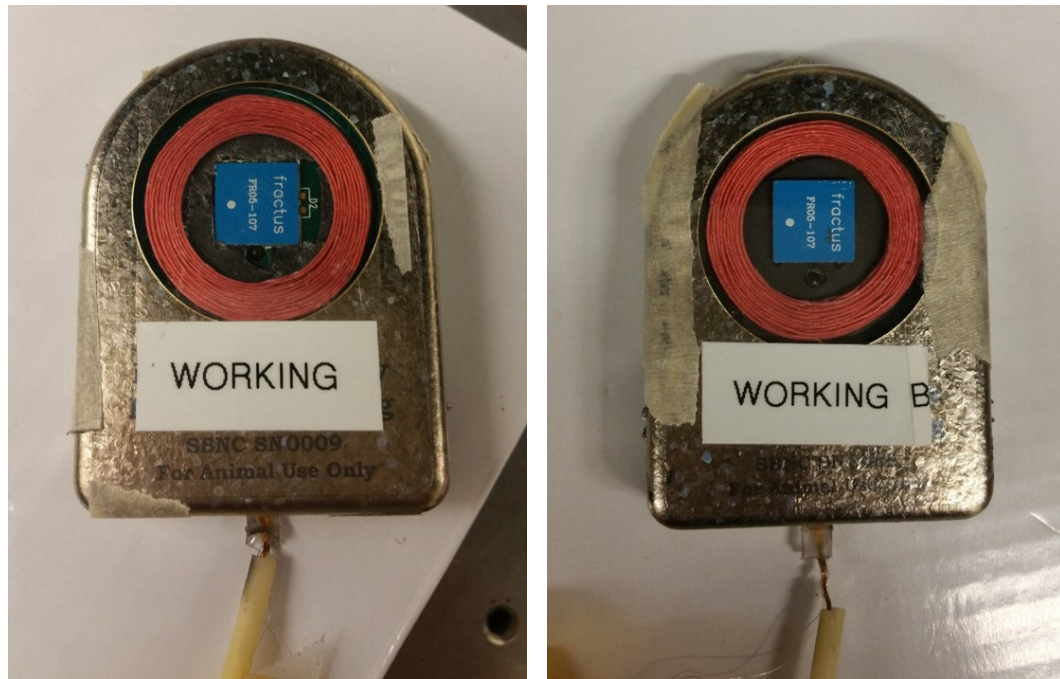
4.4 Results of Qi Integration within the Implantable Device

The implementation of Qi wireless charging into the device required testing of the amount of power being transmitted across the titanium (sapphire window). Before closing of the titanium enclosure, the amount of power reaching the battery was compared to the amount of power being drawn by the charger as well as the heat generated on the titanium can. After closing the titanium enclosure, the amount of heat generated on the can was independently measured to verify consistency with power delivery efficiency. This heat is measured utilizing commercial K-type thermocouples attached to amplifiers, as explained within the previous methodology section.

4.4.1 Results of Ferrite Configuration on the Radio Frequency Transmission Power of the Device

Though the power was delivered to an open device, the receiving (or secondary) coil was still inside the titanium, aligned with the sapphire window and all components were fitted inside of the device, which was then taped shut. Figure 4.14 shows two devices of this type, enclosed in titanium, but sealed with tape.

The initial composition of the different layers of the device required the ferrite strip (accompanying the coil) to sit over the RF antenna. Even though our chosen ferrite is RF transparent at the frequencies that we are transmitting[1] (3.4-3.6 GHz), it still had an impact on the decibel-millWatts (dBm) of the transmitted power. Figure 4.15 shows the two potential layout possibilities for the ferrite relative to the RF antenna on the PCB. The images from Fig. 4.15 correspond to the images in Fig. 4.14. What these images show is two devices that were assembled, device A had a large square hole in the middle of the ferrite to fit the RF antenna through while device B had three small holes to allow conductive wires from the PCB to reach the pads underneath the RF antenna, which was now raised and put above the ferrite sheet.

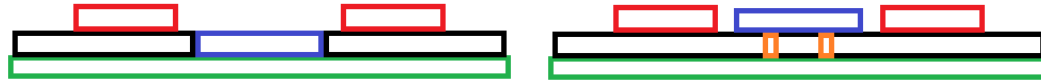


(a) An implantable device sealed with tape, with a hole in the ferrite for the RF antenna. Labelled as Device A.

(b) An implantable device sealed with tape, with a continuous ferrite layer behind the coil. Labelled as Device B.

Figure 4.14: Two types of ferrite assemblies packed inside a titanium enclosure sealed with tape. Configuration (b), with the continuous ferrite performed better on the thermal tests.)

Both configurations of devices were tested for radio frequency transmission power. These results from these tests are shown in Fig. 4.16. As can be seen from this figure, the pair of transmission frequencies from each device are relatively close to each other in signal strength and only the higher frequency from device B dips below the signal-to-noise ratio cutoff. Which means, only a small portion of the transmission signal from device B (at higher transmission distances) gets too low to be discernible from noise within the system. This shows that the two configurations of ferrite around or under the RF antenna do not have a significant impact on the transmission capability



(a) An assembly with a hole in the ferrite for the RF antenna. (b) An assembly with a continuous ferrite layer behind a raised RF antenna.

Figure 4.15: Two types of possible ferrite assembly configurations that were assembled and tested. In both images: green is the PCB, black is the ferrite, blue is the RF antenna, and red is the coil (orange in figure b are conductive pins to connect the raised RF antenna to the PCB). While both performed comparably in the RF transmission test, configuration (b) with the continuous ferrite performed better on the thermal efficiency tests.

of the device.

With this test, we were confident in utilizing either device for the remaining tests.

4.4.2 Results of Ferrite Configuration on the Efficacy of Charging Via Thermal Buildup

Utilizing the devices with two different ferrite assemblies (from Fig. 4.14) we would need to verify if design A (with a large square hole in the center of the ferrite) was a viable option as design B makes fabrication of the devices a bit difficult. The difficulty arises from the very short conductive leads that need to be extended from the PCB, through small holes in the ferrite, and then electrically connected to the bottom of the RF antenna. However, this is a better alternative than leaving a large gap in the ferrite for the RF antenna to peek through from below. Consideration of ferrite

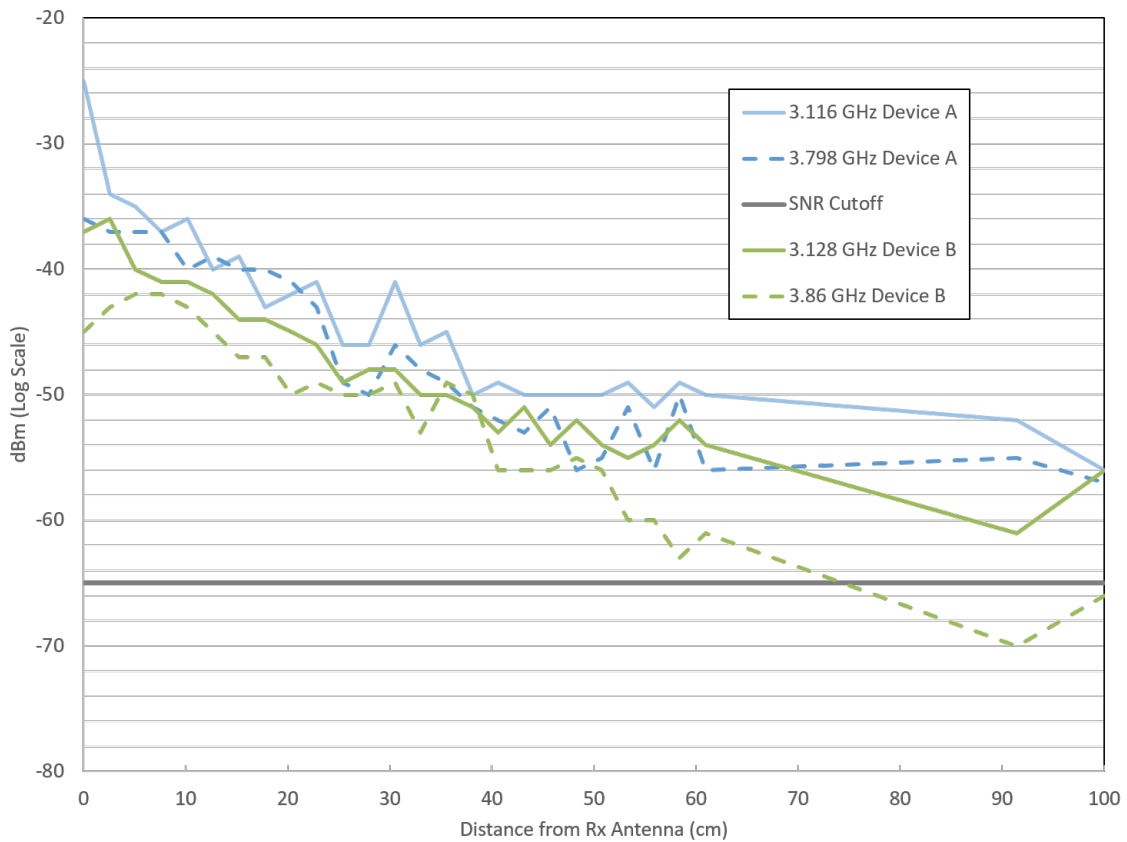


Figure 4.16: Signal strength decay over distance from transmitter. Two devices were tested (A and B), each device transmits at two frequencies (Due to Frequency Shift Keying, or FSK). The signal strength of each frequency on each device is shown here.

properties within a magnetic field state that since the magnetic field is strongest in the center of the coil (Fig 4.11) the lack of ferrite in the center will negatively affect the efficiency of power transfer. In order to verify this, thermal tests were done on the power transfer efficiency of both devices in air and compared. Fig. 4.17 shows the difference in heat generation on the titanium enclosure of each device.

As shown in Fig. 4.17, the temperature generation (higher temperature means lower efficiency) from device A and B were relatively close until about half way through charging (roughly 10 minutes in). As the charging went on, device A (with

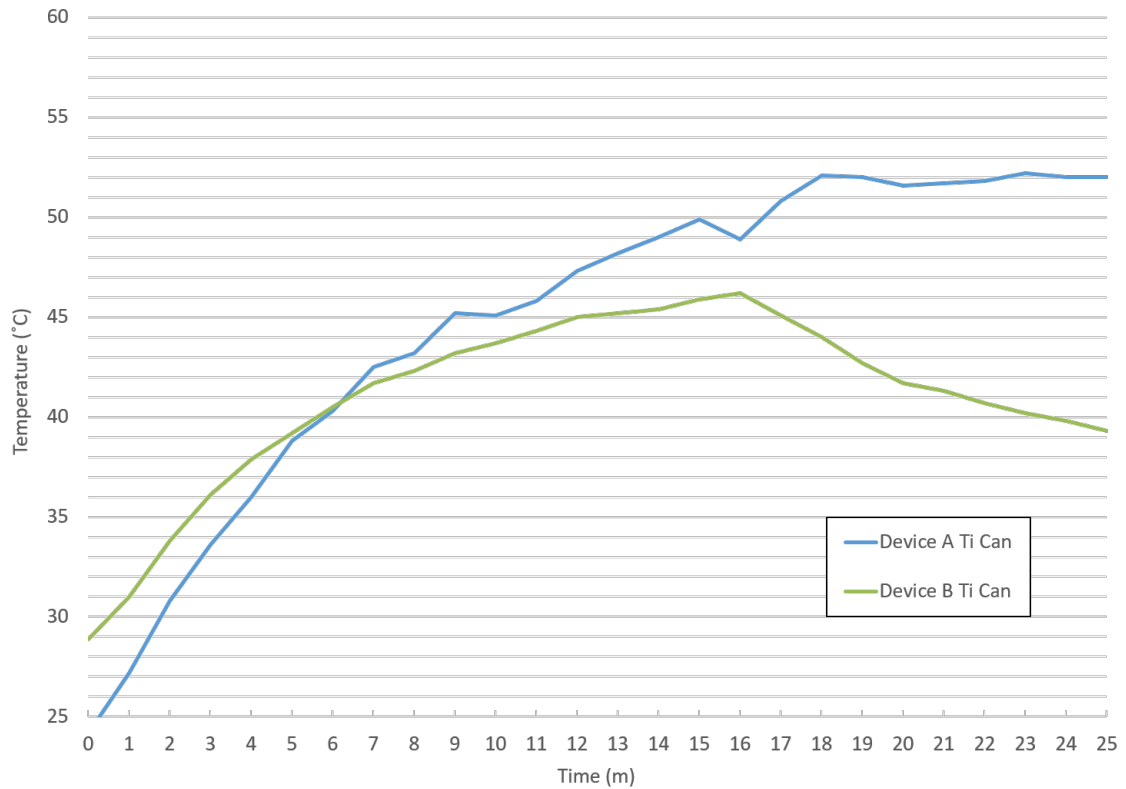


Figure 4.17: Temperature profiles of the titanium enclosure of each device with a different type of ferrite configuration, from room temperature to steady state. Device B was significantly more efficient, as it reached maximum charge much sooner and the charger switched to a low power “trickle charge” mode.

a hole in the middle) continued to heat up as the coupling efficiency was not as good (due to lack of ferrite at the B field maximum point). Device B, however, approached a high point (around 46 °C) by which point the device had been fully charged. This allowed the charger to drop the transmitting power and switch to what is colloquially known as “trickle charging”. Trickle charging is a form of very low power charging where the power delivery is active but significantly lower than the regular charging paradigm. This allows the lithium ion battery to remain topped up on charge which

would not happen if the charging ceased after full charge was reached.

4.4.3 Results of Varying Transmitting Coil Configurations

In order to determine the best coil to transmit power into the implantable device, three different coils were assessed. The efficiency of the coil was, again, verified via heat generation on the titanium can. The variation in primary coil alignment and distance from the secondary coil also has a profound effect on the efficiency, but was not directly addressed in this study. This will need to be done in thorough detail after the ideal coil within these conditions is determined. Three revisions of the transmitter were fabricated in order to determine the best coil for this construct. Revision 1 of the transmitter utilized a coil found in a commercial smartphone (Palm Pre). The Palm Pre is a now discontinued phone from 2009, which was the first smartphone released to the general public supporting wireless charging. The charging protocol was a proprietary paradigm devised within Palm and was never released or explained. However, it worked very well and their coil design was very compact and neat. An image of the Palm Pre coil is included here as Fig. 4.18. While this coil (and charging mechanism) was not Qi compatible, it was very close in design and principal. Revision 2 of the transmitter utilized the same coil from the inside of the implantable device to compliment it by applying it to the charger. The assumption was that coil coupling efficiency is greatly increased when both coils are exactly the same (or very similar, as per Fig. 4.2). Finally, Revision 3 of the transmitter design utilized the



Figure 4.18: Commercially available, machine wound, single layer, wireless power delivery coil embedded within a smartphone.

coil from Wurth Electronics (Digikey part#: 732-5673-ND). This coil was a compact, Qi compatible, commercially available coil distributed by Digikey electronics which came with a small piece of ceramic ferrite attached to it.

The first metric to determine coil viability was the inductance and the Q value of the coils. The values for all three coils are included in table 4.5. The coil within the implantable device stayed consistent and the transmitting charger was given three different coils to see which one coupled the most effectively with the internal device coil. The accompanying circuitry (i.e. coil tank circuit) was modified to accommodate for the varying inductances of each coil using equation 4.4.

The results of these coil tests are included in figure 4.19. The figure shows thermal build up on the outside surface of the titanium enclosure during wireless charging. While the coils within each revision of the charger were acceptable to begin with,

Coil	Series Inductance (μH)	Q (@100kHz)
Smartphone coil (Rev. 1)	5.5353	11.1
Device receive coil (Rev. 2)	29.504	14.8
Würth coil [732-5673-ND] (Rev. 3)	6.4527	24.1

Table 4.5: Table of inductance and quality factor values for the transmitting coils within the three revisions of the charger.

Revision 3 took the lead in lowest heat relatively soon. Revision 3 also maintained lower temperatures during the entire charging period, even though the charging period remained constant for both Revision 1 and 3. The coil used for Revision 2 seemed to be too inefficient in coupling with the coil within the device (oddly enough, it was the exact same coil). Ultimately, the Digikey provided Würth Electronics coil was chosen due to its high Q value, low inductance (closer to design ideal), and high efficiency (low heat production) while charging.

4.4.4 Results of Elevated External Temperature on the Thermal Charging Profile via Thermal Bath Testing

The thermal test consisted of using the thermal water bath with multiple thermocouples attached to the device under test. The device was assembled with glass cover slip spacers between the charger and the device. The charging (primary) coil was aligned above the sapphire window. The rest of the charger electronics were suspended above the construct in order to remain out of the heated water bath. This construct was then placed on top of a black plastic project box in order to provide a spacer between

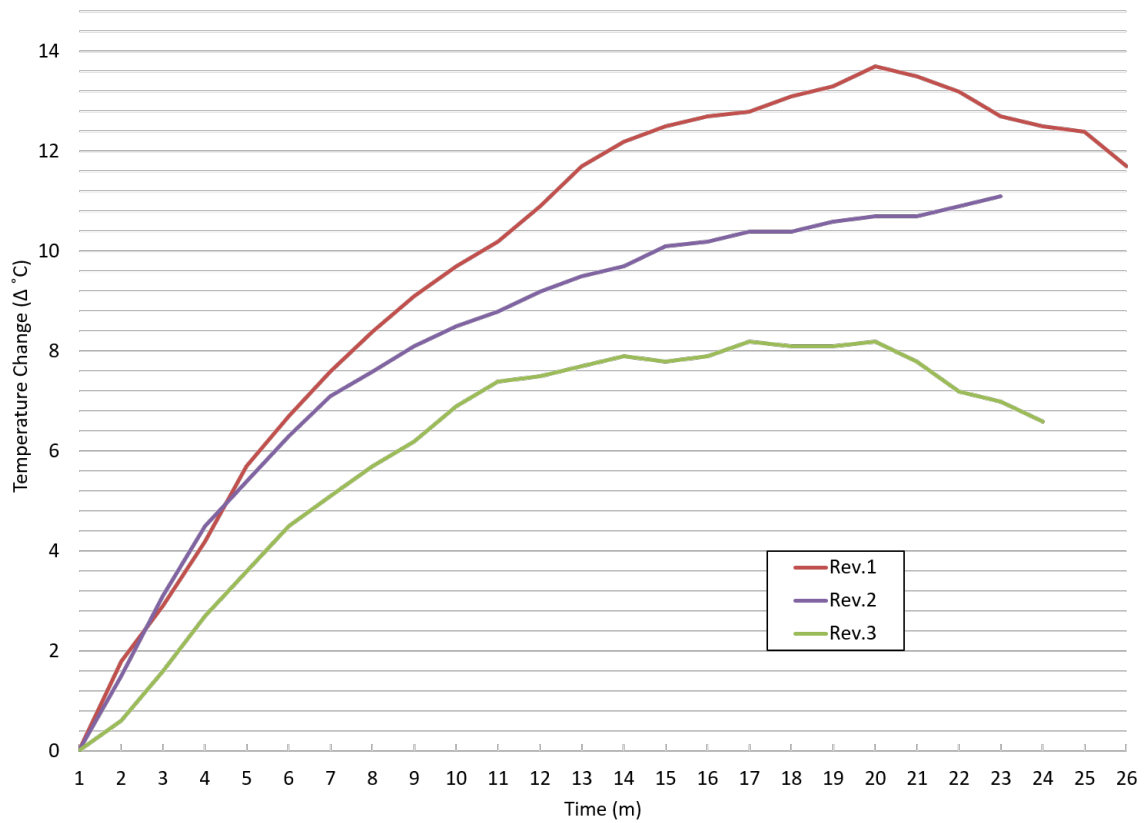


Figure 4.19: Heat generated on the surface of an implantable device using three different revisions of the external transmitting coil with the same charger. Revision 1 is a commercial smartphone coil, Revision 2 is the coil that is the same coil as the one inside the implantable device, Revision 3 is the Qi compatible coil from Wurth Electronics.

the bottom of the acrylic chamber and the device (so there could be 37 °C water underneath the device as well). This entire construct was then placed into the water bath. The water level was raised until 1 millimeter above the top of the implantable device (to make sure the entire device was submerged). Fig 4.21 shows the spacing between the charger and the device as well as the water level within the thermal bath construct. A schematic image from the top down of the device within the water bath is also included here as Fig. 4.20.

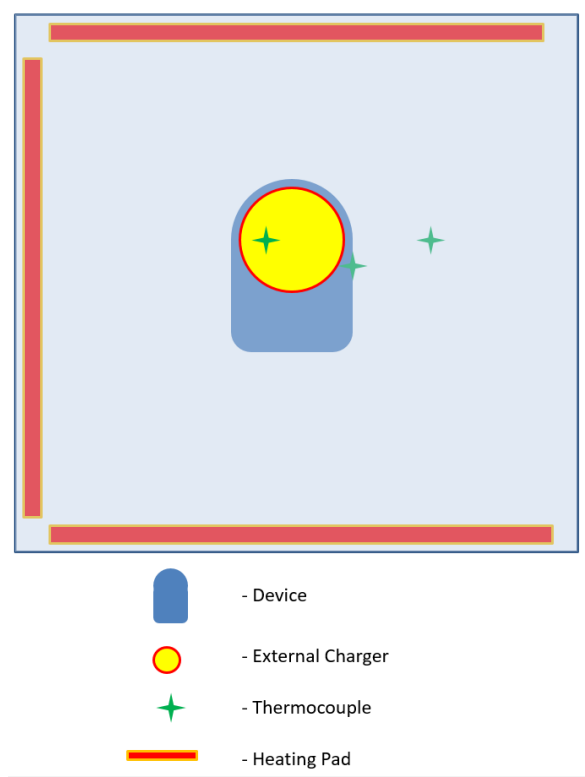


Figure 4.20: Schematic image from the top down showing the device placed within the hot water bath with thermocouples for temperature measurement and control.

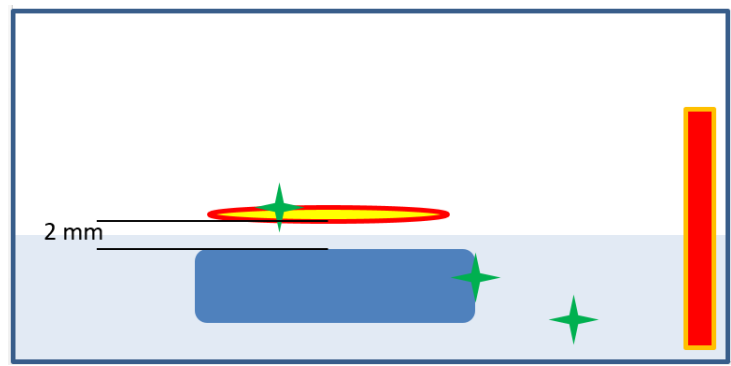


Figure 4.21: Schematic axial view showing the device placed within the hot water bath with thermocouples for temperature measurement and control.

The water bath was left for approximately 25 to 30 minutes (longer than the required charging period) and the temperature within the bath as well as the temperature of the device itself was monitored over the course of charging. During the charging period, it was observed that the water directly around the heating pads tended to get past the 100 °C and evaporate. This caused a lot of moisture and condensation within the chamber. This proved to be detrimental to the experiment in a number of ways. The condensation on the exposed electronics of the charger did not allow it to function properly. Also, hot water vapor would get trapped inside the pockets of open air created between the tape and the thermocouples. This would cause the thermocouples to reach much higher temperature than the actual temperature of the surface the thermocouple was on. Therefore, to mitigate the water vapor situation, the insulated top cover of the water bath apparatus was removed. This allowed the air in the room to blow off the water vapor. The water temperature was still maintained at 37 °C and the device itself remained submerged and maintained this temperature as well (before charging began). Once the titanium surface of the implantable device reached this 37 °C, the charger was turned on and the experiment began. The results of the experiment are shown in Fig. 4.22.

Fig. 4.22 shows the temperature from the water bath maintaining at a constant 37 °C while the charging is turned on and the device is powered. The device increases in temperature but eventually the battery approaches a full charge and the charger switches to “trickle mode” charging. These experiments showed promising

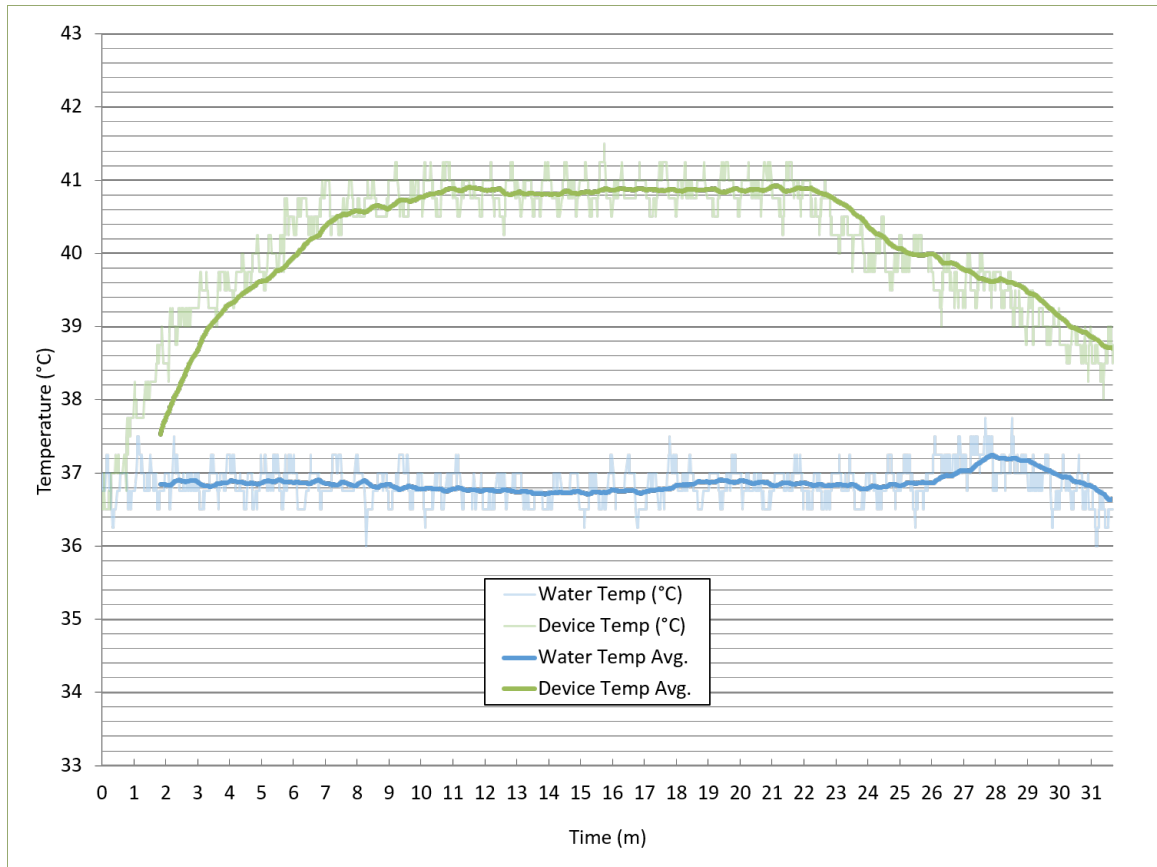


Figure 4.22: Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature.

results of incorporating Qi compatible wireless charging into an implantable device encapsulated in titanium, and allowed it to maintain a healthy, biologically viable temperature in an implanted setting.

To determine the steady state temperature profile of the implantable device during trickle charging mode from the transmitter, the experiment was continued for over ten minutes past when the maximum charge is obtained within the battery. The device is on and begins transmitting wireless data as soon as it has enough power in the battery. The results of the elongated steady state experiment are shown in

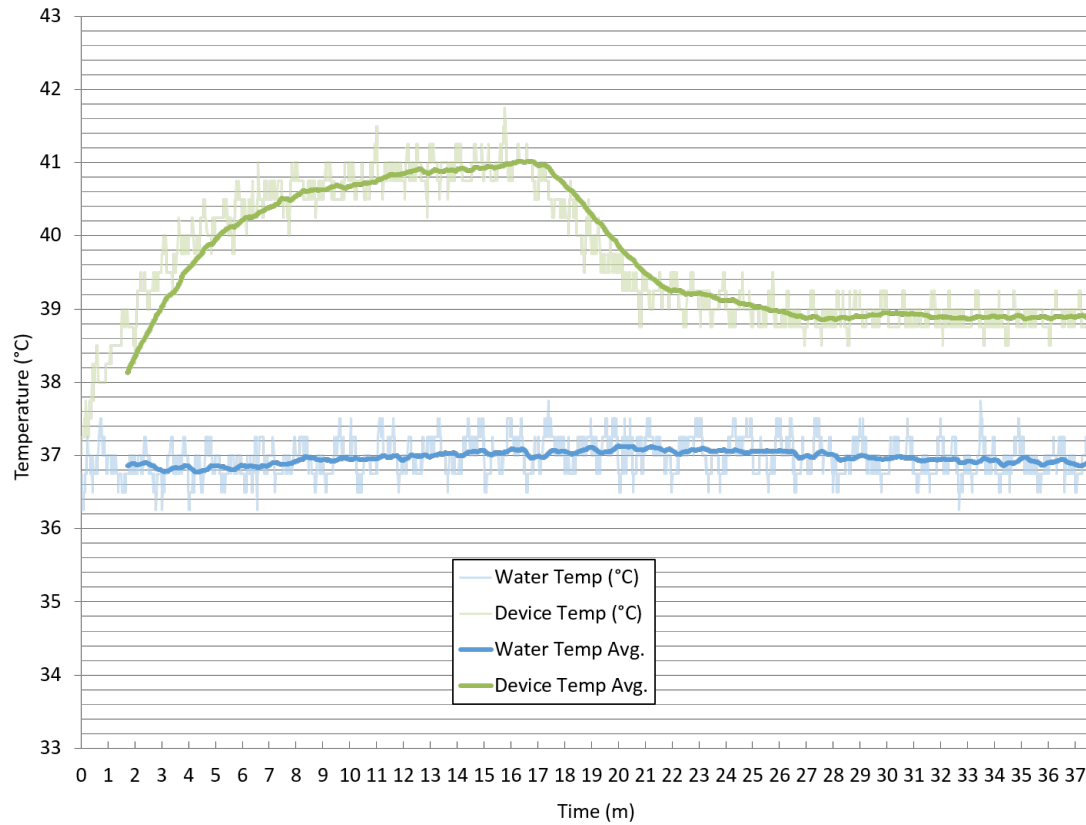


Figure 4.23: Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature.

Fig. 4.23. This figure shows how the steady state temperature reached by the device after it was finished charging remained around roughly 2 to 3 °C more than ambient temperature, half of the temperature it reaches during regular high power charging.

4.4.5 Results of Elevated External Temperature While Active Cooling via Modelled Vascular Heat Transport

The active heat dissipation modeled by the magnetic stirrer dropped the maximum temperature observed from the still water heat experiments. Average thermal profile

of the still water reached steady state just under 41 °C. With the active cooling experiments, we reached steady state of under 40 °C. There is absolutely no doubt in our minds that with proper active cooling across the large contact surface area of the device with the skin, the device will remain within the two degree celsius change in temperature from 37 °C (at or below 39 °C). Fig. 4.24 shows the thermal profile of the device in a water bath with flow incorporated into the model.

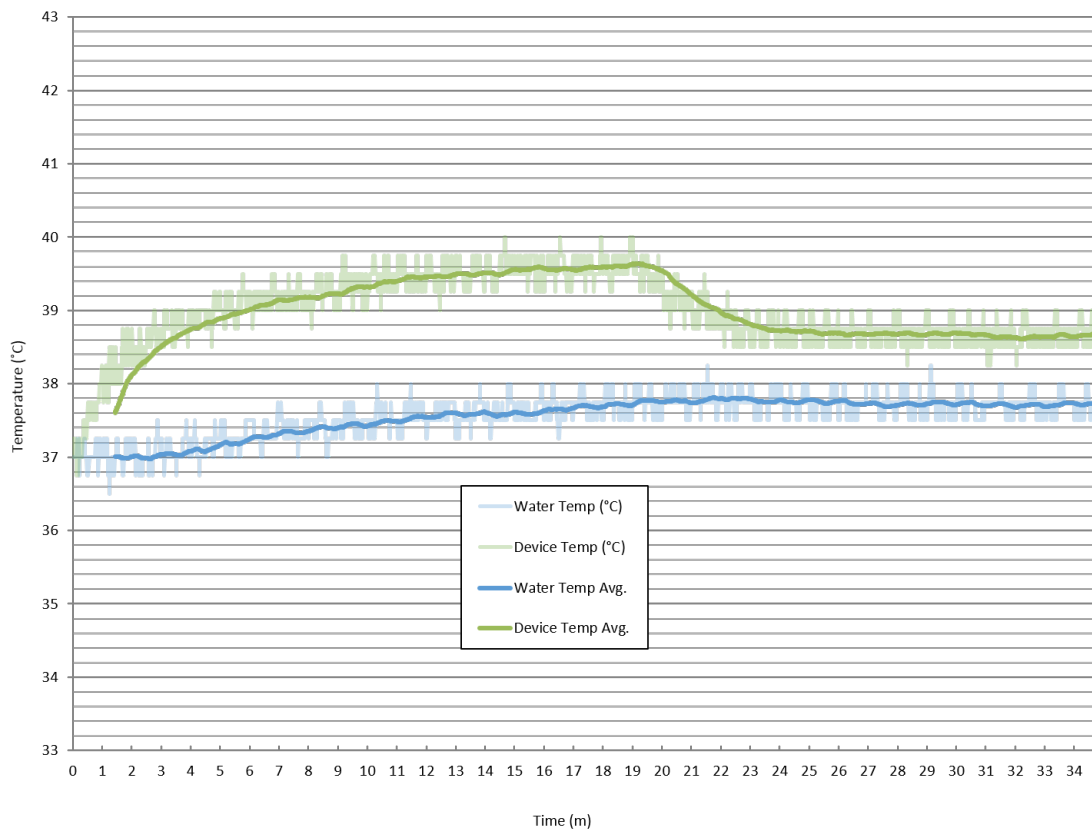


Figure 4.24: Graph of temperature of the titanium can during charging in simulated, implanted (37 °C, body) temperature with flow incorporated to mimic active heat transport.

As fig. 4.24 shows, with the proper active cooling (mimicing biological heat transport), our implantable device will be able to maintain the two degree thermal variation

limit imposed by the FDA. The heat profile in this figure remains below the 40 °C threshold, and hovers around 39 °C. 39 °C would delineate the two degree demarcation (above 37 °C) as the safety margin. With this active heat transport experiment, we can show that our device will remain at the threshold of biological safety limits while being actively charged externally.

4.4.6 Final Comparison of Air Cooling Versus Thermal Water Bath Testing As Well As Active Heat Transport Cooling

Finally, Fig. 4.25 shows a comparison of varying types of cooling methodologies used during device charging. The graph shows a normalized comparison of all three types of cooling paradigms: 1) ambient air, 2) still water, and 3) active water. This comparison outlines the necessity for a well designed thermal analog of an implanted setting, to determine a realistic level of active cooling that an implantable device can experience.

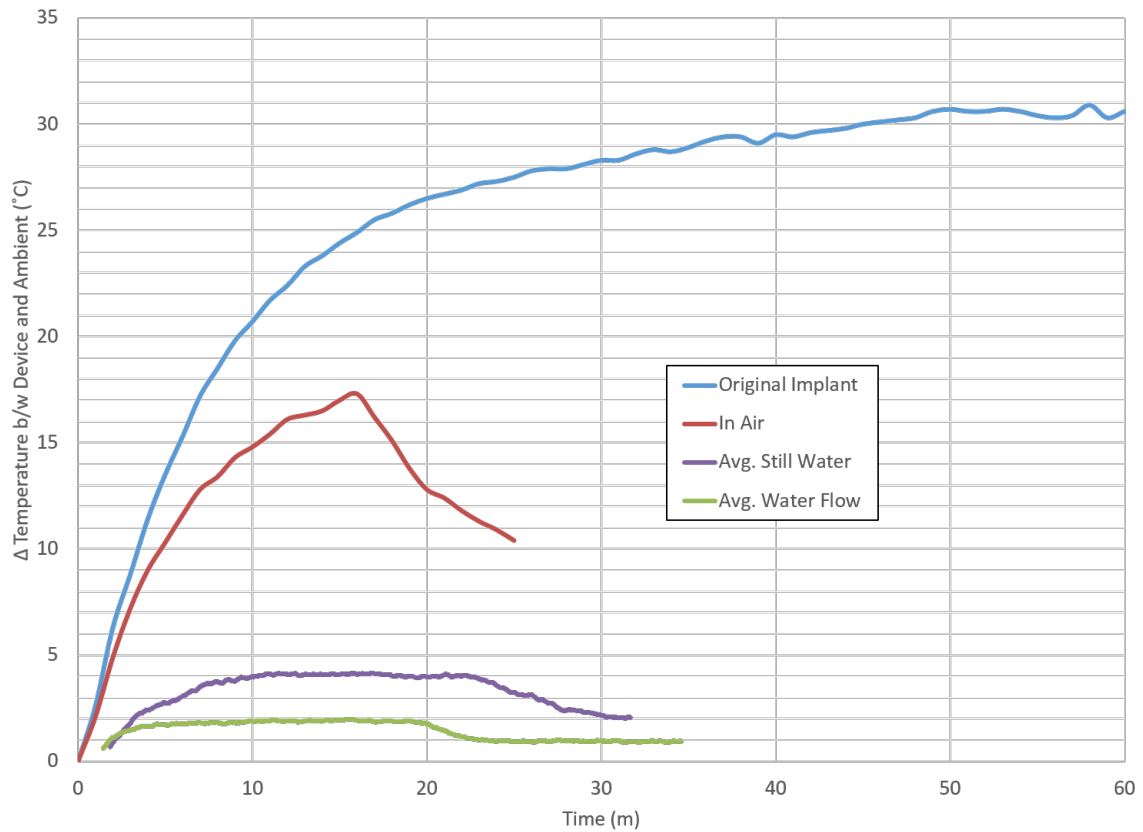


Figure 4.25: Comparison graph of thermal profiles of the titanium can during charging in air, in a simulated implanted (37 °C) body temperature bath, and finally in a 37 °C bath with flow incorporated to mimic active heat transport. The original device is without Qi integration, the other three include Qi compatible charging.

4.5 Conclusions Drawn from Integrating a Wireless Charging Industry Standard into an Experimental Implantable Device

The idea of integrating Qi wireless charging into an implantable device enclosed in titanium seemed like a monumental task. However, with the right engineering and design principles leading as far back as 1873,[12] we were able to produce a functional

device. The implantable device, in its current state, is actually 100% compatible with any Qi compatible wireless charger out in the market today. Due to the extremely compact and small size of the implantable device, however, the majority of the energy ends up being delivered into the titanium can instead of the receive (secondary) coil embedded inside. This inefficiency will generate heat on the titanium can and make the patient quite a bit uncomfortable, however, active cooling of the implant using cool water on the surface of the skin can be used to maintain the temperature. With the correct redesigning of the external charger (a smaller coil, and manipulation of the tank capacitors accompanying the coil) any charger available in the market today can be made fully compatible and efficient enough to work with the implantable device.

4.5.1 Future Qi Integration Improvement Design Ideas

There could always be more done to make the integration of this wireless charging technology better. Due to basic physics, increasing coil size would be the best way to improve the wireless coupling efficiency. Redesigning both coils to increase their mutual inductance will also help. The main design constraint for these coils is their physical size. The 30 millimeter sapphire window opening in the titanium enclosure of this implantable device forces the coil diameter to be smaller than 30 millimeters. The farther away the coil is from the edges of the titanium, the better the magnetic flux (B field) would be at transferring the energy from the primary to the secondary. This begs the coil to get smaller to maintain a clear magnetic field, however, the

smaller the coil the smaller the distance that the magnetic field can travel. Therefore the compromise of the current coil diameter was made. Further study into better coil design utilizing different types of Litz wire and varying the physical parameters of the coil could squeeze out a bit better coupling efficiency between the coils. The coil quality factor (Q) can also be improved upon by designing better, more efficient, less resistant coils. This would also greatly improve coupling efficiency and allow lower temperature charging.

4.5.2 Future Implantable Device Redesign Ideas

The biggest complication with implementing the Qi protocol compliant hardware into this device was the titanium enclosure. Even though pure titanium is not supposed to be ferromagnetic, the grade 2 titanium[2] commonly used in these type of implantable devices tend to be “impure” by design. It has traces of other elements inside to vary its mechanical/chemical properties. Table 4.6 shows a table and percentage of elements included in grade 2 titanium (used in this implantable device).

Chemical	Percentage of Total
Hydrogen	0.015
Nitrogen	0.03
Carbon	0.1
Oxygen	0.25
Iron	0.3
Titanium	99.2

Table 4.6: Table of chemical composition of Grade 2 titanium.[24, 5]

As shown in table 4.6, table of grade 2 titanium composition, the titanium enclosure used for these types of implantable devices is not pure titanium. These enclosures, in fact, have trace amounts of iron in them. This iron gives the titanium faint ferromagnetic properties, which may not be enough to cause it to become magnetic, but are definitely enough for it to affect a neighboring magnetic field. The best solution to fast, stable, efficient, and most importantly cool wireless charging is to rid the construct of any metal or ferromagnetic influence. A package of ceramic or separately packed radio frequency coil in silicone may help mitigate the deleterious effects of the titanium enclosure. However, ceramic constructs are difficult to build with 100 feedthroughs for leads to exit out of the hermetic packaging and are also not as tough and rigid as titanium but are hard and brittle. Silicone is known to be “leaky” or allow ingress of ions and conductive fluids over time so it would not make a good long term packaging solution for an active electronic implantable device. A redesign of the packaging of the device, by either increasing the sapphire window (decreasing the amount of titanium on the top surface), replacing titanium with ceramic, or separating the coil from the titanium body may be the best options for allowing this device, in its current design form, to function for a long term without increasing its temperature more than 2 degrees centigrade while charging.

To continue with the monolithic device metaphor, it would be necessary to at least increase the total surface area of the sapphire window to allow for a larger coil. A larger coil grants higher inductance which, with lower resistance, would grant a coil

with a higher Q factor. This would allow the coil to work better, giving it a higher efficiency. Larger coils would also be able to transmit across farther distances, allowing thicker skin patients to take advantage of the device and its charging capabilities. Finally, a more efficient redesign of the coil and its accompanying components, on both ends, is extremely necessary to increase efficiency. While these coils are efficient, they can always be improved by doing further analysis and modeling of the magnetic B field between the two coils with a titanium enclosure in the middle.

The Introduction of Solid Core, Ceramic, Shaped Ferrite Backing

As a final note, a ferrite construct around and behind both coils (primary and secondary) would significantly increase the mutual inductance of the two coils. There is already a small, thin, ceramic ferrite plate behind the transmitting coil, but if a similar (but properly tuned) complimentary ferrite construct could be built behind the receiving coil it would vastly improve the coupling efficiency. The two ferrites on the opposite ends of each coil would be thusly shaped, in order to force the magnetic B field to focus specifically behind, around, and through each coil. This would make sure that all the magnetic B field is focused at the exact center of each coil thus increasing power and efficiency between the two coils. While designs of these shaped ferrite are underway, implementation is complicated. The ferrite needs to be extremely thin in order to fit within the implantable device (where space is very limited to begin with). The ferrite would also have to be shaped very specifically for this application, stay

within the strict physical limits defined by the sapphire window opening, and finally, allow small holes for the radio frequency connections to go through and reconnect to the printed circuit board.

The improvements necessary to make the charging more efficient and cooler are definitely possible and will require a bit more time and research. This is considered and is being pursued for the next revision of the implantable device. The ideal goal would be to increase efficiency enough that the change in temperature on the titanium enclosure would be negligible and the device would be able to be charged at over 2.5 Watts, allowing safe, fast recharging of the implantable device.

References

- [1] API Delevan. *FFAM Series: Flexible Ferrite Absorbent Material*, January 2009.
- [2] David A Borton, Ming Yin, Juan Aceros, and Arto Nurmikko. An implantable wireless neural interface for recording cortical circuit dynamics in moving primates. *Journal of Neural Engineering*, 10(2):026010, 2013.
- [3] Nisha Charkoudian. Skin blood flow in adult human thermoregulation: How it works, when it does not, and why. *Mayo Clinic Proceedings*, 78(5):603 – 612, 2003.
- [4] Gábor Halász, Balázs Gyüre, Imre M. Jánosi, K. Gábor Szabó, and Tamás Tél. Vortex flow generated by a magnetic stirrer. *American Journal of Physics*, 75(12):1092–1098, 2007.
- [5] J.M. Holt, C. Gibson, C.Y. Ho, Purdue University. Center for Information, Numerical Data Analysis, and Synthesis. *Structural Alloys Handbook*. Number v. 2 in Structural Alloys Handbook. CINDAS/Purdue University, 1999.
- [6] H. Hori, G. Moretti, A. Rebora, and F. Crovato. The thickness of human scalp: normal and bald. *J. Invest. Dermatol.*, 58(6):396–399, Jun 1972.
- [7] ISO. Implants for surgery — Active implantable medical devices — Part 1: General requirements for safety, marking and for information to be provided by the

- manufacturer. ISO 14708-1 11:2000, International Organization for Standardization, Geneva, Switzerland, 2000.
- [8] Wilfried Jacobi and G. Eichinger. Lithium rechargeable batteries for portable telecommunication appliances-basic concepts and recent developments. In *Telecommunications Energy Special Conference, 2000. TELESCon 2000. The Third International*, pages 123–127, 2000.
- [9] WenH. Ko, SheauP. Liang, and CliffD.F. Fung. Design of radio-frequency powered coils for implant instruments. *Medical and Biological Engineering and Computing*, 15(6):634–640, 1977.
- [10] E.N. Marieb and K. Hoehn. *Human Anatomy & Physiology*. Pearson, 2013.
- [11] A.J. Marshall. *Biology and Comparative Physiology of Birds*. Elsevier Science, 2013. v. 2.
- [12] J.C. Maxwell. *A treatise on electricity and magnetism*. Number v. 1 in A Treatise on Electricity and Magnetism. Oxford: Clarendon Press, 1873.
- [13] A. Okamoto. The invention of ferrites and their contribution to the miniaturization of radios. In *GLOBECOM Workshops, 2009 IEEE*, pages 1–6, Nov 2009.
- [14] W. H. Oldendorf and Y. Iisaka. Interference of scalp and skull with external measurements of brain isotope content. 1. Isotope content of scalp and skull. *J. Nucl. Med.*, 10(4):177–183, Apr 1969.

- [15] Quallion. Quallion chemistry technology: Secondary batteries.
<http://www.quallion.com/sub-tc-secondary.asp>. Accessed: October 26, 2015.
- [16] K. S. Ryu, K. Shaikh, E. Goluch, Z. Fan, and C. Liu. Micro magnetic stir-bar mixer integrated with parylene microfluidic channels. *Lab Chip*, 4(6):608–613, Dec 2004.
- [17] M. Soma, Douglas C. Galbraith, and Robert L. White. Radio-frequency coils in implantable devices: Misalignment analysis and design procedure. *Biomedical Engineering, IEEE Transactions on*, BME-34(4):276–282, April 1987.
- [18] G. E. Strangman, Q. Zhang, and Z. Li. Scalp and skull influence on near infrared photon propagation in the Colin27 brain template. *Neuroimage*, 85 Pt 1:136–149, Jan 2014.
- [19] Texas Instruments. *bq5101xB High-Efficiency Qi v1.1-Compliant Wireless Power Receiver and Battery Charger*, 3 2015. Rev. E.
- [20] G.J. Tortora and B.H. Derrickson. *Principles of Anatomy and Physiology*. John Wiley & Sons, 2011.
- [21] Zaka Ullah, Shahid Atiq, and Shahzad Naseem. Influence of pb doping on structural, electrical and magnetic properties of sr-hexaferrites. *Journal of Alloys and Compounds*, 555:263 – 267, 2013.

- [22] E. Waffenschmidt. Wireless power for mobile devices. In *Telecommunications Energy Conference (INTELEC), 2011 IEEE 33rd International*, pages 1–9, Oct 2011.
- [23] E. Waffenschmidt and T. Staring. Limitation of inductive power transfer for consumer applications. In *Power Electronics and Applications, 2009. EPE '09. 13th European Conference on*, pages 1–10, Sept 2009.
- [24] G. Welsch, R. Boyer, and E.W. Collings. *Materials Properties Handbook: Titanium Alloys*. Materials properties handbook. ASM International, 1993.
- [25] J Werner. The concept of regulation for human body temperature. *Journal of Thermal Biology*, 5(2):75–82, 1980.
- [26] H.A. Wheeler. Simple inductance formulas for radio coils. *Radio Engineers, Proceedings of the Institute of*, 16(10):1398–1400, Oct 1928.
- [27] Wireless Power Consortium. *System Description Wireless Power Transfer*.
- [28] Würth Electronics Inc. *WE-WPCC Wireless Power Charging Transmitter Coil*, 10 2014. Rev. 1.4.

5

Discussion

5.1 A Summary of the Results of this Study

In this study, we showed the application of a unique, wireless, broadband, fully implantable device to the field of behavioral neuroscience. This device can be utilized to collect data from experiments and behavioral paradigms that no other neural data collection tool can accomplish. Table 5.1 shows all the animals that we have implanted this device into for long-term viability studies. The longevity of this device has been validated in non-human primates for almost 600 days, while its longevity in swine has been validated over 600 days.

Animal	Species	Days Implanted	Reason for Explantation
SY	Swine	613	Signal Degradation
WN	NHP	594	Signal Degradation
JA	NHP	561	Signal Degradation
JN	NHP	519	Signal Degradation
SU	Swine	321	Scalp Thickness
SM	Swine	252	Scalp Thickness

Table 5.1: Table of animal models implanted with the titanium enclosed implantable device for an extended period of time, arranged by most to least number of days implanted. All devices explanted from these animal models were fully functional at the time of explant (NHP = Non-human primate). The two swine (SU and SM) were Yorkshire swine whose scalp grew too thick for the wireless charging of the implant to work effectively. This made charging the device impossible and we were forced to explant. Upon explant, the devices were charged and were shown to be fully functional. Signal degradation is due to long term neural implants having adverse effects on the microelectrode array within the brain. The signal degradation refers to the brain/device interface which is well documented.

5.2 The Potential Impact of this Study on Implantable Devices

This device has shown great promise as the first of its kind fully implantable device to incorporate the commercial Qi charging standard into its capabilities. The ability to purchase any commercial smartphone charger and apply it to a neural device is a novel and unique capability of this device. The application of the Qi standard to different neural implants could open the door to ubiquity in implantable device charging paradigms. If it was as easy to charge an implantable device as it is to charge a smartphone, the reliability and market adoption of implantable devices could increase considerably.

5.3 Future Avenues of Pursuit for Human Clinical Trials

The next step for advancement for this device is human clinical trials. The research stage of this implantable device can be considered substantial for its application to human clinical trials. The current state of this device is in the form of an industrial technology transfer to facilitate the development of human grade versions of this device. This includes the collection and compilation of all past design and present implementation data of this device. This is a long and involved process of collecting all possible research application designs and justification of design choices to transfer over to a documentation system of a commercial company.

5.3.1 The Transition From Research Grade Tool to Human Clinical Therapeutic Device

The technology transfer to develop and manufacture human grade implantable devices is currently underway. The process of collation and collection of all pertinent design files, design documentation, and decision pathways must be followed. This technology transfer will ultimately allow all documentation from the research level of this device to be adopted into a commercial documentation system. This would allow the eventual application of this device to FDA and USDA regulation pathways. Allowing this device to be used in human clinical trials will eventually pave the way

to a fully licensed, commercially available product.

Appendix A

A Soft, Flexible, Thin, Fully-Implanted, Wireless Brain-Implantable Chip

One of the precursors of our titanium encased, implantable device, is the silicone (PDMS) encapsulated thin, flexible, polyimide based “Brain-Implantable Chip”. Extracellular electrode arrays are capable of recording neural activity with excellent spatial and temporal resolution. There are many different array designs, but the one that is most frequently used in this study is the Utah array shown in Fig A.1. While the array shown in Fig. A.1 below is 10 x 10, many smaller versions of the Utah array have been made (i.e. 4 x 4, 6 x 6 etc.). The shaft of each electrode within the matrix is made out of silicone and coated with bio-compatible parylene while the

tip is coated with platinum or platinum-iridium (Pt/Ir). The separation between the electrodes is typically a few hundred micrometers. This distance is enough to justify the assumption that the activity of a neuron is being recorded by only one electrode at any given time (See Fig. A.1b). The impedance of the electrodes is, on average, roughly $500\text{ k}\Omega$, making them particularly good at sensing events that happen on very short time-scales, such as action potentials.

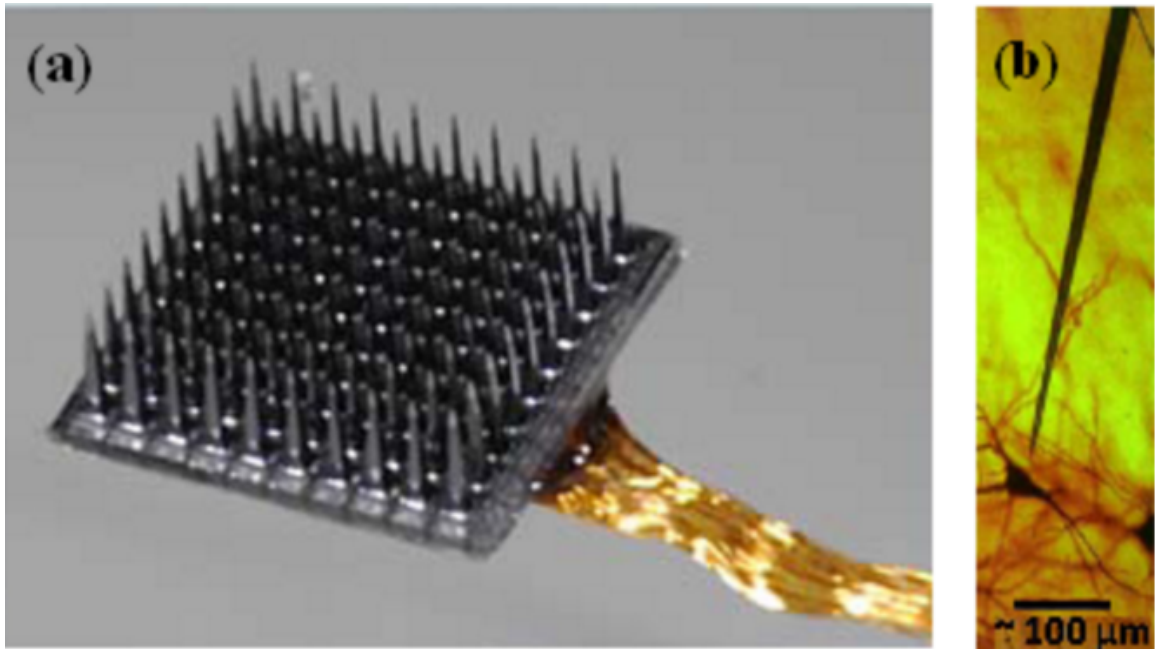


Figure A.1: Magnified images of a 1.5 mm long electrode array. (a) A 10 x 10 Utah Microelectrode Array (MEA) (b) An electrode in extracellular space.

The sensor is only a small part of the complete recording system. The analog data is typically amplified and digitized in order to make it more robust to noise. An example of a complete recording system is the Brain-Implantable Chip (BIC) developed at Brown University. The BIC is used to extract signals from the brain and transmit them through a wireless interface to an external receiver for additional signal

processing. The transmitted data can be used for a variety of applications, including real-time neuroprosthetic control. The BIC recording system is fully implantable, a design choice that reduces the risk of infection and the mechanical instability that is characteristic of recording systems that make use of transcutaneous cables. Fig. A.2 gives a system-level view of the the BIC.

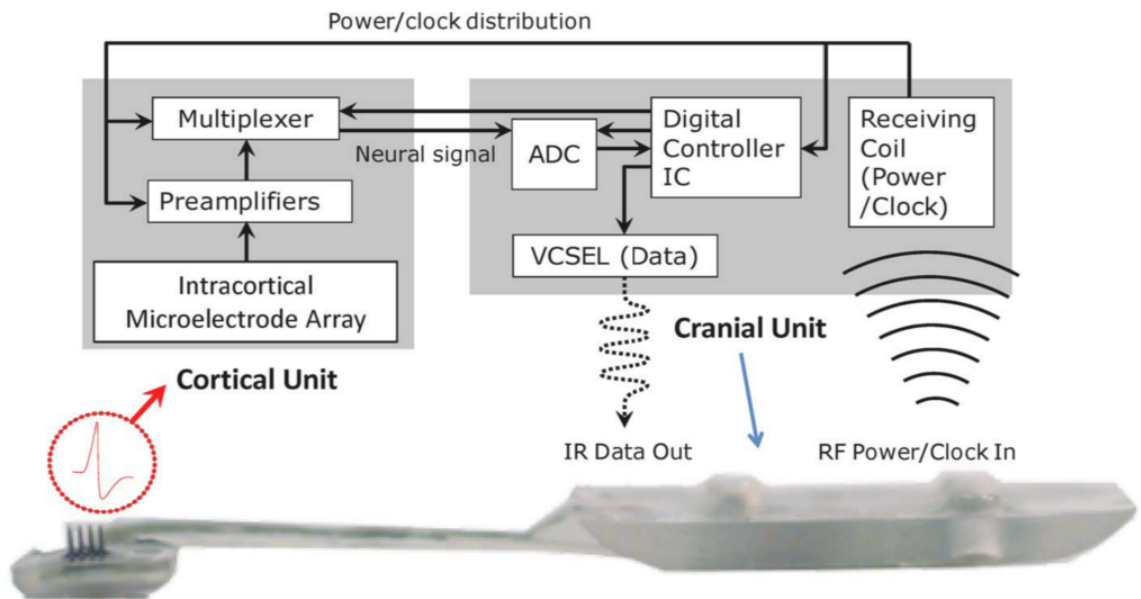


Figure A.2: A systems-level view of the Brain-Implantable Chip

The sensor used in the BIC system is the Utah Array (Blackrock Microsystems, Inc.). In a typical experiment, the 1.5mm long electrodes are inserted directly into layer IV—left hemisphere—of the motor cortex, to record activity that is correlated with movement in the upper limb. This electrode array is flip-chip bonded to an array of amplifiers developed in-house for this custom setup. The output from the preamplifiers is multiplexed into a single serial data stream. The sensor array, the preamplifiers and the multiplexer are collectively referred to as the “front-end” or

Cortical Unit of the BIC because they sit directly on top of the brain. A very thin segment of poly-imide with 7 gold traces heads out from “front-end” and meets the “back-end” of the device or Cranial Unit carrying the analog data. The power is delivered to the “front-end” from the “back-end” using the same traces.

The “back-end” of the device is responsible for three things: 1) digitizing the analog data 2) packetizing and wirelessly transmitting the data, and 3) receiving power and clock through inductive coupling. The Analog to Digital Converter (ADC) on the “back-end” operates at 34-40 ksps with 12-bit resolution for each sample. This sampling rate is more than enough to recover the high-frequency content within the neural signal. The on-board digital controller IC, packetizes the bit-stream. Using pulse code modulation (PCM), the vertical-cavity surface-emitting laser diode (VCSEL) transmits the serialized data transcutaneously as a stream of infrared light pulses. The necessary power and clock are transmitted to the “back-end” through inductive coupling. A coil is embedded around the perimeter of the “back-end”, and the induced AC current is converted to DC via a tank circuit on board. The current clock speed is 13.56 MHz and is more than capable of supporting broadband data across 16 channels.

There are a few design advantages in separating the device into a “back-end” and a “front-end”. A separated “front-end” allows us to increase the size of the Microelectrode Array (MEA) and develop larger arrays without interfering with the layout of the “back-end” electronics. A larger array would however require more

power and a higher clock speed both of which scale approximately linearly with the number of channels on the array. It is also possible to have more than one “front-end”, giving us access to multiple sites in the brain. In terms of prosthetic control, this has clear advantages; capturing limb kinematic data from the primary motor cortex (M1) and goal-oriented data from the parietal reach region (PPR) in the post parietal cortex would surely lead to better prosthetic manipulation.

An important consideration in developing a recording system such as the BIC is the functionality of the device over long periods of time. To prolong the life of an implanted device, it is necessary to protect it from the harsh environment of the human body. In order to protect itself from infection, the body has many defense mechanisms that vigorously attack foreign materials. In addition, the intracortical device must also be shielded from moisture and the ionic currents that are inherent to the cytoplasmic fluid within the brain. In order to protect the device from this humid, charged environment, it is encapsulated within a shell made out of PolyDiMethyl Siloxane (PDMS), a soft flexible silicone polymer. The low ion permeability of PDMS, keeps ions away from the device and at the same time shields the brain tissue from the potentially harmful heat being dissipated by the device.

The BIC is a complete neural recording system, capable of providing an information-rich signal that can be used in a multitude of applications. Such a device is an important milestone in developing a brain-controlled neuroprosthetic system with widespread clinical application.

Appendix B

Sleep Studies Utilizing the External Version of our Implantable Device

B.1 Background on External Wireless Transmit- ting Device

During the development of our titanium encased implantable device, the need for an intermediary to bridge the gap between our device and currently adopted standards for neuroscientific research became apparent. Current methodology for multiple single unit recording sites for neuroscience applications is the Neuroport assembly by Blackrock Microsystems. The Neuroport is a metallic cylindrical pedestal which is

screwed directly on to the skull of a patient. It has the same bundle of gold wires extending into an array of silicone electrodes which sit on the cortex of the patient. The metal pedestal, then, protrudes through the skin and leaves conductive pads on the opposite end. It's main function is to allow conductive pathways to lead neural signals recorded from the array in the brain, directly outside the skin. This is usually met with a preamplification system with a thick cable and lead to a rack of computers for computation and data storage. Our lab developed a small external version of the implantable device, which mates with the metal pedestal of the Neuroport, and transmits the data wirelessly. The internal electronics and the general design is exactly the same as the implantable version of our device.

In order to validate this external device, we decided to show its unique characteristics with a freely-moving sleep study with non-human primates. The benefit of making a "backward compatible" wireless device was that it allowed us to apply it to any animal with a Neuroport that was already under another trained behavioral study. The flexibility of this device gave us the opportunity to utilize any Neuroport application and "plug and play" our external wireless transmitting device into the study. The receiver then obtains the wireless data and directly interfaces with the commercially available neural signal processor (or NSP) from Blackrock Microsystems.

B.2 Sleep Study Methodology

The sleep study application of our device consisted of sedating the non-human primate in its home cage with ketamine. Then the animal was removed and the device was attached to the preimplanted Neuroport pedestal. While the animal was removed, its home cage was fitted with three antennas, one on top and two on either side of the cage. The fourth antenna was left on a stand outside, facing the middle of the cage. The animal was then returned to its home cage and allowed to recover. Once the animal was awake, recording was started. An infrared capable network camera was also set up to take video and synchronized through the network data stream collected from the neural data via the receiver board as well as the network video stream from the camera. The neural data was then observed by two researchers in an adjacent but separate room. The animal was allowed to fall asleep when the room lights automatically shut off on a timer at 19:00. The infrared night vision camera was able to record the animals behavior as it moved around its home cage at night and fell asleep, occasionally waking to move around or readjust its position. These movements were visually marked on the data stream as the video stream came in simultaneously. When the automated timer turned on the lights, at 6:00, the animal was then sedated with ketamine again and removed from its home cage. The device was then removed from the top of the animals head, and the receiving antennas removed from the inside of its home cage. Finally, the animal was returned to its home cage and allowed to recover from the sedative.

B.3 Sleep Study Results

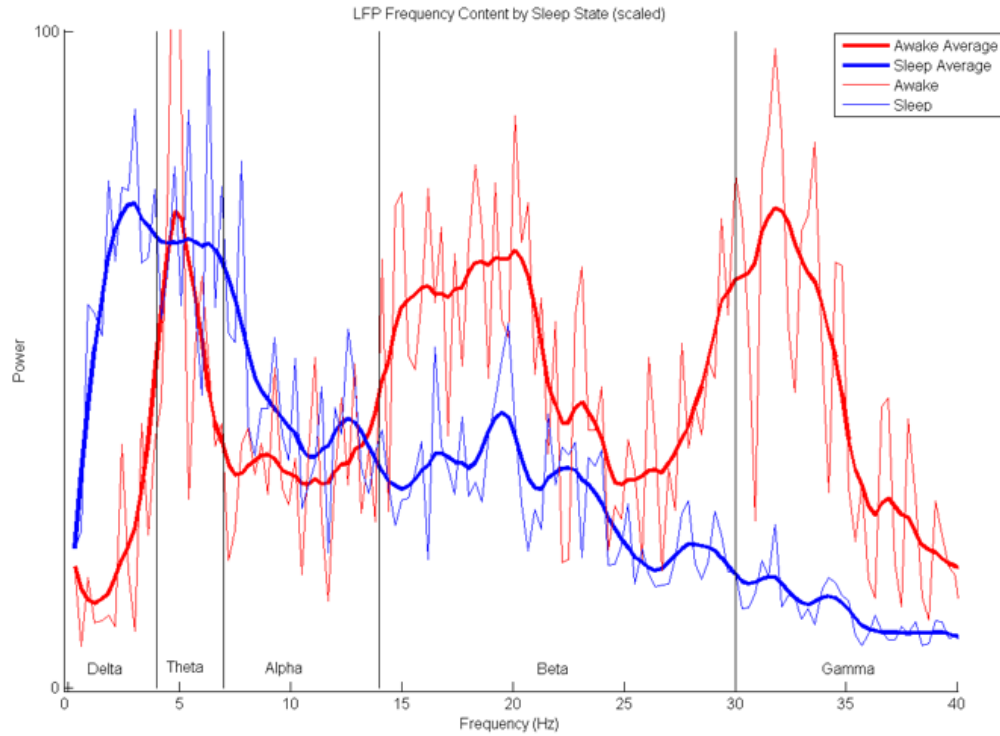


Figure B.1: Spectral analysis of sleep recordings collected from a freely-moving non-human primate in its home cage. The animal fell asleep and awoke of its own volition over the course of a 12 hour night.

The sleep study was conducted to show a unique application of a freely-moving, self-guided behavioral study. The goal of this study was to leverage our device's capability on a previously task-oriented behavioral study non-human primate and observe its application in opening new avenues of research. It is not possible to perform freely-moving naturalistic sleep pattern studies on an animal when it is head fixed in a primate restraint chair. The animal's sleep in this study was purely naturalistic from the onset. The data was then collected and analyzed using basic MATLAB

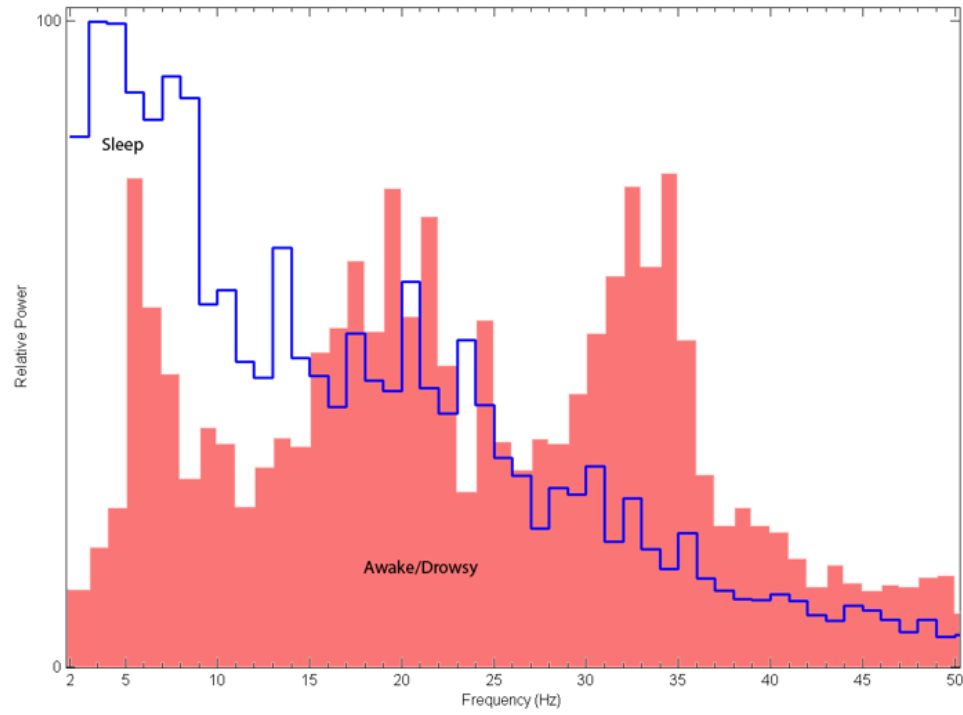


Figure B.2: Spectral analysis of sleep recordings collected from a freely-moving non-human primate in its home cage. The recorded data was binned at 1 minute intervals with some awake activity occurring within the sleep bands due to a mental “drowsy” state.

spectrum analysis tools. The separation of the sleep bands were shown, in order to isolate sleep and wake states. Fig. B.1 shows the neural activity spectrum at the local field potential (or low frequency) level. This gives a wholistic view of the neural activity. Even though single unit neural activity was also observed.

B.4 Sleep Data Analysis

Fig. B.1 shows the separation of neural states based on literature standards of sleep and awake states in lower frequency power bands. While we see some power in the sleep bands during awake, our interpretation is that this is during a “drowsy” state. The video shows the non-human primate clumsily moving around the cage in the middle of the night, so this activity can be attributed to such a mental state. However, the majority of the awake activity can be seen in the Beta and Gamma bands of the neural activity spectrum, as expected.