5-2016

Handcrafted electrocorticography electrodes for a rodent neural activity

Nishat Tasnim
The University of Texas Rio Grande Valley

HANDCRAFTED ELECTROCORTICOGRAPHY ELECTRODES FOR A RODENT NEURAL ACTIVITY

A Thesis

by

NISHAT TASNIM

Submitted to the Graduate College of
The University of Texas Rio Grande Valley
In partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

May 2016

Major Subject: Electrical Engineering

HANDCRAFTED ELECTROCORTICOGRAPHY ELECTRODES FOR A RODENT NEURAL ACTIVITY

A Thesis
by
NISHAT TASNIM

COMMITTEE MEMBERS

Dr. Yoonsu Choi
Chair of Committee

Dr. Yul Chu
Committee Member

Dr. Nazmul Islam
Committee Member

May 2016

ABSTRACT

Tasnim, Nishat**,** Handcrafted Electrocorticography Electrodes for a Rodent Neural Activity. Master of Science (MS), May, 2016, 47 pp., 19 figures, 49 references, 14 titles.

Electrocorticography (ECoG) is a minimally invasive neural recording method that has been extensively used for neuroscience applications. Although many neural recording methods exist, ECoG provides a combination of stability, high spatial and temporal resolution with chronic and mobile capabilities. This paper presents an animal study using a low cost and simple handcrafted ECoG electrode that is made of commercially accessible materials. The study is performed on a *Lewis* rat implanted with a handcrafted 32-channel non-penetrative ECoG electrode covering an area of 3 x 3 mm^2 on the cortical surface. The ECoG electrodes were placed on the motor and somatosensory cortex to record the signal patterns while the animal was active on a treadmill. Using a Tucker-Davis Technologies acquisition system and the software Synapse to monitor and analyze the electrophysiological signals, the electrodes obtained signals within the amplitude range of 200 μV for local field potentials with reliable spatiotemporal profiles.

ACKNOWLEDGMENTS

First and foremost, I will always be grateful to Dr.Yoonsu Choi, chair of my thesis committee, for all the mentoring, advice and opportunities he has provided me. I would like to thank Dr. Nazmul Islam and Dr. Yul Chu members of my thesis committee, for their advice and encouragement. I would also like to thank Raul Ramos and Ridwan Hossain for their advice, and suggestions for my thesis. Finally, I would like to express gratitude to The University of Texas Rio Grande Valley Health Science Center-Regional Academic Health Center in Edinburg (ERAHC), for all the support they have given my work.

TABLE OF CONTENTS

LIST OF FIGURES

Page

CHAPTER I

INTRODUCTION

In the study of neuroscience, there is a significant amount of interest in determining the mechanisms that explain the relationship between neural interactions in the brain and physical movements. The neural signals obtained from brain activity describes the physical behavior of human and other animals. Being able to measure brain signals to understand these mechanisms will allow to treat numerous diseases and greatly increase the quality of recovery for patients suffering from nervous tissue damage [1-6].

Identifying neural functions, by means of cortical maps, can ease the establishment of proper links for neural interfaces that can offer disabled patients an alternative solution for their lost sensory and motor functions through the use of brain-computer interface (BCI) technology [7-10]. Several recording methods that have been implemented in BCI applications are electroencephalography (EEG), electrocorticography (ECoG), magnetoencephalography (MEG), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) [11-14]. However, due to not having considerable temporal resolution and being large systems, MEG, fMRI, and PET are not practical for continuous recording of electrical signals from neurons. Alternatively, methods that have the portability, are comparably less expensive and minimally invasive are EEG and ECoG. These interfaces extract neural activity with the use of electrodes which have advanced the performance of BCI and neuroprosthetics. EEG measures

the brain activity placing the electrodes on the scalp while ECoG measures the voltage at an electrode site below the skull and directly on the surface of the brain.

Researchers prefer using ECoG over EEG for recording brain signals, as ECoG has high spatial resolution. Commercially available ECoG electrodes provide high performance and integrated amplification. However, the cost of these systems can be redundant for experiments performed at small research laboratories where a large number of animals to be continuously recorded. Therefore we have proposed a fabrication procedure for ECoG recording technique using low-cost components and without any complicated micromachining fabrication procedure. The electrode response obtained after implanting the electrodes on rat's cortical surface confirms the stability and spatiotemporal features. Chapter 1.1 describes current trends in EEG and ECoG, Chapter 1.2 describes problems with other ECoG electrodes, and Chapter 1.3 describes the motivation of this research work.

1.1 Current trends in EEG & ECoG

EEG is a commonly known recording technique for BCI applications due to its low cost, portability, and non-invasiveness. This technique measures the activity from a large population of neurons by attaching electrodes to the scalp of a subject. As a consequence, the impedance of the distance between the cortical tissue and the electrodes force the EEG to have a low spatial resolution [11, 15].

Another type of recording technology is the Utah Intracortical Electrode Array (UIEA) which has allowed implanting a large number of microelectrodes into a small area of the cortex due to its micromachined structure. This technique has been implemented in BCI systems for its ability to provide high temporal and spatial resolution and capture both action potentials and local field potentials by allowing microelectrodes to be placed close to small groups of neurons.

With this information, UIEA has allowed individuals with illnesses, such as tetraplegia, to have control over technologies such as neuroprosthetics [16-19]. However, this electrode array has also proven to be impractical due to its lack of reliability and invasive procedure. Therefore, attention has converged on electrocorticography (ECoG), a minimally invasive method that records over the cortical surface of the brain by surgically placing an array of electrodes underneath the skull.

By direct comparison with EEG, ECoG electrodes detect signals from around 50 μV to over 100 μV, while EEG obtains signals in the 5–10 μV range from scalp electrodes. The bandwidth of EEG is limited to about 50Hz and since ECoG is placed on the surface of the cortex it has a higher frequency bandwidth ranging between 40 to several hundred Hz. The ECoG also allows to obtain very accurate signal source localization because it achieves a spatial resolution in the millimeter range compared to the centimeter range with EEG neural activity. For these reasons, ECoG has become a preferable alternative approach in recording brain activity for BCI applications in numerous occasions [20-22].

1.2 Problems with other ECoG Electrodes

There are several methods for recording from individual neurons within the brain which are useful for a practical BCI, which translates brain signals into messages and commands to the external world. These methods used in BCI systems include EEG, ECoG, MEG, PET, fMRI, fNIR and SEEG, among which most commonly used are the EEG and ECoG.

The main difference between EEG and ECoG is that the electrodes are placed on the scalp for recording brain signals in EEG, whereas in ECoG the electrodes are placed directly on the brain surface. Advances in ECoG has allowed to place the electrode arrays closer to neurons for better spatial and temporal resolution. With the use of micromachining, contemporary ECoG

electrodes are highly flexible with a higher electrode density and has the feasibility to surgically place the electrodes on the cortical surface. This technology has enabled advanced investigations in patients with epilepsy and similar diseases, has demonstrated a feasibility to facilitate interactions with external devices, and has allowed to obtain larger maps of LFPs [23-28].

Although these valuable advances have improved many applications, ECoG, along with all other methods, comes with its own particular set of trade-offs. Even though the safety of ECoG has been improved, the surgical process of implanting the electrodes still runs a risk of harming the subject during and after the procedure. The only disadvantage of the current micromachined ECoG electrodes are its high cost and invasiveness. Furthermore, this technology requires MEMS fabrication techniques which grant it similar difficulties and expenses found in fabricating microdevices. Micromachining electrode arrays in case by case basis in order to control the trade-off characteristics and obtain certain capabilities for experiments having specific requirements makes the technique delicate and expensive for clinical applications.

1.3 Motivation

Over the past few years, the potential generated by the activity inside the cortex is measured using platinum or gold electrode arrays on the brain surface using micromachining techniques that result in a difficult and lengthy process which makes the device expensive. At the same time, the mapping of those traditional electrodes cannot be changed once these devices are fabricated.

The standard ECoG technique has grown to be weakly invasive and vastly applicable to a majority of BCI applications. For these reasons, I would like to propose a handcrafted microdevice that will prove to be an easier and faster fabrication process of obtaining an ECoG electrode array that will allow users the freedom to design for themselves basic unique

configurations of the electrode array with commercially available materials for various applications. The ECoG electrode developed with this process will be handcrafted, robust, and have similar spatial and temporal resolution as other modern ECoG electrodes [29]. This microdevice is entirely handcrafted using commercially available microwire and biocompatible PDMS, which is the most convenient part of this device. The amount of time and money devoted to fabricate this 32-channel ECoG electrode is significantly less than any other device reported in this field. We did not use MEMS technique for the microfabrication and we can change the design of the array of electrodes as per necessity. Furthermore, this ECoG device is flexible, adjustable and also reliable.

The quality of the electrode will be presented through the results obtained from the motor and somatosensory cortex activity of *Lewis* rats, located in the left hemisphere of the forebrain, while on a treadmill to demonstrate that the handcrafted electrode does provide a reliable performance as seen in other ECoG electrodes. In Figure 1.1, anatomical parts of the forebrain of rat is shown where we implant the ECoG device on the surface of cerebral neocortex.

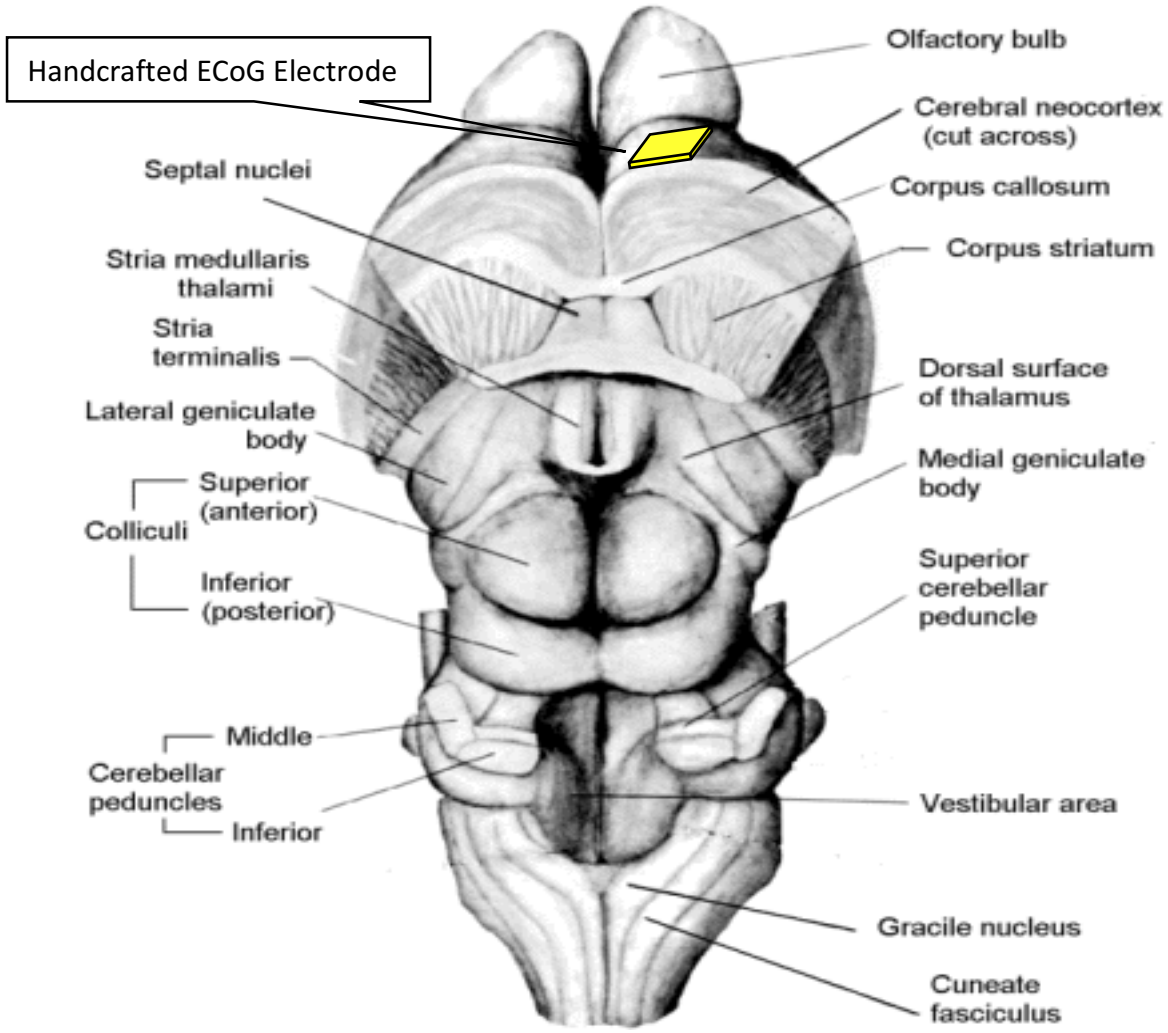

Figure 1.1: Anatomical Parts of the Forebrain of rat [30]

CHAPTER II

RELATED WORKS

The research in this thesis aims at building a low cost handcrafted micro-ECoG electrode and confirm the reliability of the device with an animal model by studying the potentials measured from its surface and comparing them to other successful micromachined ECoG electrodes. The ion pumps and ion channels create the voltages we measure at electrodes directly outside the skull (EEG) and also in our electrocorticographic (ECoG) recordings, where the electrodes are placed immediately on top of the cortex. ECoG refers to recordings that have electrodes placed either above or below the dura mater covering the brain. Cross- and auto-correlations between these electrode voltages reveal spatial and temporal correlations between neuronal activity, and from them, we can infer properties of neural computation at the population scale. Recordings are made while subjects are performing a task and the recordings are then analyzed. There are several different recording modalities that can potentially be used for providing the neural signals used in a motor BCI. One of these recording modalities is electrocorticography that has shown growing promise in the field as an intermediate solution between the two extremes of recording single unit activity and EEG. Although the signals are not as direct of representation of the underlying neural code that can be observed at the single neuron level, the surgical procedure to implant ECoG electrodes is less invasive with a lower chance of cortical tissue damage or infection. Compared to EEG, ECoG provides better spatial and spectral resolution.

It is common for many researchers in neuroscience to use microdevices developed by companies or other researchers, mainly, because of the time and expenses that come with fabricating one of their own. When fabricating non-invasive micro-ECoG electrodes, micromachining techniques are utilized to form them into various structures, sizes, and from different materials. A classic example can be demonstrated by a group of Amelia A. Schendela in 2013 who were focused on studying the tissue response in vivo when a micro-ECoG array is implanted [31]. The device used was based on a design by Thongpang et al. in 2011 where the objective of the project was to design a micro-ECoG made up of flexible film electrodes to keep pressure to the brain at a minimum and have radial subcranial placements of multiple electrodes from a single craniotomy [32]. While a more detailed and a couple other types of electrodes can be found in [32], Amelia A. Schendela et al. describes a brief fabrication process for an ECoG electrode to be implanted on a rat. A layer of Parylene C was deposited onto a silicon wafer in a vacuum deposition system. Photolithography was then used to define the electrode sites and traces on the Parylene layer. Next, gold and platinum were deposited onto the wafer in a metal evaporation system for the conductive layer. Another layer of Parylene was used as an insulator and reactive ion etching was used to form the outline of the device, open holes through the substrate, and uncover the electrode sites. Lastly, the device was removed from the silicon surface and connected to a PCB connector. In comparison to the handcrafted device, there was no need of a silicon wafer that is usually sold in large groups and must provide specific characteristics when ordered which were not significant for the fabrication of the micromachined device. Also, different metals and deposition systems were not used because the inexpensive microwires are good conductors and were easily placed to form the handcrafted device. No additional layer for insulation or etching was required because the microwires were already

insulated and any specific physical features of the handcrafted device can be formed or cut from the PDMS material. Finally, the handcrafted device did not require any additional steps to clean or remove any unwanted metal or residue during the fabrication process.

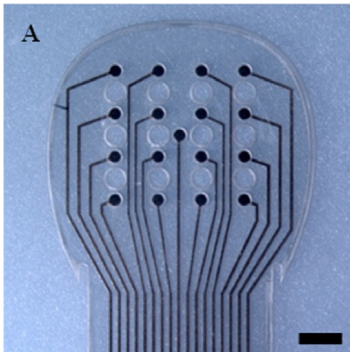

Figure 2.1: The micro-ECoG device consisted of a Parylene C substrate with 16 electrode sites. Scale bar represents 750 μm [31]

Another example is provided by Birthe Rubehn, Conrado Bosman, Robert Oostenveld, Pascal Fries and Thomas Stieglitz who developed a higher density flexible ECoG electrode array to record from a large area of the cortex [33]. Their array utilized a wafer that was spin coated with polyimide and placed on a hotplate to remove any solvents. After the polyimide was cured under a nitrogen atmosphere, hexamethyldisiloxane (HMDS) was used to bond with a photoresist that was structured with photolithography. The wafer was then etched to improve the adhesion of a metal layer to the polyimide. Platinum was sputtered onto the wafer and acetone was used to remove the unwanted platinum that landed on the photoresist only leaving the platinum on the polyimide surface for form the electrode sites and conductive paths. Then, a second layer of polyimide was spin coated and cured. Photoresist and photolithography were performed again in order to etch open the electrode and solder pad sites in addition to defining the array perimeter. After the remaining photoresist was removed with acetone the device was

removed from the wafer. The fabrication of the handcrafted ECoG electrode did not require the need for a cleanroom and, as mentioned before, no wafer was utilized. In addition, polyimide, HMDS, or photoresist were not spin coated which would mean additional expenses would take place if one did not have these chemicals and the necessary equipment to apply them. Furthermore, photolithography, etching, sputtering, and the training to perform these processes were avoided, along with the need to remove any material which does not guarantee to be completely effective. The handcrafted device made use of commercially available materials and a process that required common and inexpensive equipment. It also allows constructing the ECoG electrode into different sizes and densities. It significantly reduces the cost and time it takes to fabricate a micro-ECoG electrode without the need of a cleanroom to perform micromachining techniques.

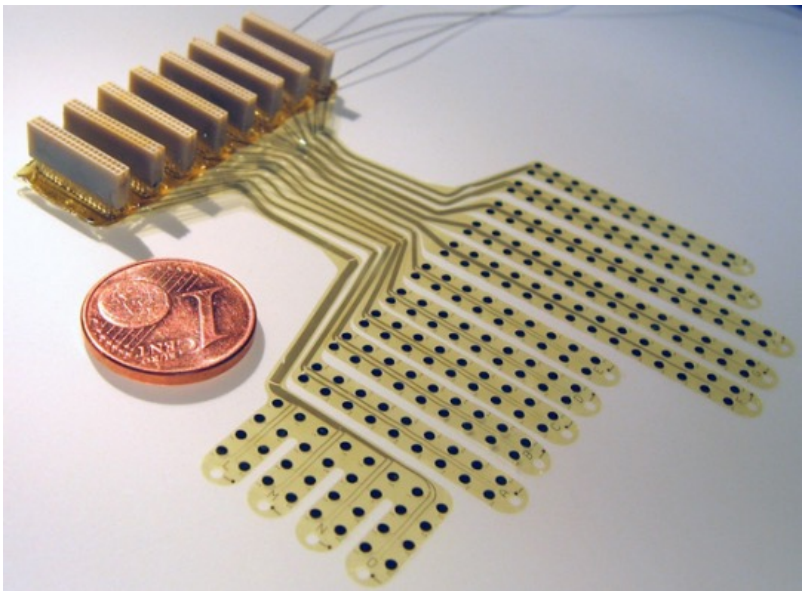

Figure 2.2: Fully assembled 252-electrode array. The diameter of the coin is 16 mm [33]

An alternative, but more invasive, type of electrodes is the penetrating ECoG electrode arrays. A typical example of such device is the Utah Electrode Array (UEA) or a

similar design known as the Utah Slanted Electrode Array (USEA) which are shown in Figure 2.3. Most UEA type of arrays contain about 100 electrodes with needles around 1.5 mm long. To achieve these kinds of specifications, penetrating electrodes go through a micro-manufacturing process consisting of basic micromachining techniques to create the necessary patterns and depositing materials that will allow the electrodes to be electrically isolated from each other [34]. These electrode arrays have been implemented in BCI systems for its ability to provide high temporal and spatial resolution and capture both action potentials and local field potentials by allowing microelectrodes to be placed close to small groups of neurons [16]. However, these electrode arrays have also proven to be impractical in some cases due to its lack of reliability and invasive procedure. Furthermore, insufficient understanding of the reaction during long term integration on a nerve causing electrodes recording single-unit to decline over time have also impeded this type of device to reach widespread clinical use [35].

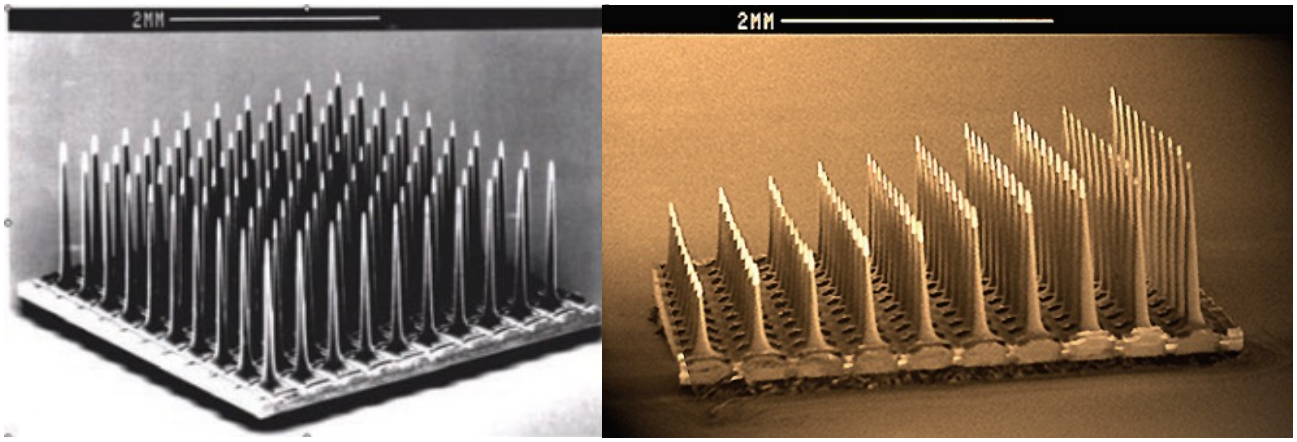

Figure 2.3: Scanning micrograph of the UEA (Left) and USEA (Right) [34]

Focusing on the type of results obtained from these kind of devices, in the past few

years, numerous groups presented precision-engineered or MEMS-based ECoG electrode arrays. To obtain an objective measure of the recording quality of our ECoG device, we performed a comparison with two other reported research [32, 37]. Much like the purpose of the handcrafted device, both their research also consisted of making an ECoG electrode for recording brain signal. They also performed their experiments on animals like monkeys and rats and recorded electrical signals from the brain. Referring back to the work done by Birthe Rubehn, Conrado Bosman, Robert Oostenveld, Pascal Fries and Thomas Stieglitz in 2009 which was then published in Journal of Neural Engineering [32]. These researchers fabricated a micromachined 252 channel ECoG electrode array, which is made of a thin polyimide foil substrate enclosing sputtered platinum electrode sites and conductor paths and implanted that on a macaque monkey's cortex. Figure 2.4 shows an example of LFP activity observed from 12 out of the 252 channels distributed over the cortex. The electrical brain signals from 12 electrodes lying on different cortex areas showed normal ECoG characteristics with a peak to peak amplitude of 80 µV.

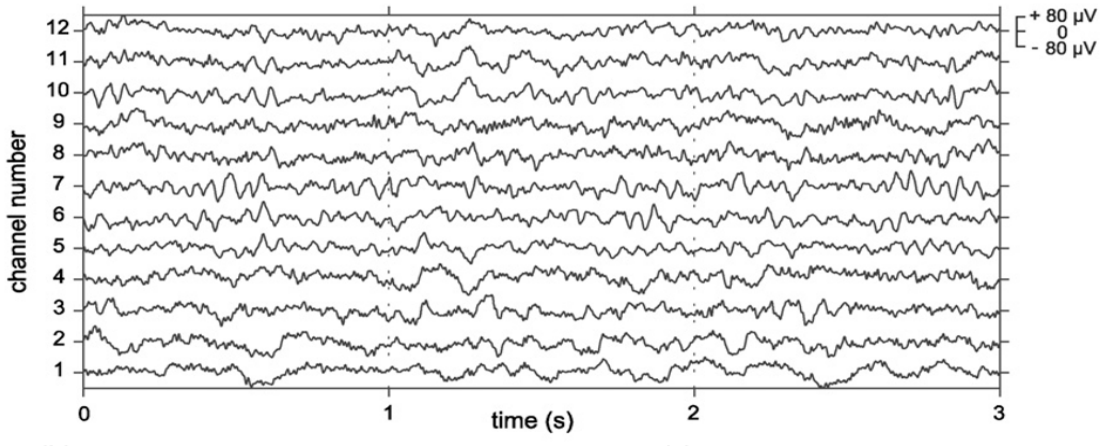

Figure 2.4: LFP activity observed from 12 channels [36]

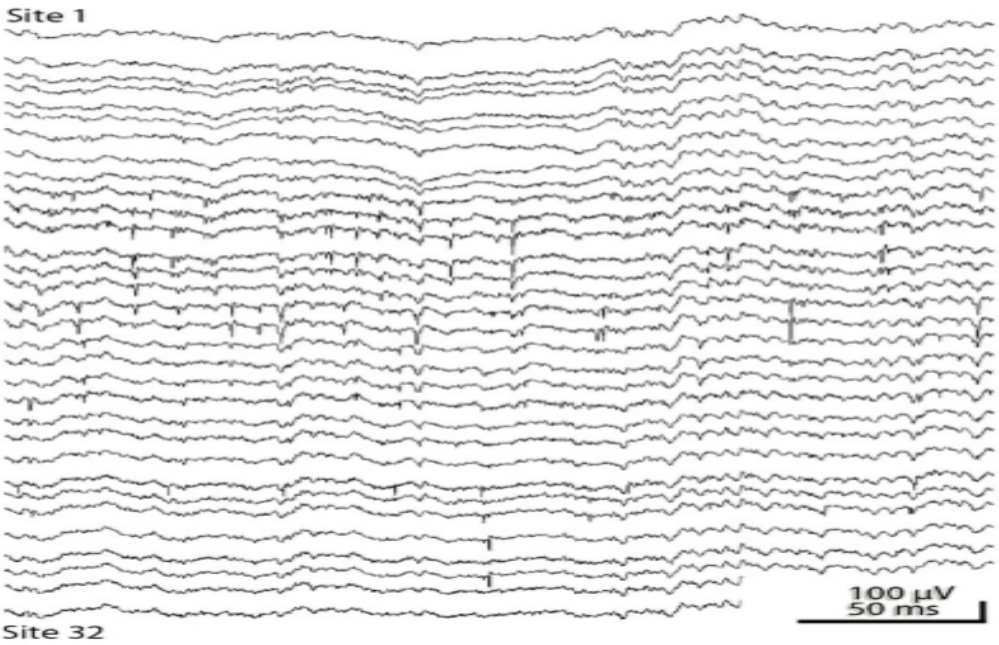

Figure 2.5: LFP activity observed from 32 channels [37]

A second research paper showing similar type of results is done by Antal Berényi, Zoltán Somogyvári, Anett J. Nagy, Lisa Roux, John D. Long, Shigeyoshi Fujisawa, Eran Stark, Anthony Leonardo, Timothy D. Harris, and György Buzsák in 2013 and was published in Neurophysiol journal titled as "Large-scale, high-density (up to 512 channels) recording of local circuits in behaving animals" describing a system that allows high-channel-count recordings using a signal multiplexing headstage that permits free behavior of small rodents [37]. They monitored single-unit and LFP activity patterns of neighboring neocortical regions. They designed an 8-shank probe with 32 recording sites on each shank. Figure 2.5 shows recorded neural signals from 32 channels of a single shank in the somatosensory cortex with a peak to peak amplitude of 100 µV. Comparing to this device, our device is more economical, simple, and achieved a better or similar signal from the cortical surface of rats as can be seen from our results

in Chapter V. Table 2.1 below shows a comparison summary between the handcrafted device and micromachined electrodes. This table provides an idea of the capabilities seen from different types of electrodes that are closely similar to commercial ECoG electrodes and compare with the handcrafted device. It can be effortlessly observed that a micro-ECoG can have a high electrode density but the average signal amplitude obtained from the electrodes reaches a limit at around 100 μV regardless of the dimensions, while the handcrafted ECoG can reach twice the amplitude.

Table 2.1: Comparing the handcrafted micro-ECoG electrodes with other electrodes

	Multichannel micro-ECoG	Utah Electrode Array	Custom micro-ECoG	Handcrafted Device
Number of electrodes	252	100	16	32
Dimensions (mm^2)	35 x 60	~ 4 x 4	~ 4.5 x 4.5	5 x 5
Signal Amplitude (μV)	Up to 80	30 – 100	Up to 100	Up to 200

CHAPTER III

SURGICAL PROCEDURE & ANIMAL MODEL

Using animal models to perform experiments have helped achieved scientific breakthroughs without the risk of human casualties. Animal models, such as rodents, have become a common test subject for experiments because of our understanding of their anatomy, shared similarities with the human race, and other characteristics that make them easy to work with. Throughout the course of numerous animal experiments, animal ethical committees of universities and research facilities have established common standard protocols.

Following these protocols have allowed to confidently proceed with our experiments without any ethical concerns and will allow others to easily build upon or make comparisons with other research. The basic surgical procedure used in the experiments for all test subjects avoids any complications with common protocols. The importance of applying the same procedure to each test subject minimizes the aspects of the experiments that would need an in-depth investigation if an unexplainable characteristic presents itself in the data. In addition, since the studies would take place *in vivo,* the level of care to the animal model is equally important to prevent situations that could result in compromising the experiment and, thus, a loss in resources available.

For these reasons, the procedures followed to implant the device onto the test subjects were reviewed and approved by the Institutional Animal Care and Use Committee UTRGV. In

Chapter 3.1 the necessity of animal model is explained and chapter 3.2 describes the implantation of the ECoG device by the surgical procedure.

3.1 Animal Model

Although human and non-human animals look different, at a physiological and anatomical level they are remarkably similar. Animals, from mice to monkeys, have the same organs (heart, lungs, brain etc.) and organ systems (respiratory, cardiovascular, nervous systems etc.) which perform the same functions in pretty much the same way. Nearly 90% of the veterinary medicines that are used to treat animals are the same as, or very similar to, those developed to treat human patients [31].

If we want to study a human disease, we cannot perform the initial experiments on humans, rather we have to develop an animal model. Sometimes the model may be *in vitro*, but we must eventually test ideas *in vivo*-in living animals. Animal models allow a closer approximation to a human response. From formulating new cancer drugs to testing dietary supplements, mice and rats play a critical role in developing new medical wonders. In fact, 95% of all lab animals are mice and rats, according to the Foundation for Biomedical Research (FBR) [32]. Scientists and researchers rely on mice and rats for several reasons. One is convenience: rodents are small, easily housed and maintained, and adapt well to new surroundings. They also reproduce quickly and have a short lifespan of two to three years, so several generations of mice can be observed in a relatively short period of time. Mice and rats are also relatively inexpensive and can be bought in large quantities from commercial producers that breed rodents specifically for research. The rodents are also generally mild-tempered and docile, making them easy for researchers to handle. Most of the mice and rats used in biomedical research are inbred so that, other than sex

differences, they are almost identical genetically. This helps make the results of researches more uniform, according to the National Human Genome Research Institute. As a minimum requirement, mice used in experiments must be of the same purebred species. Another reason rodents are used as models in medical experiments is that their genetic, biological and behavior characteristics closely resemble those of humans, and many symptoms of human conditions can be replicated in mice and rats.

Rodents also make efficient research animals because their anatomy, physiology, and genetics are well understood by researchers, making it easier to tell what changes in the mice's behaviors or characteristics are caused by. Some examples of human disorders and diseases for which mice and rats are used as models include: Hypertension, Diabetes, Cataracts, Obesity, Seizures, Respiratory problems, Deafness, Parkinson's disease, Alzheimer's disease, Cancer, Cystic fibrosis, HIV and AIDs, Heart disease, Muscular dystrophy, Spinal cord injuries etc. Mice are also used in behavioral, sensory, aging, nutrition and genetic studies, as well as testing anti-craving medications that could potentially end drug addiction.

3.2 Implantation of ECoG Device

Surgical procedures were performed under aseptic conditions at the UTRGV Animal Facility. A *Lewis* rat underwent implantation surgery in aseptic conditions at the UTRGV Animal Facility. Prior to implantation, the rat was placed into an induction chamber and Isoflurane (5.0%) was used to induce anaesthesia followed by maintenance of anaesthesia (1.0-2.0%) in oxygen until unconscious. The surgery location (the top of the rat’s head from between the eyes to behind the ears) was shaved and cleaned using a betadine scrub and isopropyl alcohol using electric barber’s clippers [36]. Its maxillary central incisors were hooked into a gas mask

through which it continued to receive small doses of anaesthesia [37]. Then the rat was mounted in stereotaxic ear bars. It was secured to a surgery table and its body temperature was regulated with a hot pad. On top of the head, two half circles from the midline outwards were cut partially removing the scalp. The bone surface was disinfected and cleaned using hydrogen peroxide. The bone was dried to make the cranial sutures more clearly visible. Screw holes were drilled into the bone and stainless still screw electrode was placed epidurally on the brain's left hemisphere. For the 5 x 5 mm^2 device, a 6 x 6 mm craniotomy must be made [38]. Before drilling the craniotomy, UV-curable dental acrylic was applied to the periphery of the craniotomy site while it was still dry and not in danger of touching the dura or pia. The dura was kept well hydrated with artificial CSF or Saline.

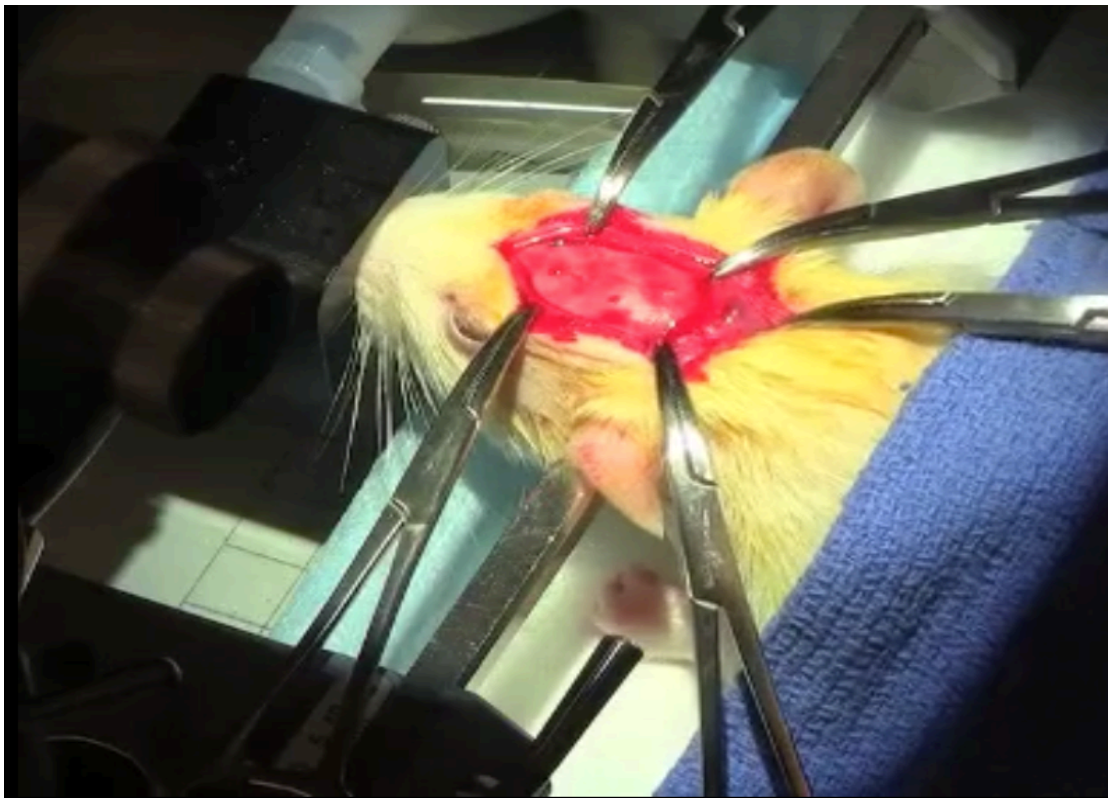

Figure 3.1: Removing the scalp

To implant the ECoG device, a stereotaxic arm was placed over the open skull, and the electrode was secured to the arm using sterile tape making sure that the electrode sites were facing downward and making contact with the dura surface. The ground wire was connected to the ground screw by wrapping around at least three times over and under itself. Small pieces of saline soaked Gelfoam was placed surrounding the electrode where there was dura or pia exposed. A small amount of saline soaked Gelfoam was placed to cover the top of the thin film electrode. UV-curable dental acrylic was applied to the top of the Gelfoam and was used to create a stable head cap. The acrylic was applied directly to the thin film cable covering it until the connector is reached. After the dental acrylic was completely hardened, the skin was sutured tightly around the head-cap and the animal was removed from the stereotaxic frame.

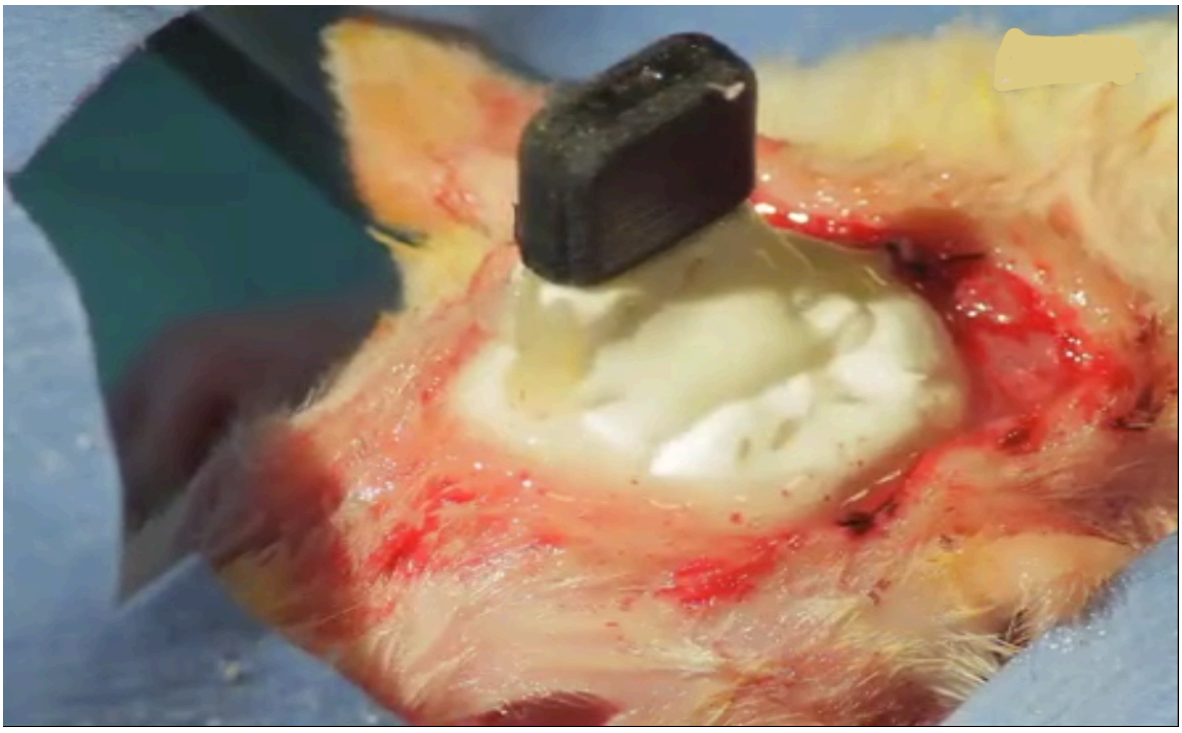

Figure 3.2: Implementation of the ECoG device and UV-curable dental acrylic was applied to create the stable head cap

Antibiotic ointment was applied copiously around the wound. Some antibiotic was placed into the ear canal for the bleeding from the ears. The same procedure was followed to implant an ECoG electrode on three additional rats. We proposed a handcrafted ECoG device as shown in Figure 3.2 to collect the brain signals. All surgical procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (National Academy Press, Washington, DC, 1996) and were reviewed and approved by the Institutional Animal Care and Use Committee UTRGV.

CHAPTER IV

PROPOSED HANDCRAFTED MICRODEVICE

The goal of this thesis is to develop a handcrafted 32-channel ECoG electrode which has the advantages of design customization, flexibility, and minimal invasiveness. ECoG electrodes that are implanted on the cortical surface in rodents at high spatial resolution requires dozens to hundreds of electrodes and must be kept to a small size forcing these devices to be fabricated using micromachining techniques. As a result, obtaining neural signals from freely behaving animals is challenging and expensive which presents a limit in the number of animals that can be simultaneously recorded. To overcome this limitation, we have designed a low-cost and handcrafted microdevice.

When developing a microdevice, there is a significant amount of effort put into reducing the necessary steps in a fabrication process which could in turn make the microdevice a more preferable choice for applications. Processes that require micromachining techniques are commonly accompanied by equipment that may not be accessible to many researchers. The equipment for such techniques are usually expensive and require to be placed in a cleanroom in order to achieve reliable results. Furthermore, use of micromachining equipment can be time consuming due to the training required to operate the equipment and time needed to complete a task. However, this is not the case for the device presented below.

The handcrafted device makes use of commercially available low-cost materials and a few common micromachining equipment making it attainable to a broader range of researchers. The flexible and adjustable design enables it to be directly implanted chronically on the brain surface of rodents. In Chapter 4.1, a microfabrication process is described for making a PDMS thin film and chapter 4.2 describes the fabrication process of the proposed handcrafted ECoG electrode.

4.1 Microfabrication

Microfabrication process used to fabricate the ECoG device is a process for making miniature structures of micrometer scales and smaller. This is actually a collection of technologies which are utilized in making microdevices such as MEMS, micromachines, microfluidics, and their subfields. These fields use microfabrication methods which are giving rise to multidisciplinary research. The major concepts and principles of microfabrication are microlithography, doping, thin films, etching, bonding, and polishing. These processes must be performed, one after the other, many times repeatedly. Microfabricated devices are usually made on silicon wafers even though glass, plastics, and many other substrates are in use. The PDMS structure used for this ECoG device was fabricated at J.J. Pickle Research Campus (The University of Texas at Austin). Polydimethylsiloxane (PDMS), the preferred material, is a highly structural, surface biocompatible, inexpensive, and flexible medium for microfluidic device fabrication like bioassays which has been used in a number of successful implants such as cochlear implants and pacemakers.

In order to produce the extremely precise PDMS structures (40 μm microchannel), a master structure mold is first needed to be fabricated using the photolithographic procedure. A

three-inch diameter silicon wafer was first sprayed with isopropyl alcohol, dried with a nitrogen gun, and placed on a hotplate to prepare and clean the surface prior to the application of the photoresist and placed in the spinning machine. Two-thirds of the wafer was covered by the SU-8 2035 photoresist. The wafer was then spin-coated 3250 rpm for 30 seconds. The sample was then placed on a level hotplate at 95º C for 6 minutes. A mask pattern was placed on a four-inch glass plate coated with chromium and AZ1518 photoresist, placed on the MJB4 Suss Microtec® mask aligner, and then exposed to UV light. After exposure, the sample was placed in a 400K developer solution for two and a half minutes, rinsed in deionized water and dried with a nitrogen gun. The sample was then placed in a chromium etchant for three minutes, rinsed with deionized water and dried with a nitrogen gun. Lastly, the sample was washed with acetone and rinsed with deionized water to remove remaining AZ1518 photoresist and form the chrome mask. The SU-8 covered silicon wafer was placed on the mask aligner with the chromium glass mask on top of it, aligned and then exposed to UV light with a light intensity of 160 mJ/cm^2. Immediately after exposure, the silicon wafer was placed on the hotplate at 95º C for 5 minutes and removed to cool. The post exposure bake solidifies the photoresist to a permanent structure. The sample was then placed in the SU-8 developer for 5 minutes to remove the unexposed portion of the photoresist. At this point, the master structure mold is complete, and the microchannel pattern can be seen. Master structure was covered by the 10:1 PDMS mixture (Sylgard® 184, Dow Corning®, MI) then spin-coated for 3000 rpm for 30 seconds. This was then cured in an oven for 30 minutes at 95º C, removed and allowed to cool. The structure was then submerged in a chloroform solution, within which the PDMS solution expanded and detached from the SU-8 master structure. The PDMS layer was then submerged in an isopropyl

alcohol solution until it retracted to its original size and simultaneously removed any chloroform remaining on it, removed from the solution, and allowed to air dry.

4.2 Fabrication of ECoG Electrode

To make the handcrafted ECoG electrode, commercially available green wire of 75 µm in diameter was used as probes (Stablohm 800A, California fine wire, Grover Beach, CA). For the preparation of the microwire, the green wire was cut segments of 15 mm in length. The length of the microwire was determined after several trials of performing the surgery and implementing on the rat's cortical surface. A longer or shorter length of microwires would present a risk of

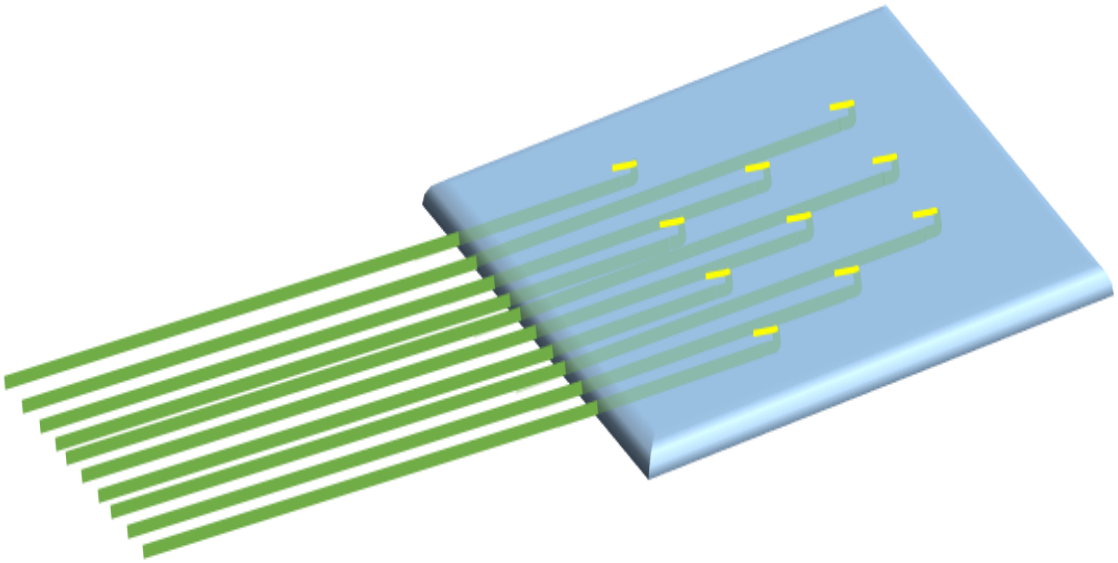

Figure 4.1: A schematic view of fabricated ECoG electrode

compromising the experiment either by the animal or a level of difficulty during surgery. With the use of a ruler, 1 mm of insulation was peeled off at one end of each wire. A comparison of a green wire with a human hair is presented in Figure 4.2 (a), in which the microwire is

uninsulated 1 mm in length. Then the uninsulated part of each wire was bent at an angle 90^0 with the help of tweezers under the microscope resulting in Figure 4.2 (b). Having the uninsulated portion of the microwires bent will become useful when it is time to insert them into the PDMS layer that was fabricated in section 4.1 of this Chapter. After all 32 wires were prepared, a paraffin wax film (Parafilm M laboratory film, Bemis Corporate, Neenah, WI) was folded to make 6 layers with an area 50 x 50 mm^2 (Figure 4.2(c)). An area of 3 x 3 mm^2 was marked on top of the wax film which was used to guide the placement of the wires into a square shape. Although the area marked in this step is dependent on the area of the PDMS film, the PDMS film is only limited by the design of the device. In this case, an area of 3 x 3 mm^2 is utilized to present a small section that can be built upon to construct an ECoG electrode of higher density.

The marked area was then covered with a thin PDMS layer within an area of 5 x 5 mm^2 on the wax film (Figure 4.2 (d)). The PDMS layer is the structure described in Chapter 3.1. Although the PDSM structure was fabricated at a different lab for time saving purposes, the structure could have also been fabricated in the same lab as the process described in this section. Instead of a wafer that is commonly used for micromachined device, the wax film was used as a supporting platform to easily separate a fabricated ECoG at the final stage because it is not adhesive to the PDMS layer. The wires were then placed row by row on the thin PDMS film by inserting the bended sides of the wire within the marked area using tweezers, making them parallel and kept apart at equal distances as demonstrated in Figure 4.3 (a, b).

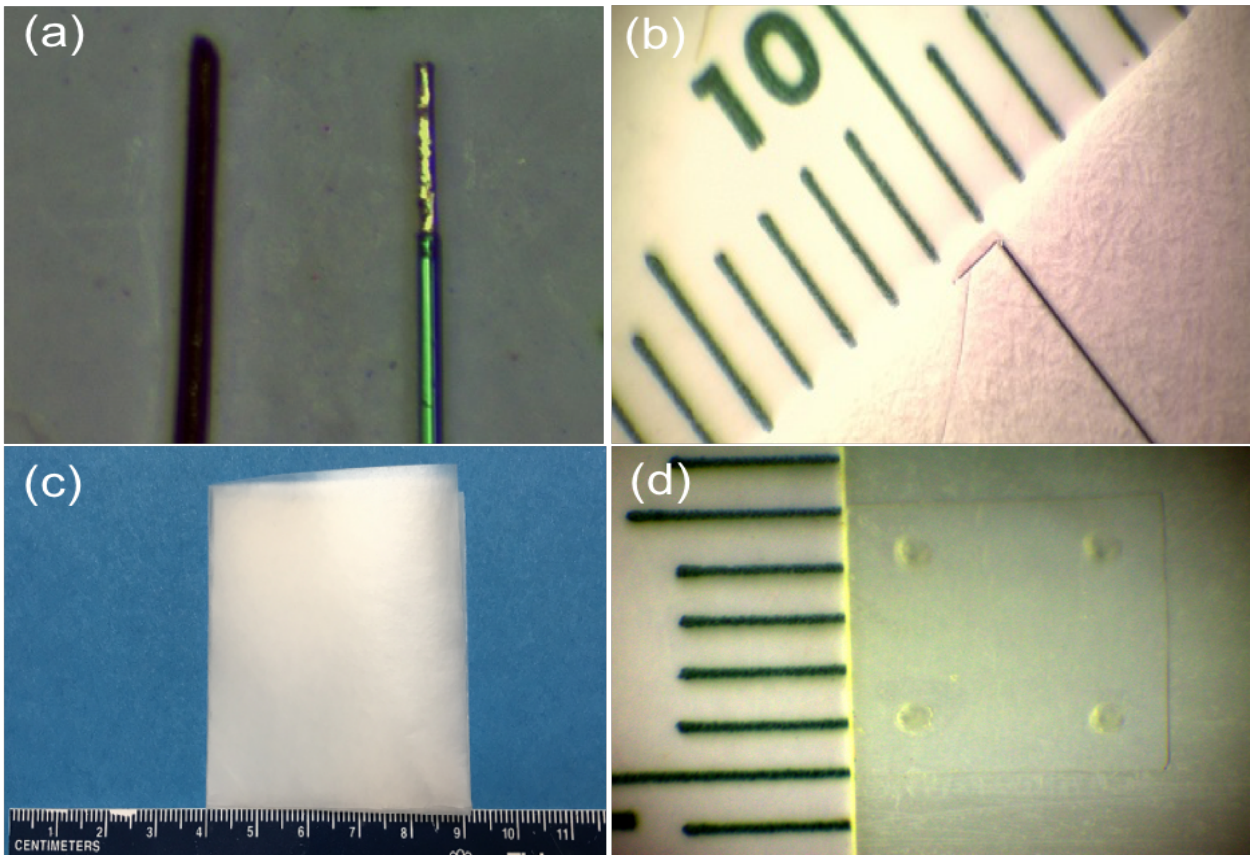

Figure 4.2: (a) Comparing the microwire with human hair. (b) Single wire specification with 90 degree bent. (c) 6 layer parafilm. (d) (5x5) mm^2 area marked on the wax film and the thin PDMS film on the top.

Once all 32 wires were inserted into the wax film, the remaining parts of the wires were arranged using a tape. The tape was placed on the wax film, as shown in Figure 4.3 (c), where strips of tape were used to keep the microwires in place by placing the tape strips in such as way that the adhesive side of the tape does not come in contact with the microwires. Then the 186 Sylgard base (Dow Corning Corporation, Midland, MI) and curing agent were mixed at a ratio of 10:1 and kept in a vacuum chamber for 20 minutes until all visible bubbles had disappeared. After this, it was then checked under a microscope for any remaining bubbles which were removed with the use of a needle. This step can be repeated if excessive bubbles are still present.

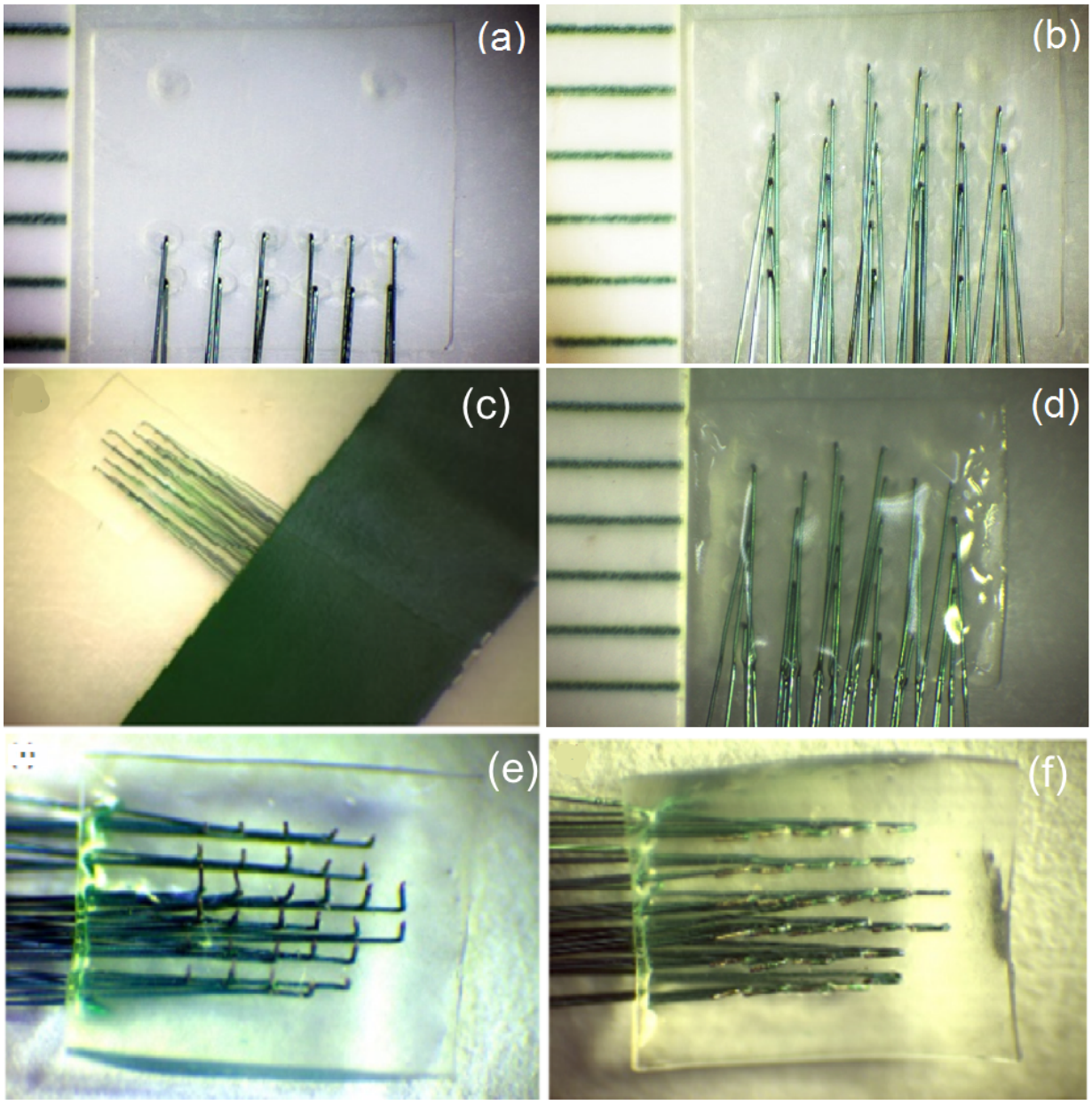

Figure 4.3: (a) Placement of the 12 wires in two rows on the wax film through the PDMS film. (b) Placement of all the 32 wires in two rows on the wax film. (c) A tape covered the wire area to keep it down to the wax film. (d) Solidified PDMS on top of the green wires after removing from the oven. (e) View of the device after the wax film is removed. (f) After the wires are cut and bent all the way down.

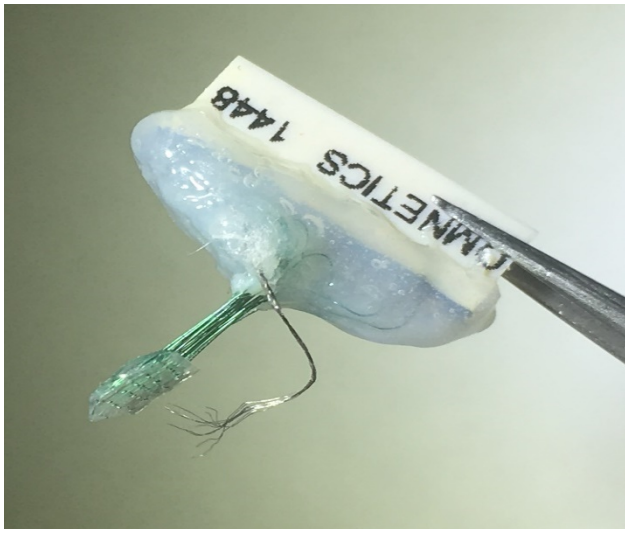

Figure 4.4: The finished ECoG devices soldered on an omnetics connector

Liquid PDMS was applied in small amounts over the wires that had been inserted into the wax film. Then the device was placed in the oven for 30 minutes at 50° C to reduce the time for the liquid PDMS to solidify, resulting in Figure 4.3 (d). This low temperature was requried to keep the wax film stable. The tape was then removed and the wax film was separated from the device. Figure 4.3 (e) shows the bottom view of the device after removing the wax film. Then the tip part of wires were further bent with tweezers until they laid along the PDMS film as shown in Figure 4.3 (f) to prevent the microwires from poking into the brain surface and potentially causing damage. The next step was to solder the other ends of the wires with the 32 pin Omnetics connector (Nano Strip Connector, A79022-001, Omnetics, MN) where the columns at each end of the connector were used as a connection to the ground or reference and the remaining 32 pins were soldered with the 32 microwires. After soldering was done, epoxy glue was applied on the pins and through the wires that had been connected to the soldering pins. The glue was then applied in between the pin gaps and filled up all the empty spaces. With this step,

the epoxy glue will serve as an insulation for each wire and a physical support between the connector and wires making it more robust. In addition, it is important to note that the device is not limited to the Omnetics connector but can be implmented using any applicable connector. Figure 4.1 shows a schematic view of the stage of Figure 4.3 (f) for a better understanding of the structure and Figure 4.4 shows the final deivce which is ready for implantation.

CHAPTER V

RESULTS

This paper discusses the fabrication of a 32-channel handcrafted ECoG electrode which was then implanted on a subject to retrieve brain signals. Now, the device is to be connected to an electrophysiological signal acquisition system to analyze the signals obtained from three test subjects. Through the acquisition system, it is observed that the ECoG electrode was able to retrieve signals that are similar to reported data obtained by various researchers who have applied different kinds of ECoG electrodes.

However, before the devices were implanted and the acquisition system was set up, the device was designed to have several pins on the connector to serve as noise cancellation. To minimize the level of noise in the signals, a notch filter and a channel acted as a digital reference on each device. It was observed that the results from each test subject shared similarities in the kind of waveforms and amplitude range signifying that a reasonable yield of the crafted devices can be attainable. It is common for a micro-ECoG to be able to read signals as high as 100 μV, therefore, it was exciting to see the handcrafted devices were obtaining signals twice the amplitude of most ECoG electrodes.

The fact that a handcrafted device can have a comparable performance to micromachined devices shows the potential that this device can have on numerous applications.

Chapter 5.1 will be discussing the experimental ECoG acquisition setup and Chapter 5.2 will be explaining and analyzing recorded brain signals.

5.1 Experimental ECoG Acquisition Setup

We were able to customize signals by linking components to create custom processing circuits using TDT 32-channel electrophysiological signal acquisition system (Tucker-Davis Technologies, Alachua, FL). In order to remove noise from the signals, we first used notch filter for removing 60 Hz and similar interferences from the waveforms and re-referenced them to one of the 32 channels. Next, we band-pass filtered the signal between 300 Hz and 7000 Hz.

This signal processing technique greatly improved the quality of ECoG signal analyses. Figure 5.1 shows the configuration of the system from the animal on a treadmill to the workstation computer to monitor and analyze the electrophysiological signals. Recorded signals were amplified and digitized in PZ5 and then transmitted to the RZ5 BioAmp Processor for further processing via an isolated, noiseless fiber optic connection. The optical interface ensured fast and reliable data transfer from the PZ5 to RZ5 and to a workstation computer.

Synapse software auto-detects the TDT hardware and uses that information to streamline the experiment design. The streamlined interface can be used to adjust experiment-specific hardware choices, such as the number of recording channels, operational modes, and input sources. As we make selections, Synapse updates the design time window with relevant choices to complete the configuration for basic neurophysiology bundles; including high-channel LFP, ECoG, and EEG recordings ranging from 0 μV to over 200 μV. Using the Synapse API, custom applications can be developed in MATLAB or Python to dynamically control timing, triggering, data storage, as well as visualize data at runtime.

Figure 5.1: The acquisition system setting. One end of a TDT zif-clip digital headstage is connected to a headstage adapter on top of the rat's head and the other end is connected to PZ5 amplifier to boost and digitize the signals

5.2 Recording Brain Signals

By using TDT 32-channel acquisition system and Synapse software, we were able to record brain signals from 32-channel ECoG electrodes. Two of these channels are shown below in Figure 5.2. The unit of y-axis was 100 μV and peak to peak amplitudes were shown around 200 μV. This plot showed 3 second period signal patterns which demonstrated the traditional local field potential patterns.

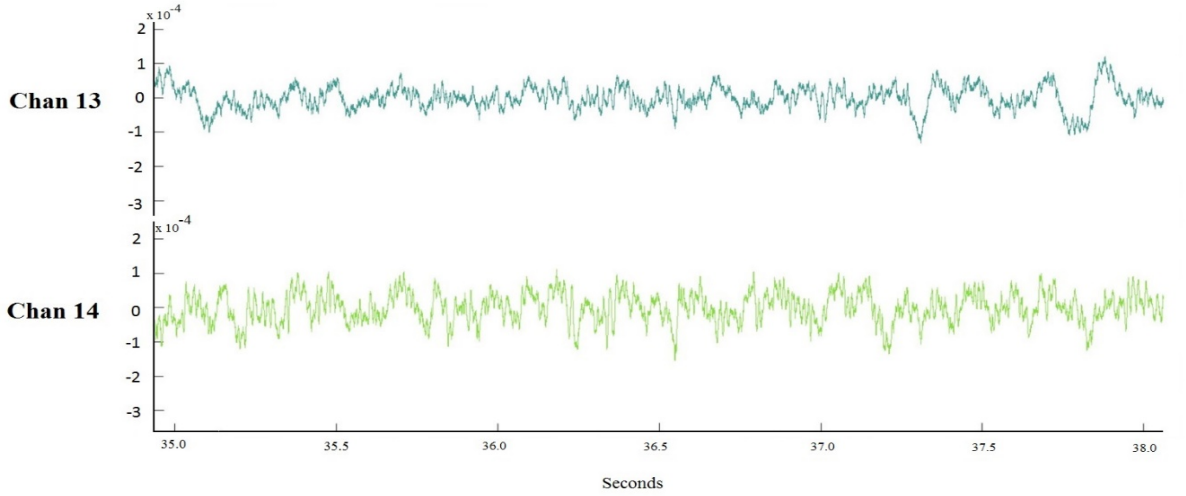

Figure 5.2: A detailed view of the recorded signals. Peak to peak amplitudes are around 200 µV. This plot shows 3 second period signal patterns which demonstrated the traditional local field potential patterns.

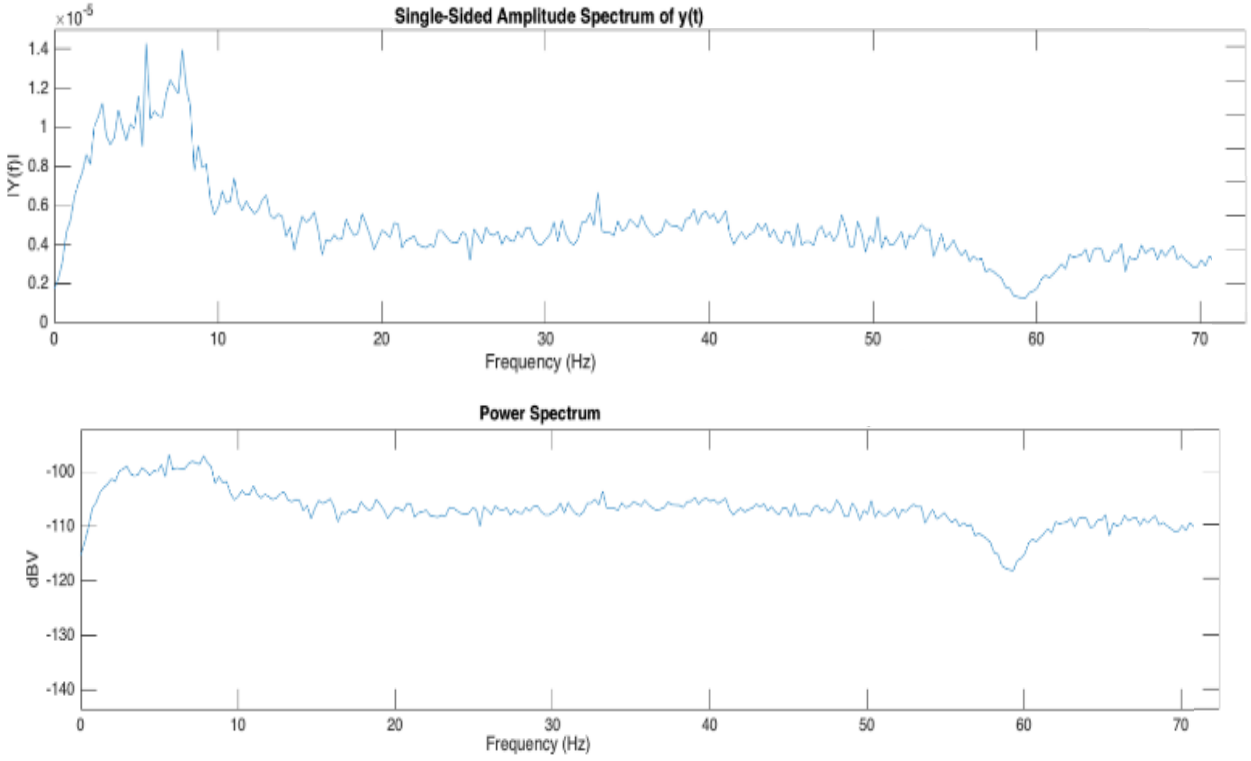

Figure 5.3: (Top) Single-sided voltage amplitude in the frequency spectrum (Bottom) Relative power of the LFP frequency spectra.

Using Synapse, TDT's graphical design software, we could control the signal presentation and data acquisition, customize the function of each signal-processing module, and control timing, triggering, and data storage. Synapse communicated directly with TDT hardware for fast, precisely timed operations. When an experiment is fully configured and saved, the data can be displayed in either preview or record mode. In Preview mode, we adjust plots and change the sorting parameters and runtime settings without any of the data being permanently stored in the data tank. For the plots in Figure 5.3, a notch filter to remove 60 Hz noise was used during the recording which showed as a deep dent at 60 Hz in the frequency spectrum. We obtained the LFP signals for all neural signals from 31 electrodes of the ECoG. One out of 32 channels (Channel 2) was used as a digital reference signal to further remove any possible noise. We obtained the local field potentials within the traditional amplitude range, 100 to 200 μV, which can be seen in Figure 5.4 while the rat was walking on the treadmill. The differential signals measured between 31-channel signals and a reference channel signal improved the signal quality. The differential recordings selectively amplify the difference in the signal from the ECoG electrodes while suppressing the common signal, i.e. the background noise.

A handcrafted micro-ECoG electrode was surgically implanted on three rats which all went through the same experiment and, as expected, obtained similar results from all test subjects. In Figure 5.4, we can see the LFP signals recorded two months after the surgery was performed on rat 1. The LFP signals on rat1 remained stable and within 100-200 μV peak to peak on each channel throughout most of the recording. Similar results can be observed one month after a handcrafted device was implanted on two other rats in figures 5.5 and 5.6.

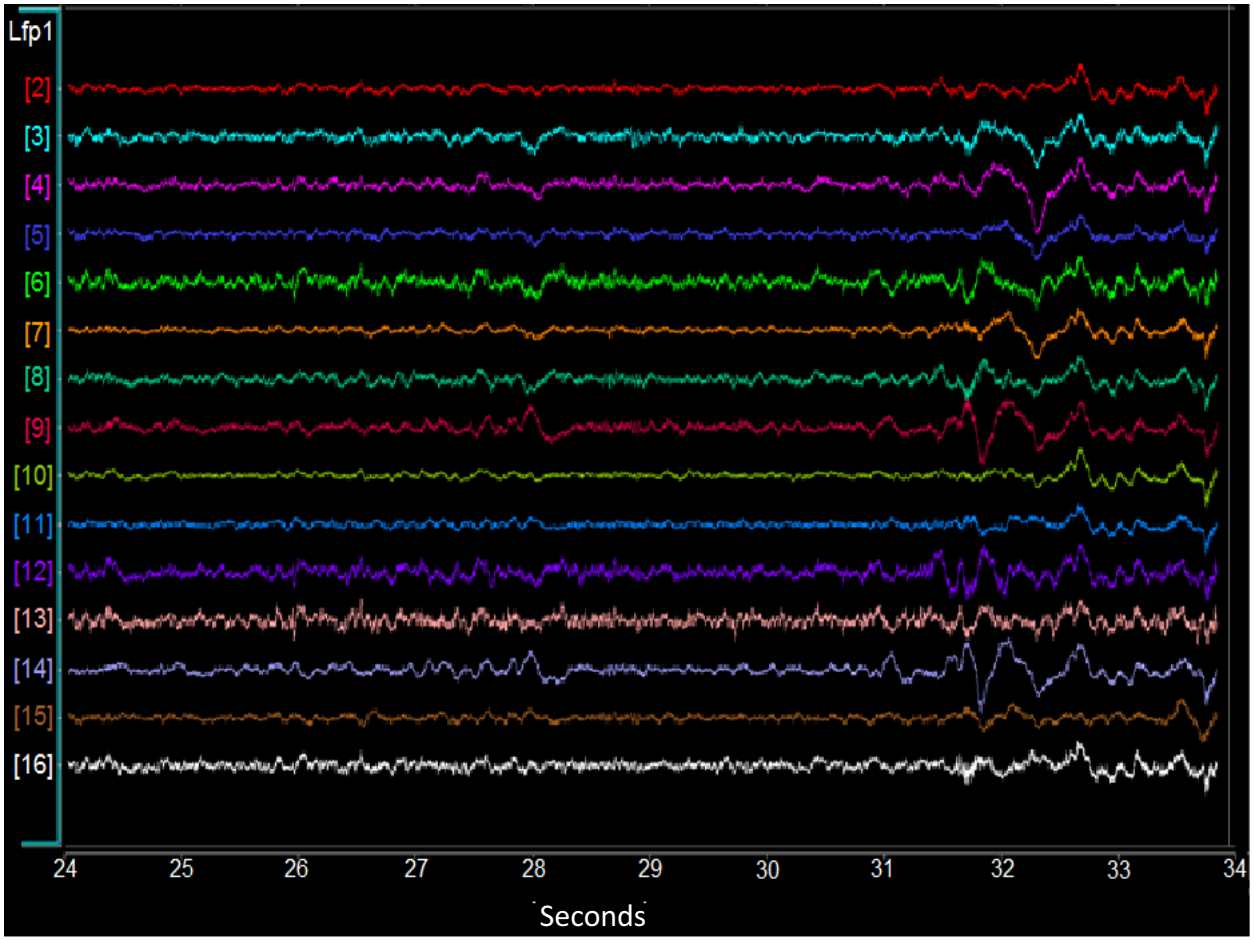

Figure 5.4: ECoG signals from 16-channel microwires of rat 1 two months after device implantation on Rat 1. Each different color signal represents a different signal acquired from a different electrode of the ECoG.

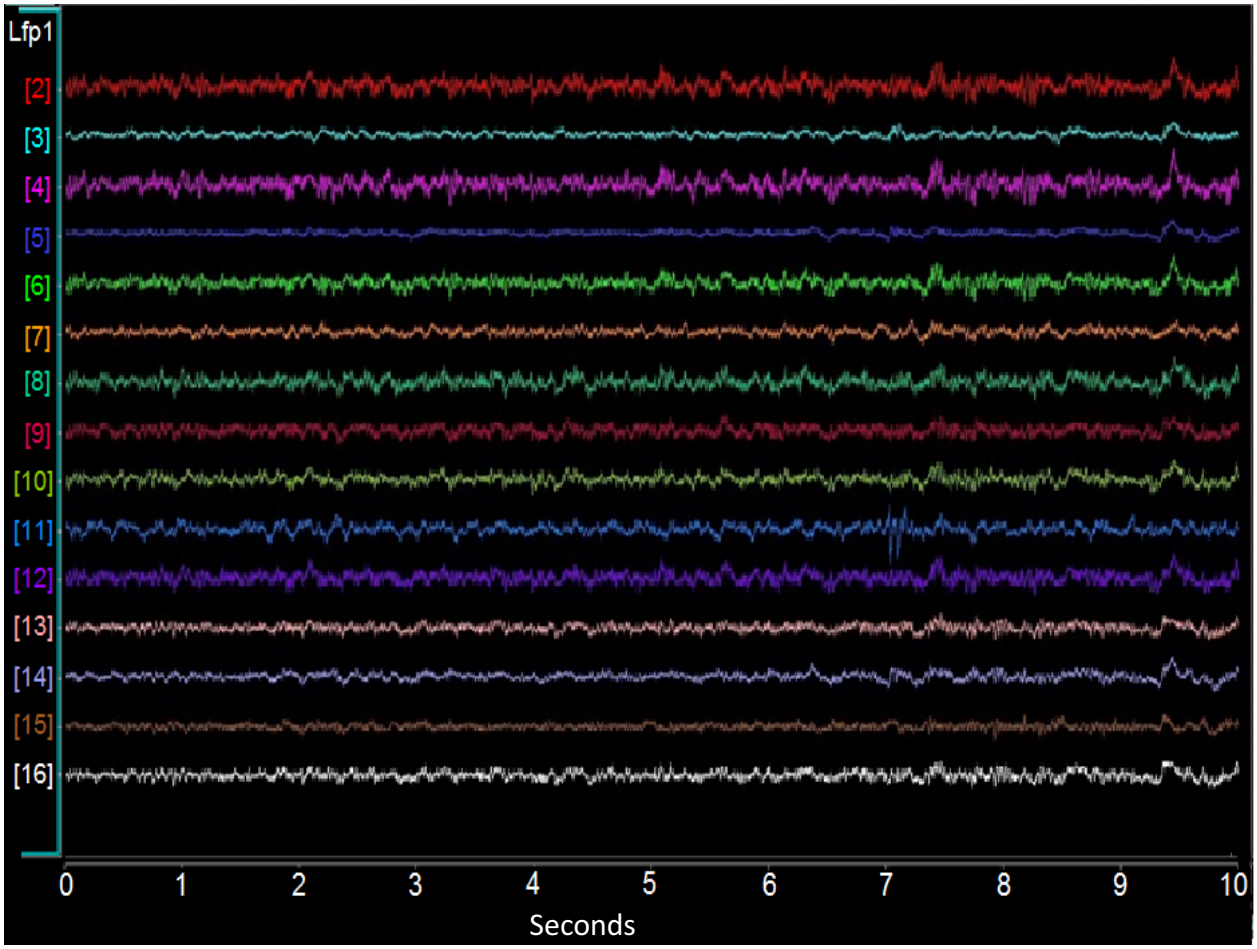

Figure 5.5: Recordings of rat 2 one months after device implantation

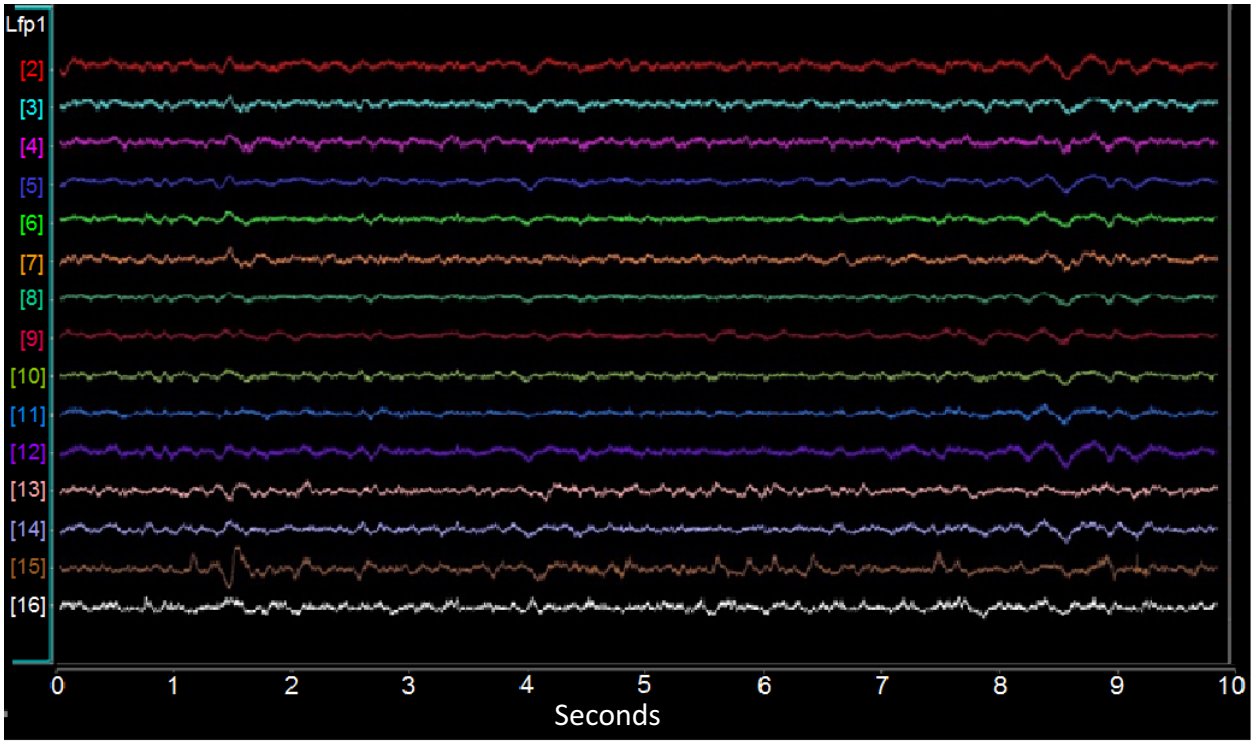

Figure 5.6: Recordings of rat 3 one months after device implantation

It is generally seen that micromachined devices gain advantages against non-micromachined devices, especially when fabricating in a small scale. The initial goal of the handcrafted ECoG was for it to be low-cost, reliable, and able to retrieve signals in approximation to the traditional amplitude range. However, from the fact that we attained local field potentials in the traditional amplitude range and patterns along with amplified signals and consistency across all plotted channels, as shown in the three previous figures, signified the success of the handcrafted device. These responses were obtained after implanting the electrodes on rat's cortical surface and confirms the stability and spatiotemporal features of the handcrafted microdevice. With the addition of the device having a dependable performance for at least two months after implementation indicate that the handcrafted device has surpassed the initial objectives and has the potential to have similar applications as micromachined ECoG electrodes.

CHAPTER VI

CONCLUSION

This research work describes in detail the design and testing of handcrafted 32-channel ECoG electrode with high resolution and small area. This device was simply handcrafted, no cleanroom facility and micromachined fabrication technique was needed. For micromachined techniques such as photolithography, etching, and deposition can be complicated and lengthy procedures where each step could take several days to complete depending on the channel numbers and other properties. The cost of these systems can be excessively high, therefore unfavorable, for small labs or for experiments that require a large number of animals to be continuously recorded at the simultaneously. Most researchers may be able to purchase commercially available ECoG electrodes which usually cost over $1000 per device [39]. Here, we have developed a handcrafted 32-channel ECoG electrode arrays for recording brain signal with high spatiotemporal resolution. Using low-cost components, we were able to reduce the cost of the multiplexed headstage to ~$10 per microdevice. Being constructed from commercially available material and not requiring micromachining techniques, a user can also make modifications to the design of the device to fit onto various cortical surfaces. Since handcrafting a device only needs several hours to prepare, a completely functional micro-ECoG electrode can be uniquely designed and fabricated as the necessity presents itself. After implementing the electrode onto a *Lewis* rat, it was confirmed that it remains stable and non-

penetrative with the high spatial and temporal features that are also observed from commercial electrodes.

The data collected from our rat model using a TDT signal acquisition system suggests that the handcrafted electrode does have the capabilities to provide reliable readings that can be used in neuroscience applications. The traditional amplitude range of the signals obtained from the electrodes and the chronic ability can be compared to other reported microelectrodes which make the device a considerable candidate for numerous applications. Currently, we are fabricating 64-channel, 128-channel, and 256-channel devices for getting more sophisticated results to analyze the brain signal in more detail. Further studies will focus on increasing its electrode density, decreasing the interelectrode distances to get signals with higher resolution, and possibly adopting known physical characteristics to optimize performances which could be able to generate sophisticated neural data comparable with animal's behavioral patterns.

CHAPTER VII

FUTURE RESEARCH

In the present study, we produced a handcrafted 32-channel ECoG electrode array for recording neural signals. We implanted this device on three rat's cortical surface and obtained reliable spatiotemporal profiles. Since the device is handcrafted, it can be easily modified in the fabrication process to satisfy any requirements. The device is also adjustable, minimally-invasive, and quick to fabricate with a minimum of expense. The size of the device can also be controlled by increasing or decreasing the length, diameter, and number of the wires which could be applied to investigate the puzzling concept of physical structures affecting the quality of LFPs in electrodes arrays [40-42]. Without the need for cleanroom facilities, this device can be fabricated and modified to fit and possibly improve on different applications, such as BCI systems [43, 44]. Since the electrode is handcrafted, users can design ECoGs with higher electrode density without any further complication and microfabrication limitation. A reliable performance, the flexibility of the device design, and simplified fabrication is highly required for multidisciplinary biological applications, along with a long-term applicable device which the presented device satisfies by providing dependable results for at least two months after implantation. We can focus on the biological mechanism in the complicated multidisciplinary research without any interruption, even if the device dimension should be modified significantly. The short turnaround time of the modification and fabrication of the handcrafted ECoG is especially preferable when we pioneer a new approach of a research.

The biocompatibility of the ECoG electrode is justified by using PDMS a suitable base material for its durability and biocompatibility. As a biocompatible material, PDMS has been used in a wide range of clinical applications and can be listed in three different categories, such as a structure itself as part of the device, an insulator, and a liquid form. PDMS cuff electrodes have been used on the extradural sacral root to sense the bladder response to stimulation in patients [45-47]. The Stablohm 800A microwire has been used widely for a variety of implantable devices which confirms the reliable biocompatibility [48, 49].

We have developed an animal model using our ECoG electrode to investigate the possibility to match the behavioral patterns of animals while recording the ECoG signals. The ECoG electrodes were placed on the motor and somatosensory cortex and the related neural signals have been recorded. Currently, we have further investigated an acquired database to find specific electrophysiological patterns from animal behavior. This requires intensive computational neuroscience approach to screen out critical behavioral data from the immense neural data. The next goal and future directions of the presented work are pursuing further analysis of the acquired neural signals possibly with a collaboration of a computational neuroscience lab for higher level analysis such as acquiring more information for BCI applications.

REFERENCES

[1] X. Navarro, T. B. Krueger, N. Lago, S. Micera, T. Stieglitz, and P. Dario, "A critical review of interfaces with the peripheral nervous system for the control of neuroprostheses and hybrid bionic systems," *Journal of the Peripheral Nervous System,* vol. 10, pp. 229-258, 2005.

[2] J. C. Sanchez, A. Gunduz, P. R. Carney, and J. C. Principe, "Extraction and localization of mesoscopic motor control signals for human ECoG neuroprosthetics," *Journal of Neuroscience Methods,* vol. 167, pp. 63–81, 2008.

[3] G. Schalk, D. J. McFarland, T. Hinterberger, N. Birbaumer, and J. R.Wolpaw, "BCI2000: a general-purpose brain-computer interface (BCI) system," *IEEE Transactions on Biomedical Engineering,* vol. 51, pp. 1034-1043, 2004.

[4] Y. Nagasaka, K. Shimoda, and N. Fujii, "Multidimensional Recording (MDR) and Data Sharing: An Ecological Open Research and Educational Platform for Neuroscience," *PLOS ONE,* vol. 6, p. e22561, 2011.

[5] D. Khodagholy, T. Doublet, P. Quilichini, M. Gurfinkel, P. Leleux, A. Ghestem*, et al.*, "In vivo recordings of brain activity using organic transistors," *Nature Communications,* vol. 4, pp. 1-7, 2013.

[6] J. P. Donoghu, "Bridging the brain to the world: a perspective on neural interface systems," *Neuron,* vol. 60, pp. 511-521, 2008.

[7] W. Wang, A. D. Degenhart, J. L. Collinger, R. Vinjamuri, G. P. Sudre, P. D. Adelson*, et al.*, "Human motor cortical activity recorded with micro-ECoG electrodes during individual finger movements," in *Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Minneapolis, MN, USA 2009, pp. 586–589.

[8] H. Toda, T. Suzuki, H. Sawahata, K. Majima, Y. Kamitani, and I. Hasegawa, "Simultaneous recording of ECoG and intracortical neuronal activity using a flexible multichannel electrode-mesh in visual cortex," *NeuroImage,* vol. 54, pp. 203–212, 2011.

[9] H. Liu, N. Tanaka, S. Stufflebeam, S. Ahlfors, and M. Hämäläinen. (2010, Functional mapping with simultaneous MEG and EEG. *Journal of Visualized Experiments (40)*, pp. 1–3.

[10] A. B. Schwartz, X. T. Cui, D. J. Weber, and D. W. Moran4, "Brain-controlled interfaces: movement restoration with neural prosthetics," *Neuron,* vol. 52, pp. 205-220, 2006.

[11] N. J. Hill, T. N. Lal, M. Schr¨oder, T. Hinterberger, G. Widman, C. E. Elger*, et al.*, "Classifying event-related cesynchronization in EEG, ECoG and MEG signals," in *Pattern Recognition*, K. Franke, K.-R. Muller, B. Nickolay, and R. Schafer, Eds., ed: Springer Berlin Heidelberg, 2006, pp. 404-413.

[12] A. K. C. Lee, E. Larson, and R. K. Maddox. (2012, Mapping cortical dynamics using simultaneous MEG/EEG and anatomically-constrained minimum-norm estimates: an auditory attention example. *Journal of Visualized Experiments (68)*, pp. 1-7.

[13] N. J. Hill, D. Gupta, P. Brunner, A. Gunduz, M. A. Adamo, A. Ritaccio*, et al.* (2012, Recording human electrocorticographic (ECoG) signals for neuroscientific research and real-time functional cortical mapping. *Journal of Visualized Experiments (64)*, pp. 1-5.

[14] C. R. Conner, T. M. Ellmore, T. A. Pieters, M. A. DiSano, and N. Tandon, "Variability of the Relationship between Electrophysiology and BOLD-fMRI across Cortical Regions in Humans," *Journal of Neuroscience,* vol. 31, pp. 12855-12865, 2011

[15] T. Pistohl, T. Ball, A. Schulze-Bonhage, A. Aertsen, and C. Mehring, "Prediction of arm movement trajectories from ECoG-recordings in humans," *Journal of Neuroscience Methods,* vol. 167, pp. 105–114, 2008.

[16] E. M. Maynard, C. T. Nordhausen, and R. A. Normann, "The utah intracortical electrode array: a recording structure for potential brain-computer interfaces," *Electroencephalography and Clinical Neurophysiology,* vol. 102, pp. 228-239, 1997.

[17] N. Y. Masse, B. Jarosiewicz, J. D. Simeral, D. Bacher, S. D. Stavisky, S. S. Cash*, et al.*, "Non-causal spike filtering improves decoding of movement intention for intracortical BCIs," *Journal of Neuroscience Methods,* vol. 236, pp. 58-67, 2014.

[18] J. A. Perge, S. Zhang, W. Q. Malik, M. L. Homer, S. Cash, G. Friehs*, et al.*, "Reliability of directional information in unsorted spikes and local field potentials recorded in human motor cortex," *Journal of Neural Engineering,* vol. 11, p. 046007, 2014.

[19] M. L. Leavitt, F. Pieper, A. Sachs, R. Joober, and J. C. Martinez-Trujillo, "Structure of spike count correlations reveals functional interactions between neurons in dorsolateral prefrontal cortex area 8a of behaving primates," *PLOS ONE,* vol. 8, p. e61503, 2013.

[20] P. Ponce, A. Molina, D. C. Balderas, and D. Grammatikou, *Brain Computer Interfaces for Cerebral Palsy*: InTech, 2014, pp. 28-58.

[21] J. A. Wilson, E. A. Felton, P. C. Garell, G. Schalk, and J. C. Williams, "ECoG factors underlying multimodal control of a brain–computer interface," *IEEE Transactions on Biomedical Engineering,* vol. 14, pp. 246-250, 2006.

[22] R. Pashaie, P. Anikeeva, J. H. Lee, R. Prakash, O. Yizhar, M. Prigge*, et al.*, "Optogenetic Brain Interfaces," *IEEE Reviews in Biomedical Engineering,* vol. 7, pp. 3-30, 2014.

[23] G. J. Ortega, R. G. Sola, and J. Pastor, "Complex network analysis of human ECoG data," *Neuroscience Letters,* vol. 447, pp. 129-133, 2008.

[24] V. L. Towle, Hyun-AhYoon, M. Castelle, J. C. Edgar, N. M. Biassou, D. M. Frim*, et al.*, "ECoG gamma activity during a language task: differentiating expressive and receptive speech areas," *Brain,* vol. 131, pp. 2013-2027, 2008.

[25] W. Wang, J. L. Collinger, A. D. Degenhart, E. C. Tyler-Kabara, A. B. Schwartz, D. W. Moran*, et al.*, "An Electrocorticographic Brain Interface in an Individual with Tetraplegia," *PLOS ONE,* vol. 8, p. e55344, 2013.

[26] M. A. Escabí, H. L. Read, J. Viventi, D.-H. Kim, N. C. Higgins, D. A. Storace*, et al.*, "A high-density, high-channel count, multiplexed uECoG array for auditory-cortex recordings," *Journal of Neurophysiology,* vol. 112, pp. 1566-1583, 2014.

[27] E. H. Chang, S. A. Frattini, S. Robbiati, and P. T. Huerta. (2013, Construction of Microdrive Arrays for Chronic Neural Recordings in Awake Behaving Mice. *Journal of Visualized Experiments (77)*, pp. 1-8.

[28] L. R. Hochberg, M. D. Serruya, G. M. Friehs, J. A. Mukand, M. Saleh, A. H. Caplan*, et al.*, "Neuronal ensemble control of prosthetic devices by a human with tetraplegia," *Nature,* vol. 442, pp. 164-171, 2006.

[29] G. Schalk and E. C. Leuthardt, "Brain-computer interfaces using electrocorticographic signals," *IEEE Reviews in Biomedical Engineering,* vol. 4, pp. 140-154, 2011.

[30] John Kiernan. "Anatomical Foundations of Neuroscience". Internet: https://instruct.uwo.ca/anatomy/530/ratbsl.gif. 2008 [May 1, 2016]

[31] A. A. Schendel, S. Thongpang, S. K. Brodnick, T. J. Richner, B. D. B. Lindevig, L. Krugner-Higby*, et al.*, "A cranial window imaging method for monitoring vascular growth around chronically implanted micro-ECoG devices," *Journal of Neuroscience Methods,* vol. 218, pp. 121-130, 2013.

[32] S. Thongpang, T. J. Richner, S. K. Brodnick, A. Schendel, J. Kim, J. A. Wilson*, et al.*, "A micro-electrocorticography platform and deployment strategies for chronic BCI applications," *Clinical EEG and Neuroscience,* vol. 42, pp. 259-265, 2011.

[33] B. Rubehn, C. Bosman, R. Oostenveld, P. Fries, and T. Stieglitz, "A MEMS-based flexible multichannel ECoG-electrode array," *Journal of Neural Engineering,* vol. 6, p. 036003, 2009.

[34] WTEC workshop, Arlington, VA. " Review of North American Research on Brain Computer Interfaces ". Internet: http://www.wtec.org/bci/BCI_US_Proceedings.pdf. 2006 [May 1, 2016]

[35] M. B. Christensen, H. A. C. Wark, and D. T. Hutchinson, "A histological analysis of human median and ulnar nerves following implantation of Utah slanted electrode arrays," *Biomaterials,* vol. 77, pp. 235-242, 2016.

[36] J. D. Yeager, D. J. Phillips, D. M. Rector, and D. F. Bahr, "Characterization of flexible ECoG electrode arrays for chronic recording in awake rats," *Journal of Neuroscience Methods,* vol. 173, pp. 279–285, 2008.

[37] G. J. Gage, C. R. Stoetzner, T. Richner, S. K. Brodnick, J. C. Williams, and D. R. Kipke. (2012, Surgical implantation of chronic neural electrodes for recording single unit activity and electrocortiographic signals. *Journal of Visualized Experiments (60)*, pp. 1-4

[38] E. Tolstosheeva, V. Gordillo-González, V. Biefeld, L. Kempen, S. Mandon, A. K. Kreiter*, et al.*, "A multi-channel, flex-rigid ECoG microelectrode array for visual cortical interfacing," *Sensors,* vol. 15, pp. 832-854, 2015.

[39] J. Wang, M. Trumpis, M. Insanally, R. Froemke, and J. Viventi, "A low-cost, multiplexed electrophysiology system for chronic mu ecog recordings in rodents," in *36TH Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, Chicago, IL, 2014, pp. 5256-5259.

[40] S. A. Boppart, B. C. Wheeler, and C. S. Wallace, "A flexible perforated microelectrode array for extended neural recordings," *IEEE Transactions on Biomedical Engineering,* vol. 39, pp. 37-42, 1992.

[41] B. J. He, A. Z. Snyder, J. M. Zempel, M. D. Smyth, and M. E. Raichle, "Electrophysiological correlates of the brain's intrinsic large-scale functional architecture," *Proceedings of the National Academy of Sciences of the United States of America,* vol. 105, pp. 16039-16044, 2008.

[42] M. J. Nelson and P. Pouget, "Physical model of coherent potentials measured with different electrode recording site sizes," *Journal of Neurophysiology,* vol. 107, pp. 1291-1300, 2012.

[43] M. Lee, H.-S. Shin, and J. H. Choi, "Simultaneous recording of brain activity and functional connectivity in the mouse brain," in *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Mineeapolis, MN, 2009, pp. 2934-2936.

[44] N. J. Hill, T. N. Lal, M. Schr¨oder, T. Hinterberger, B. Wilhelm, F. Nijboer*, et al.*, "Classifying EEG and ECoG Signals without subject training for fast BCI implementation: comparison of non-paralysed and completely paralysed subjects.," *IEEE*

Transactions on Neural Systems and Rehabilitation Engineering, vol. 14, pp. 183-186, 2006.

[45] G. A. M. Kurstjens, A. Borau, A. Rodriguez, N. J. M. Rijkhoff, and T. Sinkjaer, "Intraoperative recording of electroneurographic signals from cuff electrodes on extradural sacral roots in spinal cord injured patients," *The Journal of Urology,* vol. 174, pp. 1482–1487, 2005.

[46] A. Mercanzini, K. Cheung, D. L. Buhl, M. Boers, A. Maillard, P. Colin*, et al.*, "Demonstration of cortical recording using novel flexible polymer neural probes," *Sensors and Actuators,* vol. 143, pp. 90-96, 2008.

[47] P. Ledochowitsch, R. J. Félus, R. R. Gibboni, A. Miyakawa, S. Bao, and M. M. Maharbiz, "Fabrication and testing of a large area, high density, parylene MEMS μECoG array," in *2011 IEEE 24TH International Conference on Micro Electro Mechanical Systems (MEMS)*, Cancun, Mexico, 2011, pp. 1031-1034.

[48] S. Hattori, T. Yoon, J. F. Disterhoft, and C. Weiss, "Functional Reorganization of a Prefrontal Cortical Network Mediating Consolidation of Trace Eyeblink Conditioning," *Journal of Neuroscience* vol. 34, pp. 1432-1445, 2014.

[49] T. R. Farrell and R. F. Weir, "A Comparison of the Effects of Electrode Implantation and Targeting on Pattern Classification Accuracy for Prosthesis Control," *IEEE Transactions on Biomedical Engineering,* vol. 55 pp. 2198 - 2211, 2008.

BIOGRAPHICAL SKETCH

Nishat Tasnim was born in Dhaka, Bangladesh in 1991. The majority of her life was spent growing up in Dhaka, developing a fascination for technology and engineering. Nishat Tasnim received her Bachelor's degree from the Ahsanullah University of Science and Technology in 2013 and her Master's degree from the University of Texas Rio Grande Valley in 2016. While pursuing her Master's degree, she has presented research in Neural Regeneration conference, Bioscience research collaborative. Additionally, she has published her research in "Engineering Journals". Her main research interests are ECoG devices and her conducted research includes fabricating micro peripheral nerve scaffold and peripheral neural interface. She has maintained a 4.00 average throughout her graduate career. Upon graduation from the University of Texas Rio Grande Valley, Nishat Tasnim is looking forward to beginning PhD program in the United States.

Permanent address: House 52/3, South Bashabo, Dhaka, Bangladesh.

Permanent email address: tasnim.nishat2@gmail.com