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A High Density Micro-Electrocorticography Device for a Rodent Model

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A HIGH DENSITY MICRO- ELECTROCORTICOGRAPHY DEVICE FOR A RODENT MODEL

A Thesis

by

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ABSTRACT

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Electrocorticography (ECoG) is a methodology for stable mapping of the brain surface using local field potentials (LFPs) with a wide cortical region, high signal fidelity, and minimal invasiveness to brain tissue. To compare surface ECoG signals with inter-cortical neuronal activity, we fabricated a flexible handcrafted ECoG electrode made with economically available materials. This handcrafted ECoG electrode is non-penetrative with 256 channels that cover an area of 7mm X 7mm on the cortical surface of a Lewis rat. This device was placed on the motor and somatosensory cortex of the brain to record signals of an active animal. The recordings are acquired by using the Synapse Software and the Tucker-Davis Technologies acquisition system to monitor and analyze electrophysiological signals within the amplitude range of 200μV for local field potentials. This demonstrates how reactive channels and their spatiotemporal and frequency-specific characteristics can be identified by means of this method.

DEDICATION

The completion of my master studies would not have been possible without the blessing and support of my family. I would like to thank and dedicate my work to my parents, Veera Venkata Satya Narayana and Subba Lakshmi (late) for their love and support. I would also like to thank to my grandmother, stepmom, and Yoga Sree. The completion of my master studies would not be possible without their support.

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CHAPTER I

INTRODUCTION

1.1 Introduction

In the research of neuroscience, micro ECoG electrode are a common tool in the study of cortical brain functions. The use of micro ECoG electrodes as means of recording has the advantages of design customization, flexibility in material, minimal invasiveness and low cost. The brain is organized into different regions, during the information processing brain regions interact with one another. Thus, important target in neuroscience research is to determine the mechanisms that are responsible for neuronal interaction between several neuronal populations in brain. There are many ways to approach but one way is approach neuroscience is to study neuronal communications. The Local Field Potential(LFP) is a measure of pre- and postsynaptic activity within an area of nerve tissue and it appear to convey relevant information that is not present in neuronal spike activity. Different studies which says that significant LFP modulations are related to sensory processing, visuomotor interactions, motor planning, and higher functions such as attention, memory and decision-making [1].

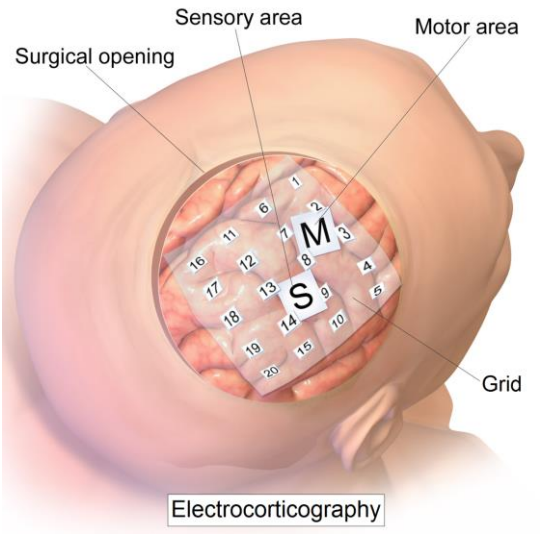


Figure 1.1 Human Brain with Ecog [2]

The neural signals obtained from micro ECoG electrodes and other neural recording devices describe the physical behavior of humans and other living beings. As we able to measure brain signals to understand these mechanisms. These mechanisms will allow us to treat a number of diseases and increase the quality of recovery for patients suffering from nervous tissue damage. The identification of neural functions is by means of maps in the cortical surface of brain, can establish proper links for neural interfaces that can offer disabled patients an alternative solution for their lost sensory or motor functions through the use of brain-computer interface (BCI) technology.

1.2 History of ECoG

Recording the electrical activity of the exposed brain, known as an electrocorticography (ECoG), which has a long history. An animal's exposed brain exhibited a characteristic waxing and waning rhythmic activity was first reported by Caton in 1875 in England, he used a Thomson reflecting telegraphic galvanometer with a frequency response to about 5 Hz. But, Caton made no photographic recordings, but his descriptions are most

convincing. The first human recordings obtained from scalp electrodes, known as electroencephalograms (EEGs), were made by Berger in 1929 that used the string galvanometer created by Einthoven in 1903 for electrocorticography. Berger, a psychiatrist, thought that the EEG might be of value in diagnosing mental disease, but this research proved that was not the situation. After that EEG are clinically evolved from the confirmatory studies in 1935 in the USA by Jasper, Carmichael, Gibbs, and others. Clinical EEGs expanded quickly in the early 1940s and found a niche in the diagnosis of the many types of epilepsy, a dysrhythmia of neurons in the brain. The EEG also permitted localization of the region of abnormally active neurons. However, the EEG had its limitations that lead to developing a more effective way of measuring neural activity, which is the ECoG [2].

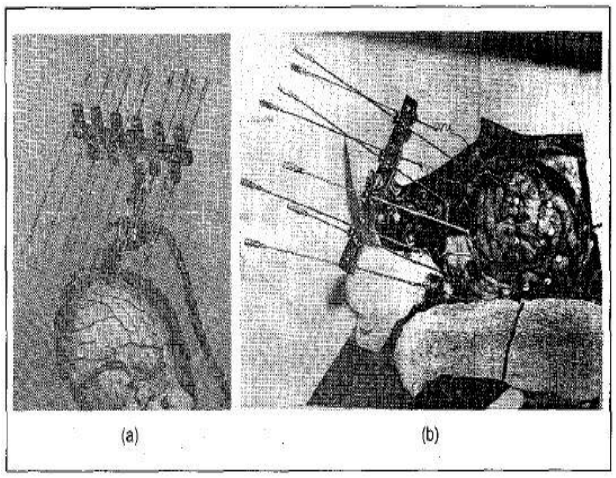


Figure 1.2: In (a) is shown the electrode assembly clamped to a skull. In (b) the electrodes are in contact with the cortex of a patient [2].

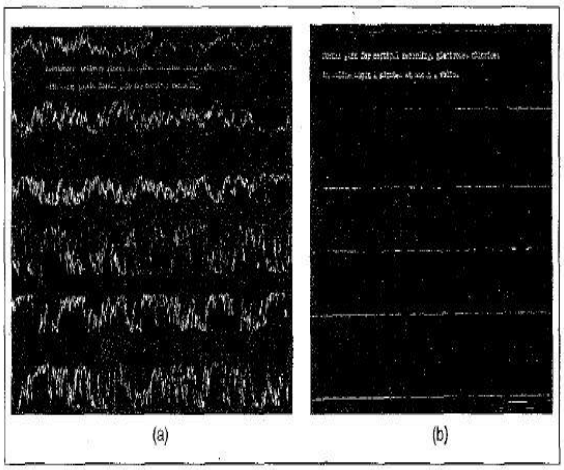


Figure 1.3: Electrode noise from polished silver-ball electrodes in saline (a) and a record obtained after chloriding the same electrodes in the same saline bath (b) [2].

1.3 EEG Vs ECoG

The EEG technique is a commonly known for recording BCI applications due to its reduced cost, portability, and non-invasiveness. This EEG technique measures highly populated neuronal activity by attaching electrodes to the scalp of a subject, the impedance between the cortical tissue and the electrodes force the EEG to have a decreased spatial resolution. Electroencephalography is a domain concerning recording and interpretation of the electroencephalogram. 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 micro machined 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. This is done by allowing microelectrodes to be placed close to each other in small groups of neurons. With this information, UIEA has allowed individuals with illnesses, such as tetraplegia, to have control over technologies such as neuroprosthetics[3-6]. 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 those 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 50μV to over 100μV, while EEG obtains signals in the 5–10μV 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. For these reasons, ECoG has become a preferable alternative approach in recording brain activity for BCI applications [7-9].

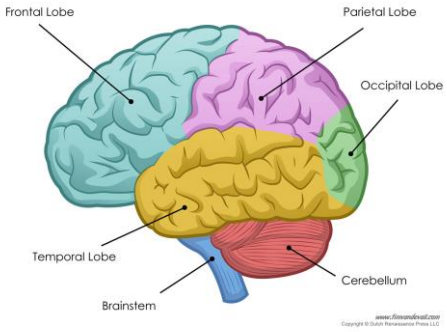


Figure1.4: Human Brain [10]

1.4 Related Works

The main motive of this research is to build a handcrafted micro-ECoG electrode with a low cost and to 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 ECoG electrodes are placed directly on top of the cortex to measure and record voltages created by the ion pumps and ion channels, while the EEG electrodes have to same function but are placed on the epicrania. ECoG refers to recordings that have electrodes placed either above or below the dura mater covering the brain. Cross-correlation and autocorrelations between these electrode voltages reveal spatial and temporal correlations between neuronal activity, and from them, it can infer properties of neural computation at the population scale. Recordings are analyzed when subjects are performing a task. ECoG provides better spatial and spectral resolution when compared with EEG. ECoG electrodes are minimally invasive with a low 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 micro devices 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 various materials. An example can be demonstrated by a group led by Amelia A. Schendel in 2013 that were focused on studying the tissue response in vivo when a micro-ECoG array is implanted [11,12]. The device used was based on a design by Thongpang 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 sub cranial placements of multiple electrodes from a single craniotomy [13]. More detailed and other types of electrodes can be found in [13], Amelia A. Schendel 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, so photolithography can be used to define the electrode sites on the Parylene layer. Next, gold and platinum were deposited onto the wafer in a metal evaporation system to act as 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 micromachined devices, handcrafted devices do not need silicon wafer that is usually sold in large groups and must provide specific characteristics when ordered. Also, different metals and deposition systems were not used because the inexpensive micro-wires are good conductors and were easily placed to form the handcrafted device. No additional layer for insulation or etching was required because the micro-wires 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.

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 a large area of the cortex [14]. Their array utilized a wafer that was spin coated with polyimide and placed on a hotplate to remove any solvents. The wafer was then etched to improve the adhesion of a metal layer to the polyimide. Platinum was sputtered onto the wafer, and an 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 so that photoresist and photolithography could be performed again in order to etch open the electrode and solder pad sites in addition to defining the array perimeter. Lastly, the remaining photoresist was removed with acetone and 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, 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 with the use of commercially available materials and a process that required only 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.

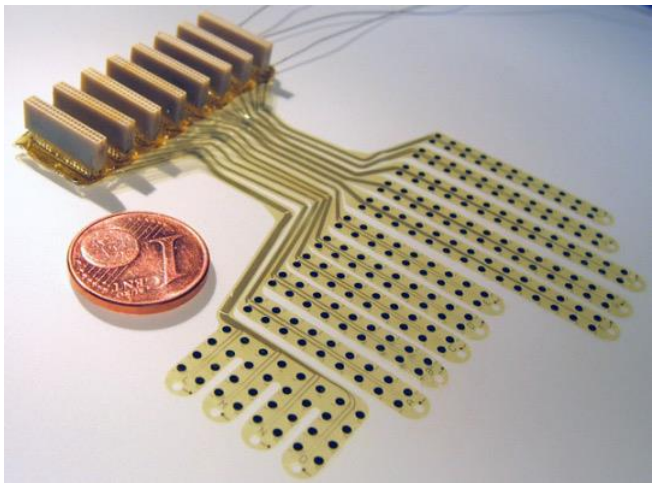


Figure 1.5: Fully assembled 252-electrode array with the diameter of the coin is 16 mm[14]

An alternative type of electrodes is the penetrating ECoG electrode arrays. A typical example of such device is the Utah Intracortical Electrode Array (UIEA) or a similar design known as the Utah Slanted Electrode Array (USEA). Most UIEA type of arrays contains 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[15]. 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 electrode recordings to decline over time has also impeded this type of device to reach widespread clinical use [16,17]. The results obtained from these kinds of related devices, in the past few years, numerous groups presented precision-engineered or MEMS-based ECoG electrode arrays.

CHAPTER II

FABRICATION PROCESS

The main motive of this research is to develop a fabrication of handcrafted, 256-channel ECoG electrode that has the advantages of design customization, flexibility, and minimal invasiveness. ECoG electrodes that are implanted on the cortical surface in rodents require dozen to hundreds of electrodes and must be kept to a small size to achieve high spatial resolution for accurate results. 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 high-density handcrafted micro device.

2.1 Required Materials

The fabrication procedure of a 256-channel, handcrafted ECoG electrode starts with some basic materials, which are listed below:

- Micro-wires
- Polydimethylsiloxane (PDMS)
- Dental cement
- Ribbon cables
- Para film

Micro-wires:

The micro-wires are commercially available wires that are going to act as the electrodes (Stablohm 800A, California fine wire, Grover Beach, CA). These wires have a diameter of 75μm and are thinner than the human hair, which is shown in the figure below.

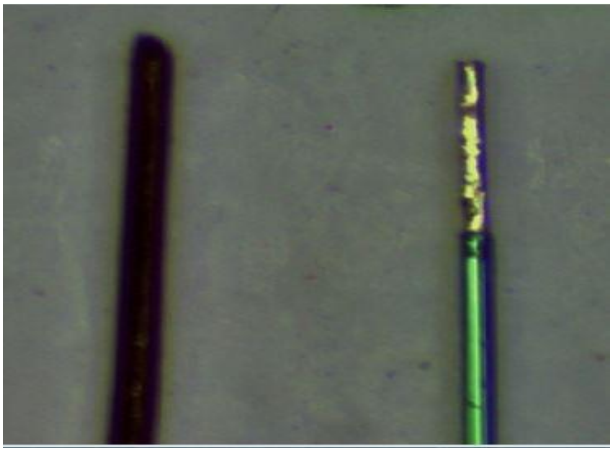


Figure 2.1: Comparing the micro-wire with human hair

PDMS layer:

Polydimethylsiloxane (PDMS) belongs to a group of polymeric organosilicon compounds referred to as silicones. PDMS is optically clear, inert, non-toxic, bio compatible and non-flammable. It was generally used in contact lenses, and medical devices.

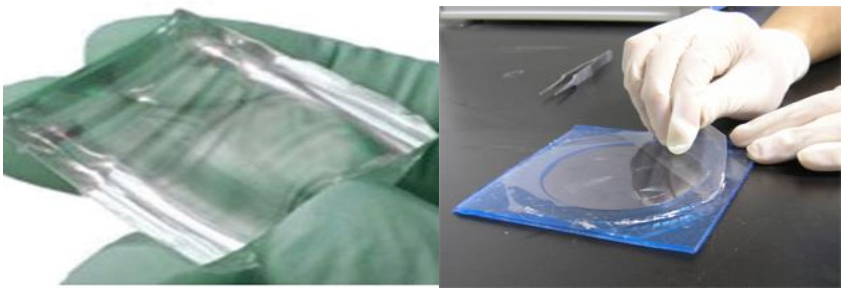


Figure 2.2: Sample of PDMS

Para film:

Para film is a plastic paraffin film with a paper backing primarily used in laboratories. It is a waterproof, translucent, and cohesive thermoplastic. It is from "Para film M laboratory film, Bemis Corporate, Neenah, WI".

Figure 2.3: Sample of Para film

Dental Composite Resin Cement:

Dental cements are hard material formed by mixing powder and liquid together. The powder is a basic metal oxide and the liquid is acidic. An acid base reaction occurs with the metal salt that acts as the cementing matrix. Dental cements are used for a variety of purposes such as dental and orthodontic applications, luting agents, pulp-protecting agents, and cavity-lining material. These can be also used to form an insulating layer under metallic or ceramic restorations to protect the pulp from injuries.

Figure 2.4: Sample of dental cement

Multi-Wire Planar Cable:

Multi-wire planar cable, also known as ribbon cable, is a cable with many conducting wires running parallel to each other on the same flat plane. As a result, the cable is wide, flat, and flexible. These cables are used for transferring data for communication. Its name comes from its resemblance to a piece of ribbon.

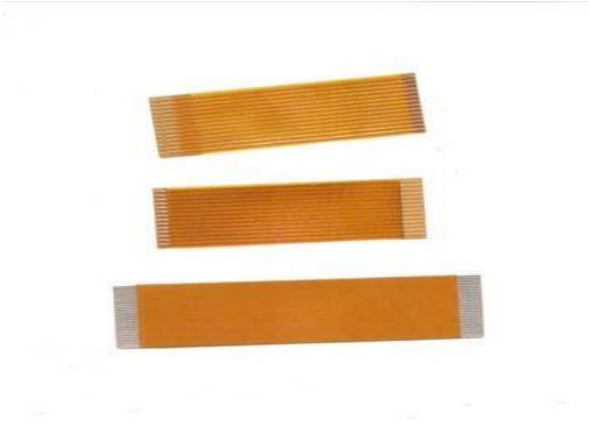


Figure 2.5: Sample of ribbon cables

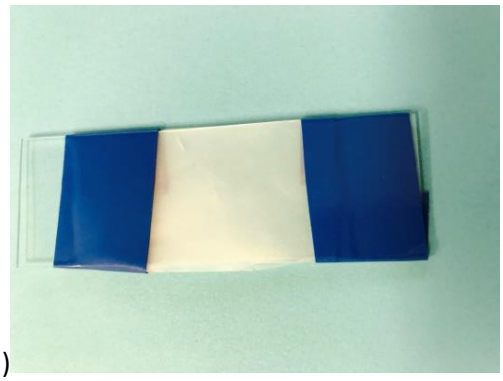
2.2 Fabrication Procedure

In the initial stage of fabricating the handcrafted ECoG electrode, the commercially available micro-wire of 75μm in diameter (Stablohm 800A, California fine wire, Grover Beach, CA) is cut into 256 segments of 1 inch in length, which are used as electrodes. The length of the micro-wire was fixed after several trials of performing the surgery and implementing on the rat's cortical surface. A longer or shorter length of micro-wires would present a risk of compromising the experiment either by the animal or a level of difficulty during surgery.

Figure 2.6: 1 inch wire

After 256 wires are cut, para film (Para film M laboratory film, Bemis Corporate, Neenah, WI) is folded into 2 layers and placed on a glass slide. Tape is attached to the para film and the glass slide in order to secure the para film on the glass slide. An area of 7x7 mm^2 is marked on top of the para film to be used to guide the placement of the wires into a uniformly square shape. After marking the area on para film, a PDMS layer of 8x8 mm^2 is then placed on the para film at the center of glass slide. The para film is used as a supporting platform to easily separate a fabricated ECoG at the final stage because it is not adhesive to the PDMS layer and also to maintain a consistent length of the micro-wires protruding through the PDMS layer. Then the micro-wires are inserted in the PDMS layer, which are arranged row by row on the thin PDMS film by using tweezers, making them parallel and kept apart at equal distances. Once all the wires are inserted into the PDMS film, the upper 256 wires are tied together using the string. Next step is to mix the PDMS liquid with 184 Sylgard base (Dow Corning Corporation, Midland, MI) and curing agent at a ratio of 10:1 and kept in a vacuum chamber for 20 minutes until all visible bubbles disappear. Afterwards, the mixture is checked under a microscope for any remaining bubbles, which are removed with the use of a needle. This step can be repeated if excessive bubbles are still present. Then, liquid PDMS is applied in small amounts over the

wires that had been inserted into the para film so that all the sides of the wires must be covered. The device is then placed in the oven for 30 minutes at 50° C to expedite the solidification process of the liquid PDMS. This low temperature was required to keep the para film stable. A higher temperature would cause the para film to start melting and adhere to the PDMS film making it difficult to separate the device from the para film as shown in the following figures.

(a)  (b) 

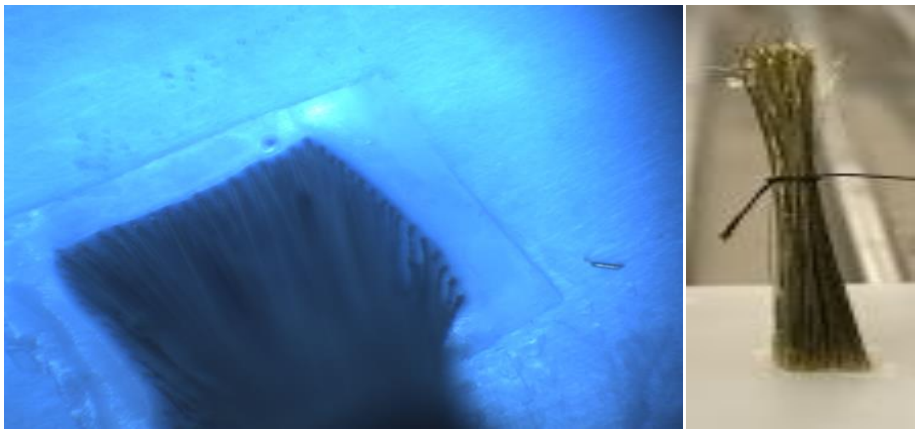
© 

Figure 2.7: (a) Arranging parafilm (b) Arranging PDMS on parafilm (c) Inserting and tying wires

Once the PDMS has solidified, remove the device from the oven and apply dental glue over it to hold the micro wires stronger. After separating the device from the para film, the device should look like Figure 2.8.

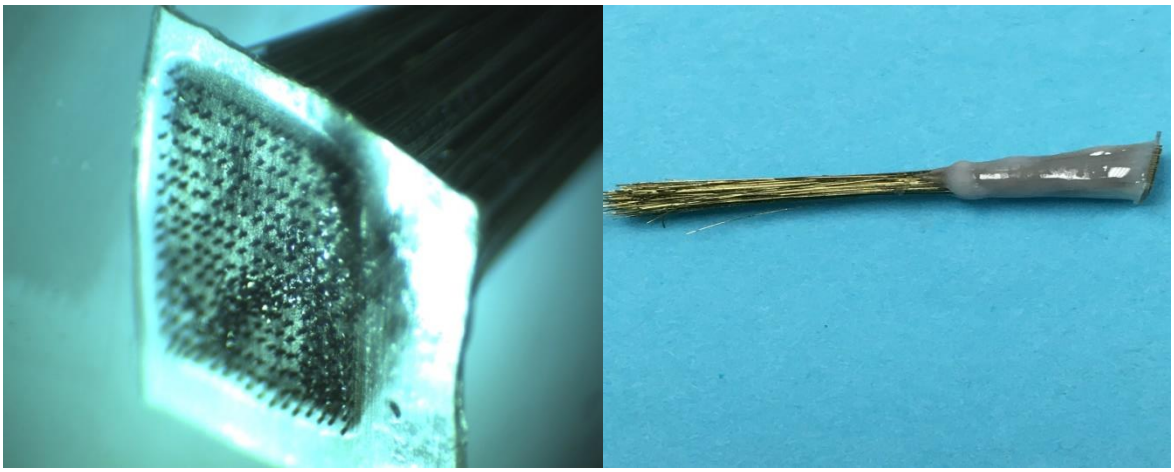


Figure 2.8: ECoG Device after separating from the glass slide

The final step of the fabrication process is soldering ribbon cables to serve as a link between the ECoG device and TDT 128 channel interface board connectors. Four commercially available Molex 33-channel ribbon cables will be inserted into each TDT input connectors. The ribbon cables will act as a bridge from the stablohm micro-wires to the TDT input connectors. Each of these ribbon cables have 33 conducting wires running parallel to each other on the same flat plane, shown in Figure 2.9(a), while the 17th conducting wire is marked and used as ground. Each of the four ribbon cables are cut with a sharp blade into two separate pieces in which one piece is of length 15 mm and the another piece is of length 22mm. Afterwards, 0.2 mm of insulation is removed at the end of the each ribbon cable and up to 5 mm of each wire of the ribbon cable is separated from the rest of the cable, as shown in Figure2.9 (b), to prevent the wires from making contact after they have been soldered with the stablohm micro-wires. The ribbon cables are then organized in such a way that they are arranged parallel to each other. Then, 0.2mm of the insulation is removed on each of the 256 micro-wires, and then we

solder the micro-wires to the ribbon cable with the help of a sharp blade placed in between the individual wires of ribbon cable to isolate a single wire from the rest of the ribbon cable.

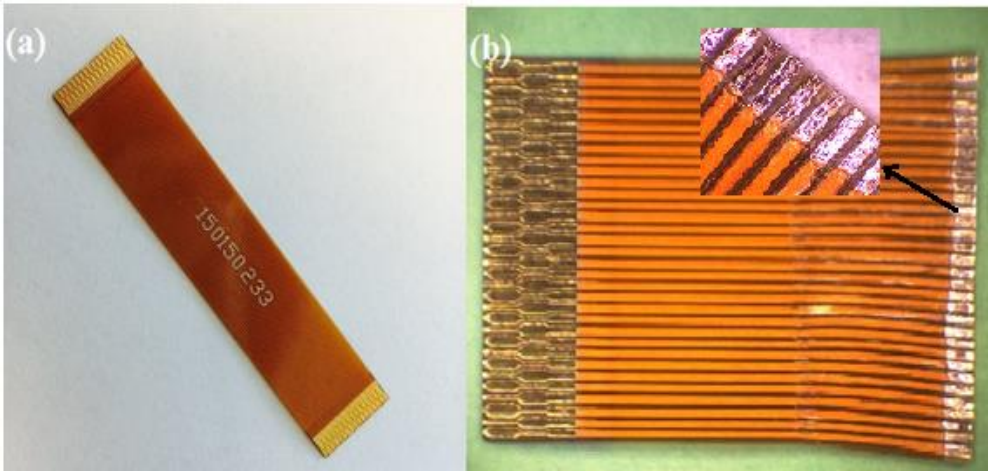


Figure 2.9: (a) Single ribbon cable. (b) Uninsulated 15 mm ribbon cable separated

The result of 32 micro-wires soldered onto each ribbon cable is shown in Figure2.10 (a). After finishing soldering the 256 micro-wires, two 1.5-inch wires (AS631, Cooner Wire, Chatsworth, CA) were connected to the 17th wire on two ribbon cables, which should be connected to two TDT input connectors to act as the ground. Figure 2.10 (b) shows the device after completion of soldering part. All ribbon cable wires were isolated from each other by applying dental cement on each wire and using UV light to harden it. Dental cement is then applied between all wires to prevent the wires from becoming unattached shown in Figure2.11 This dental glue will act as insulation for each wire and provide physical support for the eight ribbon cables and wires.

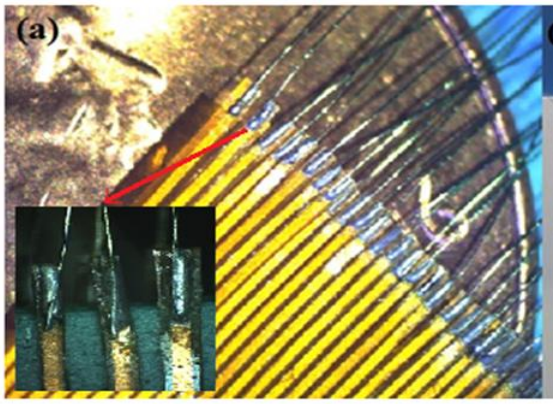


Figure 2.10(a): ECoG Device detail soldering part **Figure 2.10**(b): ECoG Device after soldering the micro wires

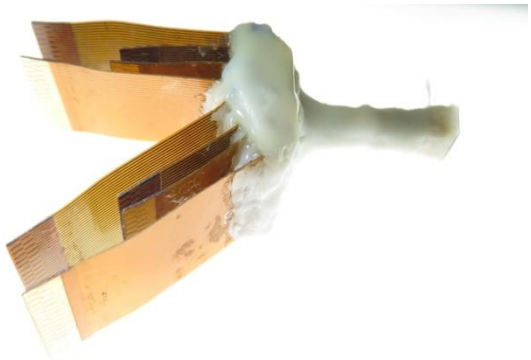


Figure 2.11: ECoG Device with dental cement in two views

The connection of the ribbon cables to the TDT interface board is shown in Figure2.12. After ensuring the stablohm micro-wires will not become loose, the device was completed and ready for implantation.

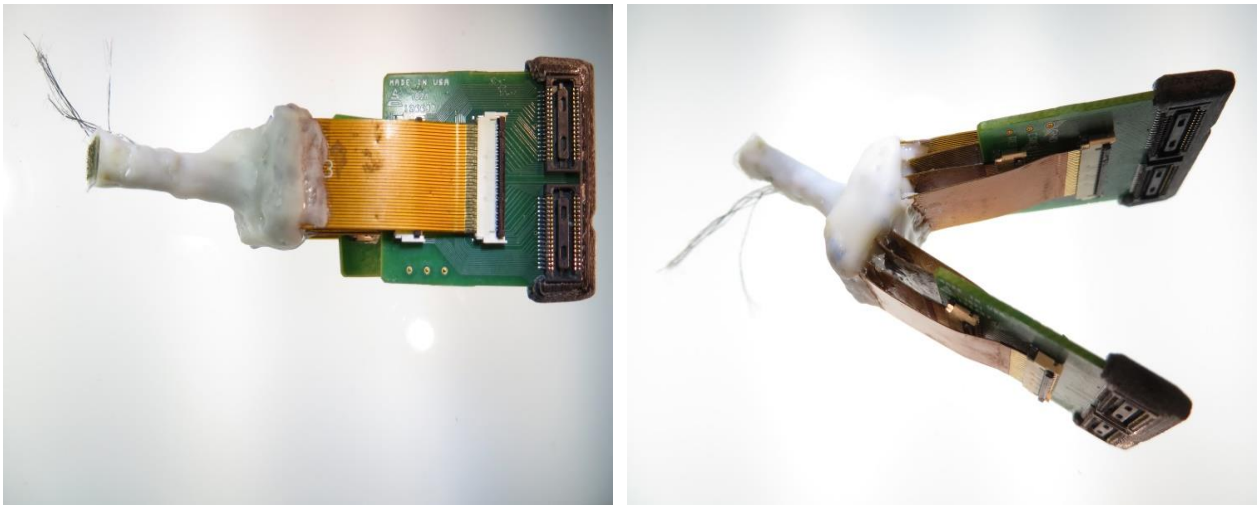


Figure 2.12 (a) ECoG Device connected to the TDT interface board in (b) Side View

CHAPTER III

SURGICAL PROCEDURE

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 us to confidently proceeding 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 [17]. 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.

3.1 Animal Model

Although human and non-human animals look different, at a physiological and anatomical level they are similar. Animals have the same organs (heart, lungs, brain etc.) and organ systems (respiratory, cardiovascular, nervous systems, etc.) that perform the same functions in, pretty much the same way. Many of the medicines that are used to treat animals are the same as, or very similar to, those developed to treat human patients. If we want to study a human disease, we cannot perform the initial experiments on humans. In such a case, we have to develop an animal model. Sometimes the model may be *in vitro*, but we eventually test ideas *in vivo*. Animal models allow an approximation to a human response. Mice and rats play a major role in developing new medical drugs. In fact, 95% of all lab animals are mice and rats, according to the Foundation for Biomedical Research (FBR). One reason we used rats is convenience: rodents are small, easily housed and maintained, and adapt well to new surroundings. They also reproduce relatively quickly and have a short lifespan of two to three years. Mice and rats are also relatively inexpensive and can be bought in large quantities from commercial producers that breed rodents specifically for research [18]. Rats and mice are also generally mild-tempered and docile, so it is easy for researchers to handle them. Most of the mice and rats used in biomedical research are inbred so that, other than sex differences, they are almost identical genetically. 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, Alzheimer's disease, Cancer, HIV and AIDs, Heart disease, Muscular dystrophy, and Spinal cord injuries. Mice and rays 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 anesthesia followed by maintenance of anesthesia (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 [19, 20]. Its maxillary central incisors were hooked into a gas mask 18 through which it continued to receive small doses of anesthesia. 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 epidurals on the brain's left hemisphere. For the 7x7 mm^2 device, an 8x8 mm^2 craniotomy must be made [21- 25]. 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.

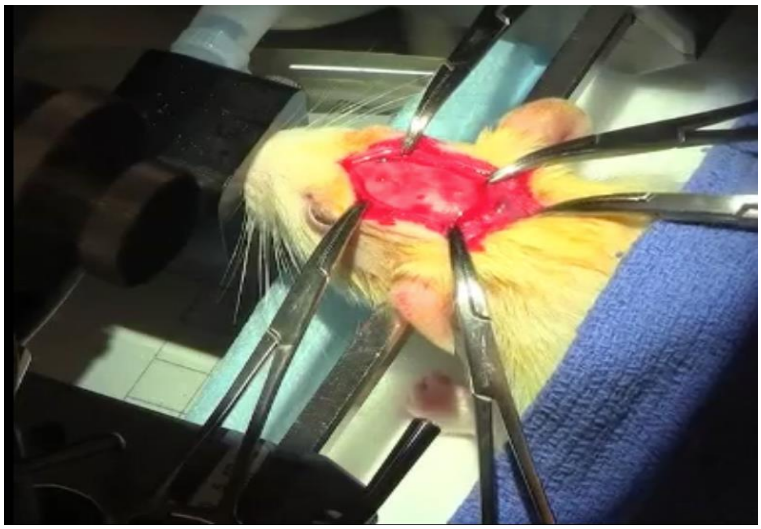


Figure 3.1: Removing the scalp

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 cement was applied to the top of the Gelfoam and was used to create a stable head cap [25-29]. The cement 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.

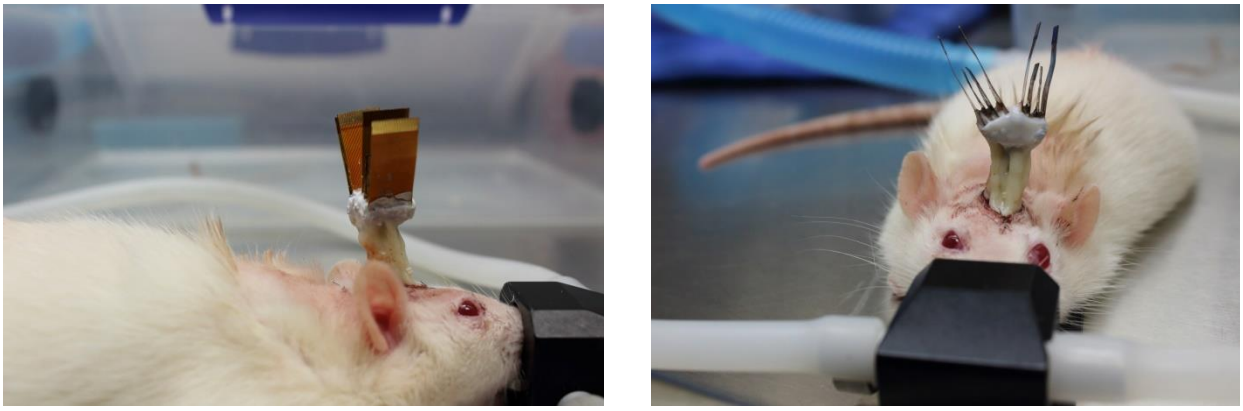


Figure 3.2: Implementation of the ECoG device and UV-curable dental cement was applied to create the stable head cap

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 other 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

RESULTS

The goal of this research is to fabricate a high-density, handcrafted electrocorticography device and use it to record brain signals from the subject by implanting the device. To record brain signals, the implanted device is connected to an electrophysiological signal acquisition system. It was observed from those brain signals that the handcrafted ECoG electrode was able to retrieve signals that are similar to reported data obtained by various researchers who have constructed and used ECoG electrodes with different fabrication methods.

To minimize the amount of noise in the signals, a channel and a notch filter acted as a digital reference on each device. Each device was designed to have multiple pins on the connector to serve as noise cancellation. After observing that results from the test subject shared similarities in waveforms and amplitude range, a reasonable inference can be made that handcrafted devices are be attainable. micro ECoG electrodes are commonly able to read signals as high as 100μV, but the handcrafted devices was able to read signals nearly twice the amplitude of most ECoG electrodes. Showing that a handcrafted device's performance can be similar to micro-machined devices establishes the potential this device can have on various applications [30-33].

4.1 ECoG Acquisition Setup and Software

To record brain signals from the subject, two main systems are required which are the TDT electrophysiological acquisition system (Tucker-Davis Technologies, Alachua, FL) and

Synapse software. To customize signals, components were linked to create custom processing circuits using the TDT 256-channel electrophysiological signal acquisition system. To remove noise, a notch filter is used to remove 60 Hz and similar interferences from the waveforms and re-referenced them to one of the 256 channels. Next, a band-pass filter was used on the signal between 300 Hz and 7000 Hz. The ECoG signal analyses' quality was significantly improved using this signal processing technique.

Figure 4.1: Shows the configuration of the system to monitor and analyze the electrophysiological signals.

Recorded signals were amplified and digitized in PZ5M and then transmitted to the RZ2 Bio Amp Processor for further processing via an isolated, noiseless fiber optic connection. The optical interface ensured fast and reliable data transfer from the PZ5M to RZ2 and to a workstation computer, the following describes the details of each and every system which is used for setup to acquire neuro signals [34].

4.1.1 RZ2 Bio Amp Processor:

The RZ2 Bio Amp Processor has been designed for high channel count neurophysiology recording and signal processing. The RZ2 features two, four, or eight digital signal processors cards. Any card can be either a single standard processor card or a quad-core processor card. Standard single processor cards use a single digital signal processor, where quad-core processor cards use four digital signal processing cores with the potential to more than double the power of the RZ2. All cards are networked on a multiprocessor architecture that features efficient onboard communication and memory access. The highly optimized multi-bus architecture uses four dedicated data buses to eliminate data flow bottle necks all transparent to the user. This architecture yields an extremely powerful system capable of sophisticated real-time processing and simultaneous acquisition on all channels. The RZ2 is typically used with a Z-Series Amplifier (such as the PZ5). High bandwidth data is streamed from the amplifier to the RZ2 over a lossless, fast, fiber optic connection. Both single and quad-core processors cards may include an optical interface for connection to devices such as the RS4 Data Streamer. Each onboard optical connection can support 256 channels at sampling rates up to ~25 kHz and 128 channels at sampling rates up to ~50 kHz. The RZ2 also features 16 channels of analog I/O, 24 bits of digital I/O, two Legacy optical inputs for Medusa Preamplifiers, and an onboard LCD for system status display.

Figure 4.2: RZ2 Bio Amp Processor[34]

The RZ2's Optibit optical interface ensures fast and reliable data transfer from the RZ2 to the PC and is integrated into the device. This system has connectors on the back panel and are color coded for correct wiring. Touch screen facilities are available in the system to configure easy and fast way which shows the information about each DSP, the optical PC interface, a connected PZ preamplifier, and system I/O. A histogram shows cycle usage for each DSP with the bottom section (blue) shows the cycle usage taken up by circuit operation and the top section (pink) shows the cycle usage required for data transfer. If the cycle usage surpasses 100%, a bar is drawn above the 100% line in the cycle use histogram and will persist until the RZ2 is rebooted. In the interface section virtual Status lights display status of the interface (Status), zTrig-A, and zTrig-B. In the I/O blocks a LED will light for an input bit or it will show the logic level for an output bit.16 lights indicate the signal level, green when a signal is present and red to warn that the signal is approaching the maximum voltage. Flashes yellow when no amp is connected and will be light green when the amplifier is correctly connected as the figure shown below.

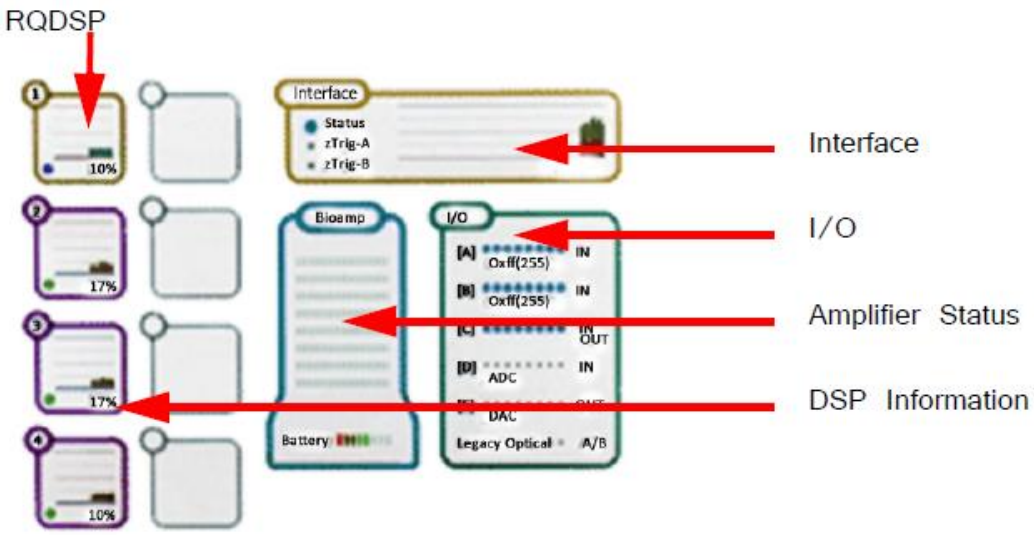


Figure 4.3: Touch screen details of RZ2 Bio Amplifier

Architecture of the RZ2 Bio amplifier is mainly based on the digital signal processor. The RZ2 processor utilizes a highly optimized multi-bus architecture and offers four dedicated, data buses for fast, efficient data handling. While the operation of the system architecture is largely transparent to the user, a general understanding is important when developing circuits in RPvdsEx. As shown in the figure below, the RZ2 architecture consists of three functional blocks. The DSPs Each DSP in the DSP Block is connected to a local interface to the four data buses, two buses that connect each DSP to the other functional blocks and two that handle data transfer between the DSPs [34]. Each standard DSP is connected to 64 MB SDRAM and each core in a QZDSP is connected to 256 MB DDR2. This architecture facilitates fast DSP-to-off-chip data handling. Because each DSP has its own associated memory, access is very fast and efficient. However, large and complex circuits should be designed to balance memory needs as data across processors. Memory use can be monitored on the RZ2 front panel display. The zBus interface provides a connection to the PC. Data and host PC control commands are transferred to and from the DSP Block through the zBus Interface Bus, allowing

for large high-speed data reads and writes without interfering with other system processing. The I/O interface serves as a connection to outside signal sources or output devices. It is used primarily to input data from a PZ amplifier via the high speed optical port, but also serves the Legacy amplifier inputs and digital and analog channels. The I/O Interface Bus provides a direct connection to each DSP and the Data Pipe Bus.

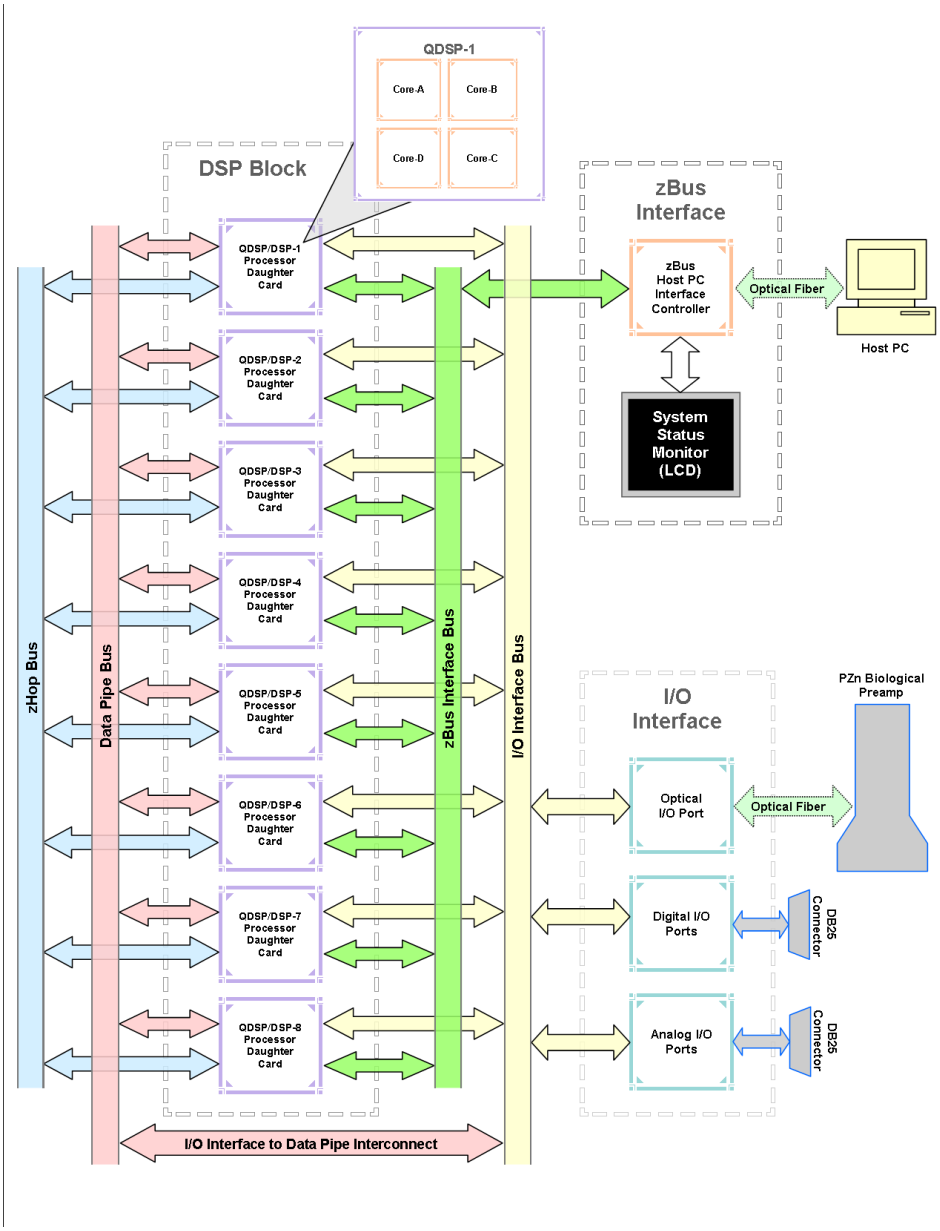


Figure4.4: RZ2 Multi- DSP Architecture Functional Diagram

4.1.2 PZ5M Medically Isolated Neuro Digitizer:

The next system device setup the connection for amplifying and digitizing a neuron signals is PZ5M multi-modal neuro digitizer, suitable for recording a broad range of biological potentials, combining the functionality of high and low impedance amplifiers in a single device. The device is battery operated and with an alternative main power switch which is used for charging the system, with full biomedical isolation for subject safety. The rack mountable PZ5M-512 can be used for simultaneous input of EEG, EMG, ECoG, LFP and Single Unit signals. It is available with 256 channels (PZ5M-256) or 512 channels (PZM-512). By oversampling the signal with very fast instrumentation grade converters, TDT's custom hybrid A/D circuit yields 28 bits of resolution and unparalleled dynamic range. Optional DC coupling offers zero phase distortion across the signal bandwidth. Sampling rate and down-sampling filters can be optimized on each logical amplifier, ensuring the best possible signal fidelity for the intended input type. The 500 mV input range is large enough to accept any biological potential and most stimulus artifacts without saturating. The neuro digitizer inputs are organized into multiple banks of 64 channels. Each bank is electrically isolated, meaning the ground and reference channels are not inherently shared between banks. Multiple banks can be grouped into a single logical amplifier that shares the same settings and ground/reference across each bank in the logical amplifier. There are several different referencing modes, optimizing ground and reference for different types of recording. Each logical amplifier can use the ground as a reference, use a shared reference, use a unique reference on each bank or implement full per-channel differential referencing.

Figure 4.5: PZ5M Medically Isolated Neuro Digitizer

The system PZ5M neuro digitizer accepts inputs from a variety of electrode/head stage combinations via the back-panel connectors. It includes up to eight DB80 connectors, each inputting 64 recording channels (or 32 differential channels) along with ground and reference. Recorded signals are amplified, digitized, and then transmitted via fiber optic connection to the RZ base station for further processing. Configuration information is also sent from the RZ to the PZ5M neuro digitizer across the same fiber optic connection. The PZ5M-512 uses two of these connections, each transferring data for up to 256 channels. A standard system configuration includes electrodes appropriate to the input signals, a connection manifold, PZ5M neurodigitizer and an RZ base station [34]. The diagram below illustrates this flow of data and control information through the system.

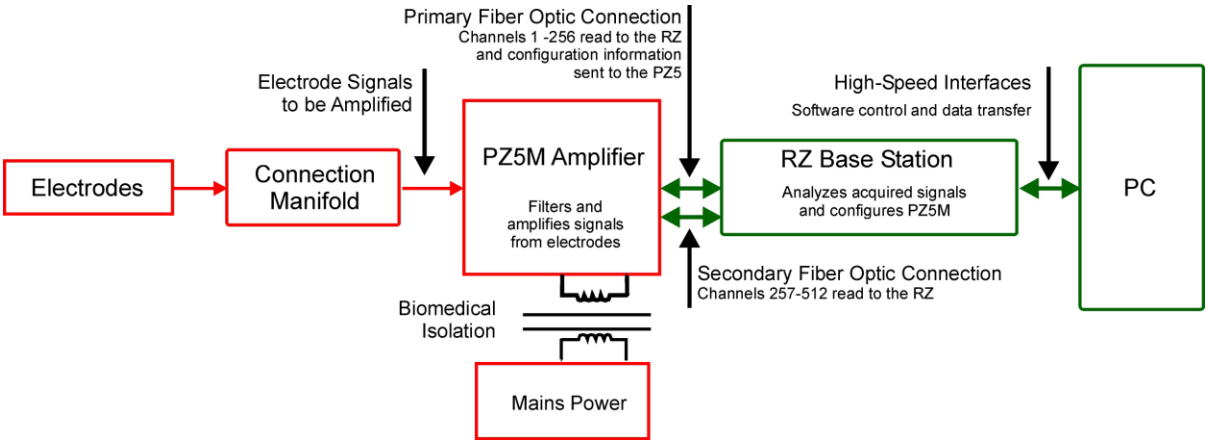


Figure4.6: PZ5M Data and Control Flow Diagram

The hardware setup is done by using 5-meter paired fiber optic cables (up to 256 channels per duplex cable) are included to connect the neuro digitizer to the base station. The connectors are color coded and keyed to ensure proper connections. The diagrams below illustrate the connections necessary for PZ5M neuro digitizer operation, two fiber optic ports are available on the back panel for transferring digitized channels to the RZ device. The first 256 channels are handled by the primary fiber optic port and the second 256 channels (257-512) are handled by the secondary fiber optic port. The connection to the processor can be made in a number of ways, including using the standard PZ Amp Port for the device (RZ2 shown below) and a RZDSP-P port mounted in the back panel of an RZ device.

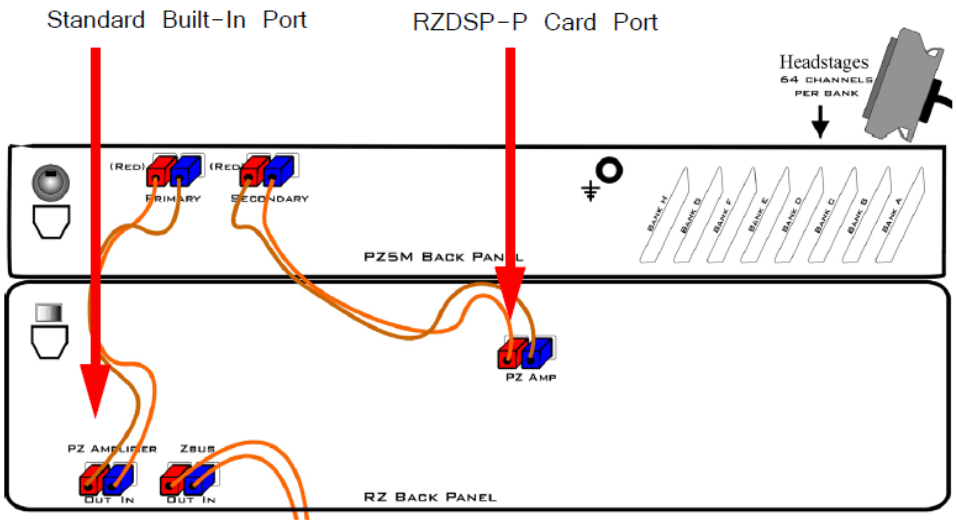


Figure 4.7: System Connection Diagram for PZ5M-512 with RZ2

4.1.3 RS4 Data Streamer:

The RS4 Data Streamer is a high performance data storage array designed to store data streamed from the RZ2, our most powerful processor for high channel count data acquisition. Off-loading data streaming tasks from an RZ2 to the RS4 improves real-time performance and allows you to acquire continuous data over several days or weeks. Access to the RS4 storage array can be provided through a network connection, direct connection to a PC, or data transfer to a USB storage device. The RS4 allows streaming of up to 1024 16-bit channels at rates up to ~25 kHz and fewer channels at rates up to ~50 kHz. Streamed data is stored as individual channels and can be stored in different numeric formats (Short, Float, etc.). Stored data can be easily reincorporated into the OpenEx data tank format for post processing. The RS4 is available with either 4 terabytes or 8 terabytes of storage and features 1 or 4 streaming ports. Data is transferred to the RS4 through its streaming ports located on the back panel of the device. A special version of the RZ2 provides matching ports used to connect and stream data to the RS4 [34]. These ports ensure fast and reliable data transfer from the RZ2 and are color coded for

correct wiring. Communication to the RS4 is provided through a touch screen user interface independent from the TDT system. The RS4 contains an integrated switched-mode power supply. The power supply auto-detects your region's voltage setting and no further configuration is needed. A switch located on the back panel of the RS4 is used to enable/disable the power supply.

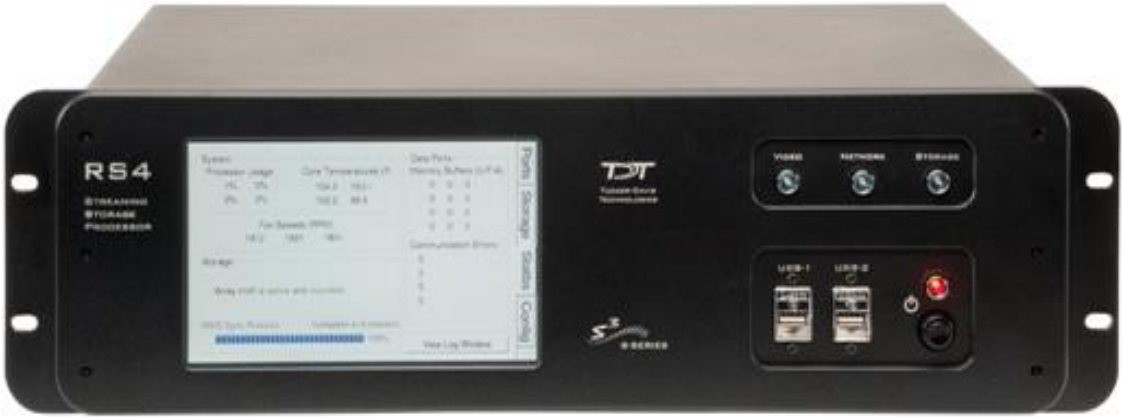


Figure 4.8: RS4 Data Streamer.

Hardware requirements for connecting the device include: RS4, RZ2 equipped with at least one streaming port, and one fiber optic cable for connection between the RS4 and RZ2. Optional requirements for accessing data on the RS4 include a PC equipped with an Ethernet port connected to a local area network. In the diagram below, a single RZ2 provides one streaming input to the RS4. Additional RZ2 devices can be connected to the same RS4 provided it has vacant streaming ports (B, C, or D) available. The RZ2 is also connected to a preamplifier and PC. The fiber optic cables are color coded to prevent wiring errors.

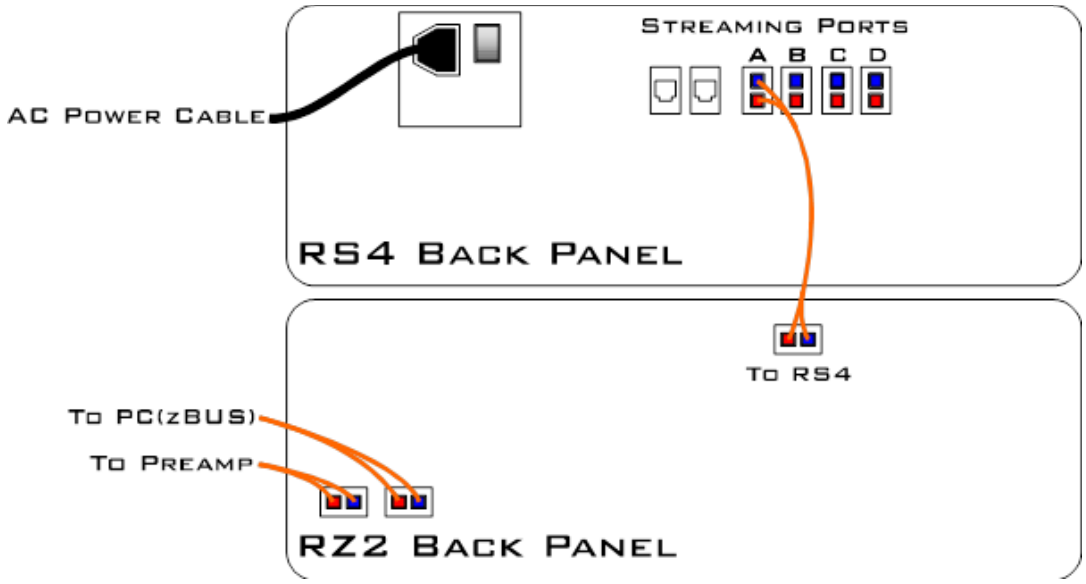


Figure 4.9: RS4 to RZ2 Connection Diagram

4.1.4 IZ2 Stimulator:

Figure 4.10: IZ2 stimulator

This IZ2 used for activating the brain signal by using electrical shock that leads to an brain activity. The IZ2 Stimulator converts digital waveforms into analog waveforms as part of a computer controlled neural micro stimulator system that delivers user-defined stimuli through multichannel electrodes. The IZ2 can output either a voltage-controlled waveform or a

current-controlled waveform and provides feedback of the actual voltages delivered to the electrodes. The IZ2 is a high current range version of the IZ2 and is available with 128 stimulus channels. A typical system consists of a Stimulator (IZ2-256) a battery pack and an RZ processor equipped with a specialized DSP and additional fiber optic connector on the back panel. The block diagram below illustrates the functionality of the system.

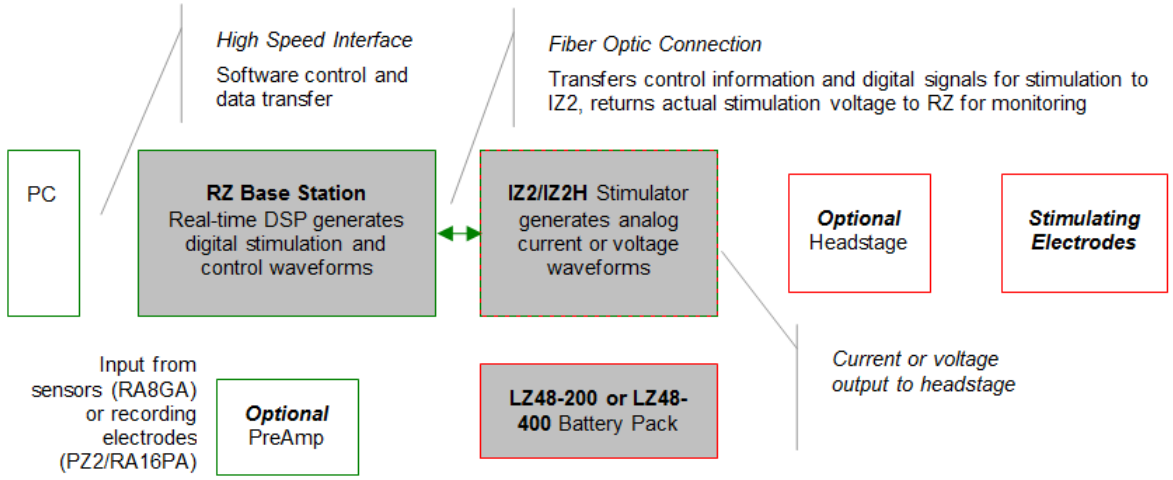


Figure 4.11: Functionality of the system

Stimulation control waveforms for each electrode channel are first defined on the RZ base station and digitally transmitted over a fiber optic cable to the battery powered stimulator. On the stimulator, specialized circuitry for each electrode channel generates an analog voltage waveform. In current mode, the driving voltage is adjusted according to Ohm's law (V=IR), where I is the desired stimulation current and R is the electrode impedance. Eight analog-to-digital (A/D) converters on the IZ2/IZ2H read the output voltage for a chosen bank of channels and send that information back to the RZ for monitoring. In Current mode, the IZ2 Stimulator System is capable of delivering up to 300 µA of current simultaneously across up to 128 stimulating electrodes (impedance up to 50 kOhm). The IZ2H Stimulator System is capable of delivering up to 3 mA of current simultaneously across up to 16 stimulating electrodes

(impedance up to 5 kOhm). In Voltage mode, both the IZ2 and IZ2H are capable of delivering up to +/-12V across each individual electrode. Individual channels can be open circuited or shorted to ground, A 1 MOhm shunt resistor to ground can be applied to all channels. This is most useful for electrodes with very high impedance and that would normally produce large quiescent voltages when in Current mode.

The IZ2 stimulator features128 channels that can deliver arbitrary waveforms of up to 80 kHz bandwidth, each channel uses PCM D/As to ensure sample delays of only 4 samples and square edges on pulse stimulation waveforms. The stimulator uses a rechargeable battery from the battery pack (VC) for logic control and D/A converter operation. Special circuitry on the stimulator draws on the high voltage batteries (VA and VB) to convert low voltage waveforms from the D/A converters to constant voltage or constant current waveforms as shown in the diagram below

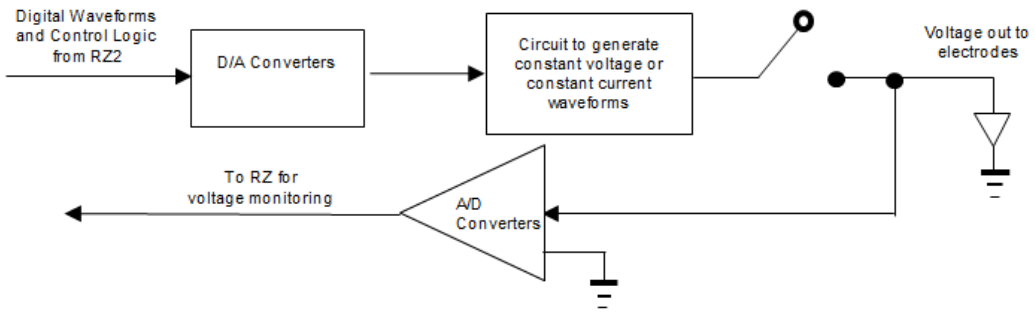


Figure 4.12: Stimulator Diagram

Setup the hardware connections by ensuring TDT drivers, PC interface, and RZ and Zbus devices are installed and configured according to the installation guide provided with the system. Connect the battery pack cable to the back panel of the stimulator via the connector labeled battery, as shown in the diagram below.

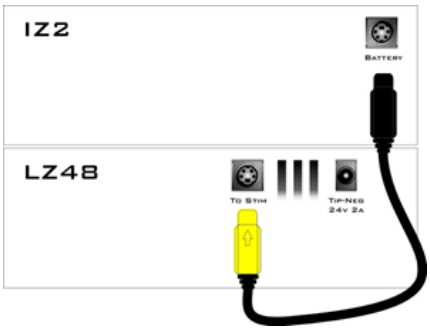


Figure 4.13: Battery connection for stimulator

Connect the stimulator to the base station using the provided fiber optic cable Connect the fiber optic cable from the IZ2/IZ2H fiber optic port labeled Fiber to the fiber optic port labeled To IZ2 on the back side of the RZ. Be sure to note the difference in the two sides of the fiber optic cable connectors and ensure they are inserted with the correct side up. Connect the DB26 output connectors on the stimulator to the stimulating electrodes using your preferred method such as direct wiring or a custom pass through connector (available from TDT). Power on the base station, then power on the LZ48 using the power switch on the LZ48's front panel. This will also power on the stimulator. Ensure that the LZ48 rechargeable batteries are fully charged before starting your protocol. The hardware is ready for use. If using the system with other devices, such as a switching head stage or preamplifiers, see the documentation for those devices for hardware connection information.

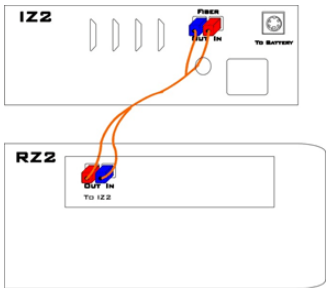


Figure 4.14: Connection of stimulator

4.1.5 ZIF Clip:

ZIF-Clip® standard head stages are analog head stages recommended for use with probe impedance that range from 20 Kohm to 5 Mohm. They are designed to connect directly to a PZ preamplifier but may be connected to an RA16PA with the use of an adapter. Analog signal are buffered inside the head stage and digitized on the preamplifier for transfer to a base station processor RZ2. By default, ground and reference are separate on all ZIF-Clip® headstages yielding a differential configuration. Reference and ground may be tied together on the headstage adapter or ZIF-Clip micro wire array for single-ended configurations. Head stages are design that ensures quick, easy connection with almost no insertion force applied to the subject. It contacts seat inside the probe array and snap in place, firmly locking the head stage and probe with very little applied pressure. These self-aligning head stages provide long lasting low insertion performance for a variety of channel number and electrode configurations. An aluminum finish provides increased durability. The following are the commercially available ZIF-Clips from TDT systems**.** ZC16 – 16,32,64,96,128 channel Aluminum ZIF-Clip head stage [34].

We are using two 128 channels head stages clips as the device is of 256 channels. The figure below shows the standard ZIF Clip. These are connected to the head stage by firmly pressing and holding the back to open the head stage, Align the notch guide of connector to the black square guide of the fully opened head stage then move head stage into position then press the front of the head stage together to lock the connector in place. You should hear an audible click when the locking mechanism is engaged.

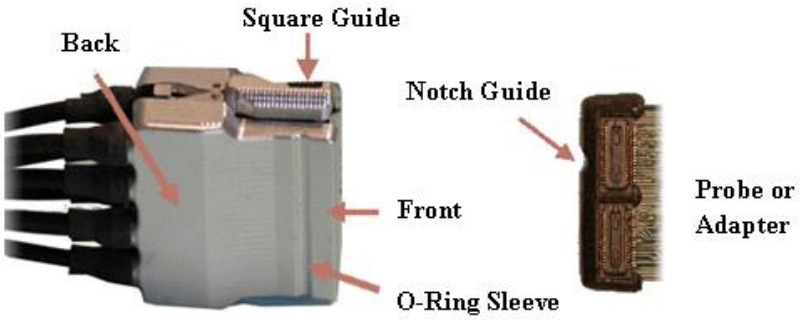


Figure 4.15: Standard ZIF-Clip and adapter

ZIF-Clip 128 channel head stage pinouts are looking through the head stage shell (or into a matching board connector). All board dimensions are in millimeters and are identical for both sides, board thickness is 0.75 mm, and connectors are centered as shown below.

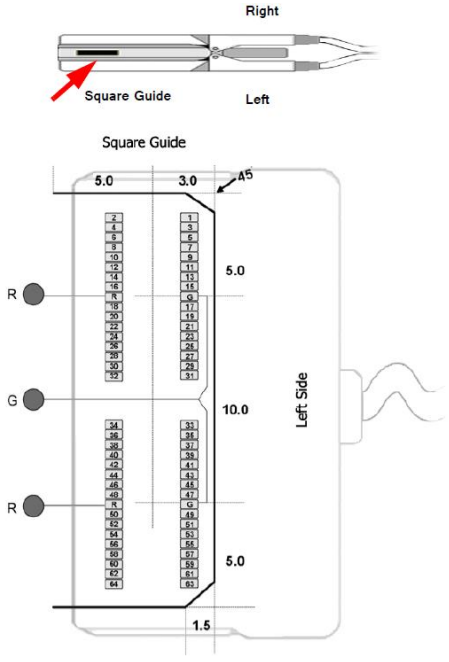
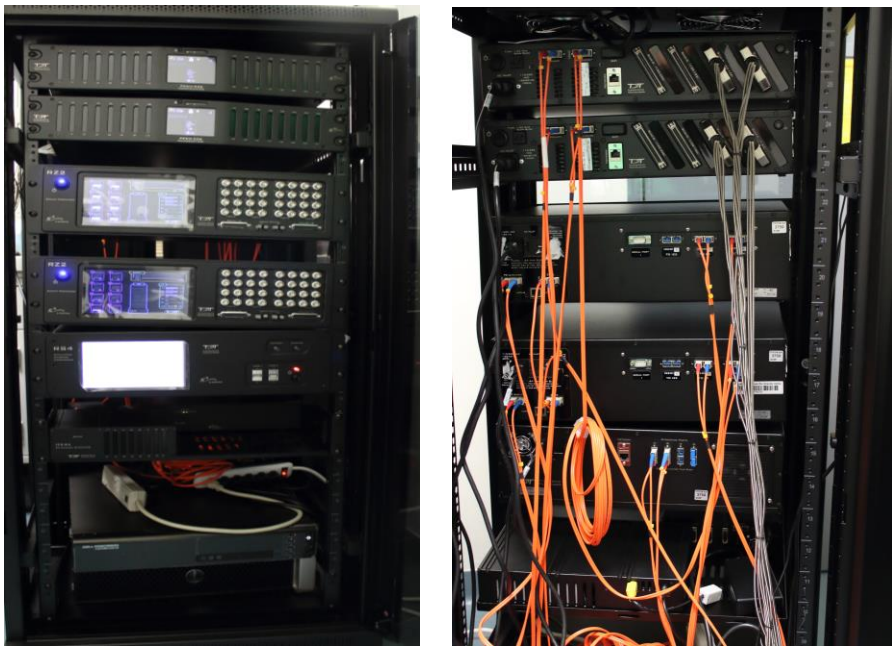


Figure 4.16: ZIF-Clip Pinpoints

By using this information we setup the devices using optical fibers, as shown in the following figures. Figure (a) shows the front view of the device connections and figure (b) shows the back view.



(a) (b)

Figure 4.17: different views of TDT system (a) Front (b) rear

4.1.6 Synapse Software:

The software that is used to run the TDT hardware is called Synapse. Synapse is the software used to design, manage, and collect data from neurophysiological experiments. Synapse has advanced automation, underlying relational database, and sophisticated hardware interface. The streamlined interface can be used to adjust hardware choices, such as the number of recording channels, operational modes, and input sources. As we make selections to fit the experiment, Synapse updates the design time window with relevant choices to complete the configuration for basic neurophysiological bundles that includes high-channel LFP, ECoG, and EEG recordings ranging from 0µV to over 200µV. 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. We discussed below how to operate the synapse software for recordings by using TDT synapse manual which gives every detail information getting started with software, install the software in the computer using CD-ROM are by downloading from the TDT website. PC requirements for installing the software is 2.0 GHz processor speed, 2.0 GHz RAM and 1 GB hard disk after installing.

Before running an experiment we must allow Synapse to gather information about the System hardware components in your system. TDT processors come in many configurations that have different abilities. Once Synapse knows which devices are using, it will keep track of the device details. In Synapse, hardware system is referred to as the ‘rig’ and it is remembered each time you open the software. The first time launching the software, the Rig Editor is displayed automatically [34]. Configuring the rig starts with letting Synapse detect your system devices.

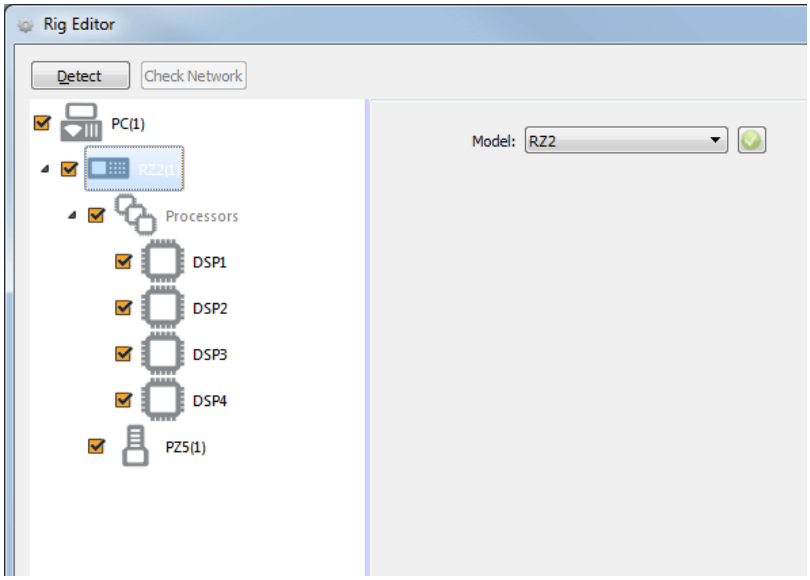


Figure 4.18: Rig Editor RZ2 Selected

Detected devices in your hardware configuration are displayed in a hierarchical diagram. Configuration settings for the selected (highlighted) device are displayed in the area to the right. There are some device and configuration information that Synapse can't automatically detect. Based on the equipment detected, such as the RZ2 and DSP-I, an IZ2 stimulator is likely to be a part of the attached system. Synapse added the IZ2 to the diagram, but it hasn't been enabled. You would need to click the check box to enable it. You can also enable or disable devices to control whether they are automatically added to the Processing Tree in new experiments. Only enabled devices are added by default. Disabled devices can still be added later and enabled manually in the Processing Tree.

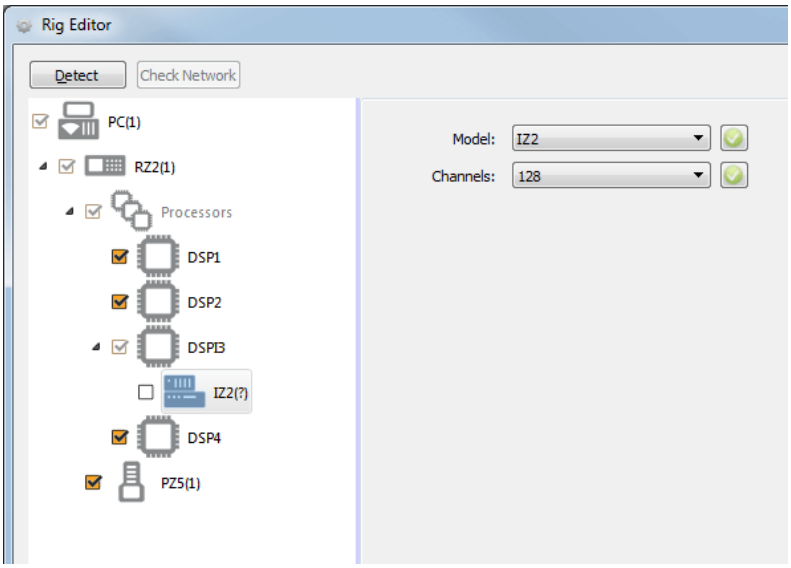


Figure 4.19: Rig Editor: IZ2 Selected

The most common item need to configure is your PZ amplifier, select the number of channels available in your amplifier. In the rig, your device settings should exactly match your hardware. You'll be able to reduce the number of channels actually used or make other experiment-specific changes to settings in individual experiments. When everything is configured, you can update the rig by clicking OK to commit the changes and return to the

Processing Tree. After the rig is initially configured, you won't need to repeat this process in future sessions unless your hardware changes. If you do need to make changes, you can return to the Rig Editor, using the EDIT RIG command on the main menu.

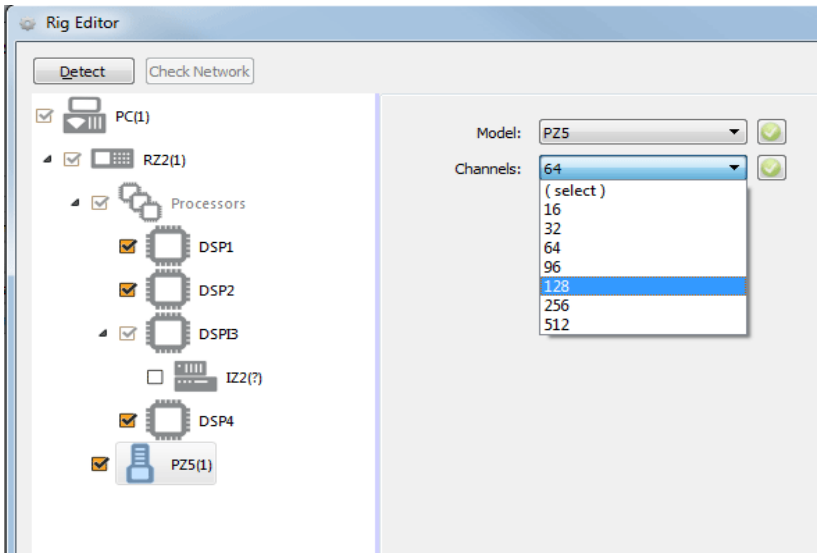


Figure 4.20: Selected Amplifier Icon with Channels Drop-Down Menu

Templates are pre-built experiments created by TDT to speed up experiment creation. Each Synapse template is a basic working experiment that can be run as configured or modified to meet our needs. We can access any saved experiments by clicking the EXPERIMENT button on the command bar, then clicking MORE. Templates are stored in special category folders within the templates folder. With this templates a current experiment window is designed for current Experiment or Experiment Selection in similar to a standard Windows Explorer window with folders, or categories, on the left and experiments in the category on the right as shown in figure.

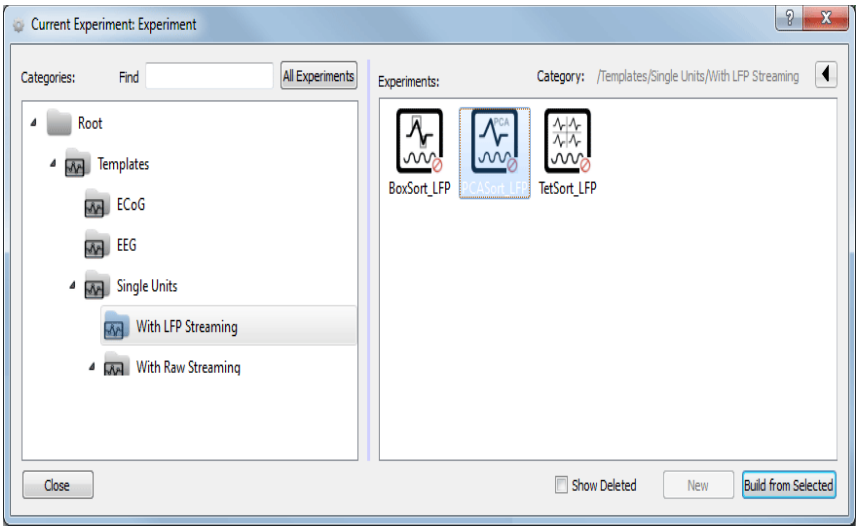


Figure 4.21: Current Experiment Window

After that we start new experiment for recording signals from the subject. In the new experiment there are mainly two task blocks are added to the Processing Tree beneath the PZ amplifier, one for LFP filtering (Lfp1) and another for PCA spike sorting (Neu1). The Processing Tree represents the path of data flow and in the example below the hierarchy shows that the LFPs and Single Units are being acquired in parallel from the same signal source (PZ5). When a block is selected in the tree, its configuration options are displayed in the Options area to the far right.

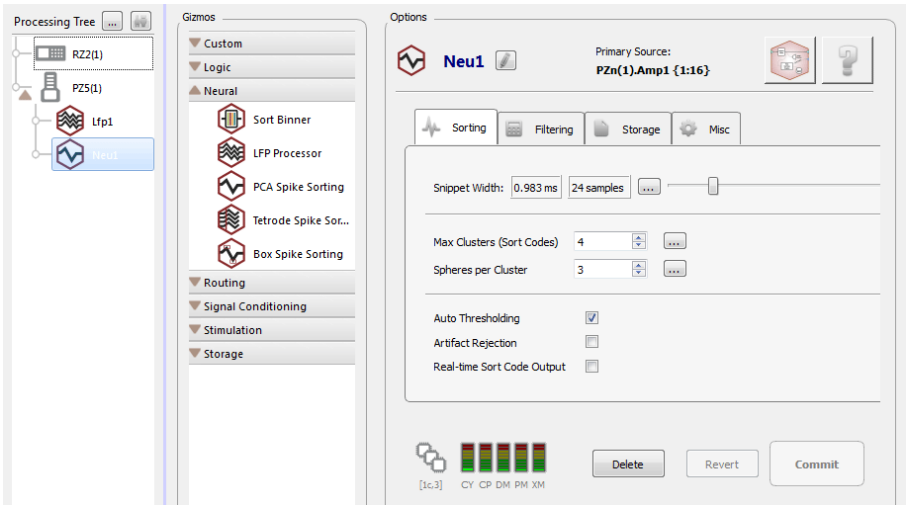


Figure 4.22: Viewing the New Experiment

Before you can begin collecting data, the new experiment needs to be named and saved. In the dialog box you can enter an experiment name, description, or add notes. The experiment is saved under the ROOT directory. You can add and move categories and experiments using right-click menus. When you return to the main design time interface, the experiment has been saved, a new tank name is displayed under the tank icon, and the RECORD button is available.

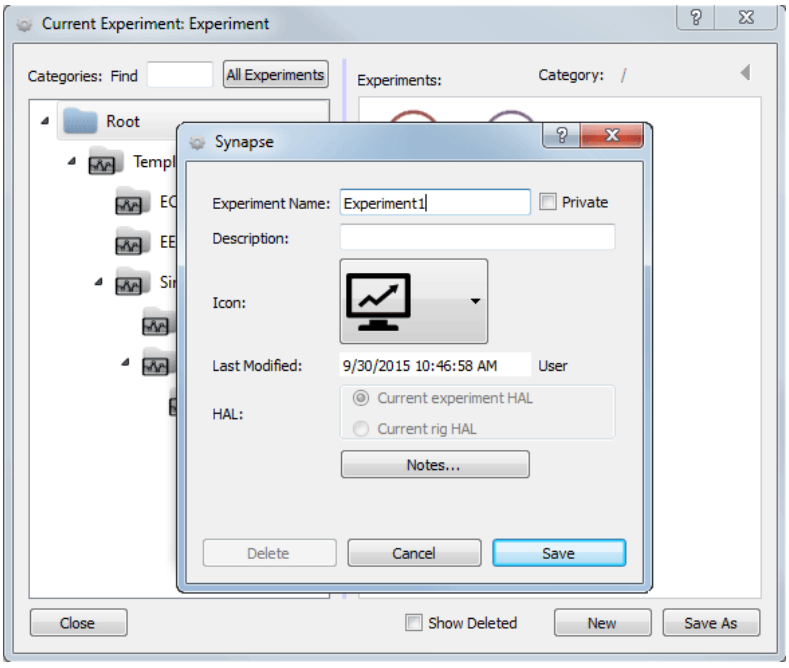


Figure 4.23: Naming the experiment

The next step in the software is to add the name of the subject on which we are going to record. To add a subject, click the SUBJECT button in the command bar, then click NEW, then enter a name in the SUBJECT NAME field. You can also enter a description, password, or notes and choose an icon. When you're done adding information, click SAVE. The steps to add users and subjects are same.

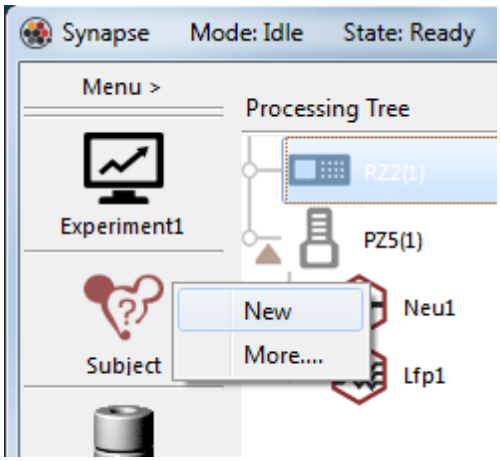


Figure 4.24: Adding Subject Name

When an experiment is fully configured and saved, the PREVIEW and RECORD buttons are enabled. In preview mode you can display data, adjust plots, and change runtime settings without any of the data being permanently stored to the data tank. This is particularly useful for tasks like spike sorting, where you might want to establish the sorting parameters before collecting data. For more straightforward tasks, like recording streamed data, you might choose to skip preview and go straight to record mode. There are three mode buttons as Idle Mode in this mode devices are not loaded and are not running just viewing. In Preview Mode data is acquired, but deleted after the recording ends. The final mode is Record Mode where data is acquired and stored to the data tank permanently. The following picture shows the mode buttons.

Figure 4.25: Mode Buttons

Lastly, after configured everything we can able to view the runtime window includes tabs with the main data plot and runtime controls for each block. The data displayed is pulled directly from the hardware and sent to the display in parallel with data storage. The basic window includes a plot for each type of data being stored and each plot is automatically configured according to the type of data, for example snippet, streamed waveforms, or epoch events. We might need to scale the plots to display the waveforms appropriately. The second tab in the template is derived from the PC sort block and is an interactive display with plots for cluster cutting and provides runtime access to many of the configuration setting, such as filter values, display options and even the sorting algorithm. By default, Synapse saves the state of all experiment variables, including filter settings, threshold values, and cluster definitions in its relational database during each recording sessions. Any changes made to a setting is logged in the database as well as in the user or subject information. All of these values are retained and saved as part of a history of the experiment. This database of experiments and history of its past states support several useful features including persistence and history browsing, filtering, and export features.

4.2 Recording Brain Signals

By using the TDT 256-channel acquisition system and Synapse software, we recorded brain signals using the 256-channel ECoG electrodes. To set up the acquisition system, one end of a TDT zif-clip digital head stage is connected to a head stage adapter on top of the rat's head and the other end is connected to PZ5M amplifier to boost and digitize the signals. Using Synapse, we could control the signal presentation and data acquisition, 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. A notch filter was used to remove noise during the recording. We obtained the LFP signals for all neural signals obtained from the 255 electrodes of the ECoG. One out of 256 channels (Channel 2) was used as a digital reference signal to further remove any possible noise. We obtained the local field potentials within the amplitude range, 100μV to 200μV. The differential signals measured between 255-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.

Figure 4.26: Recorded signals that were made after device implantation

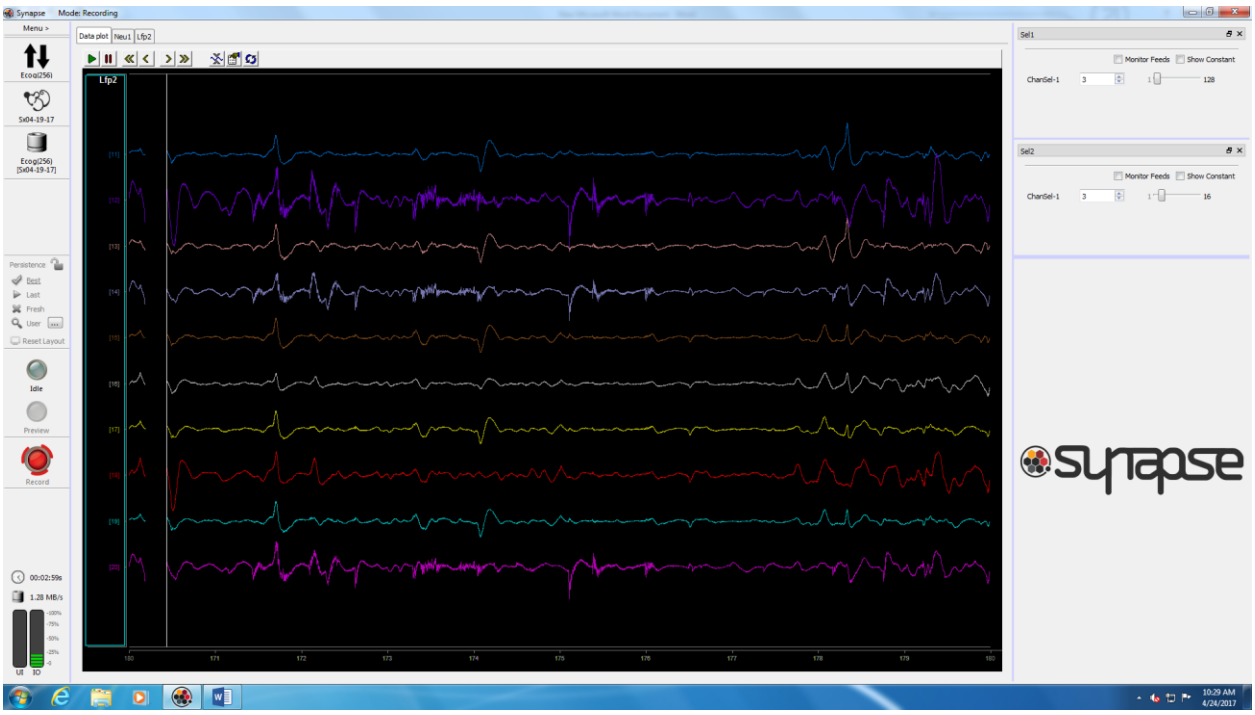


Figure 4.27: Recorded signals that were made after device implantation in a closer view of 10 channels with time period of 10 sec

These LFP signals on rat remained stable and within 100-200µV on each channel throughout most of the recording. Similar results can be observed one week after a handcrafted device was implanted on the rat as shown in the figure below.

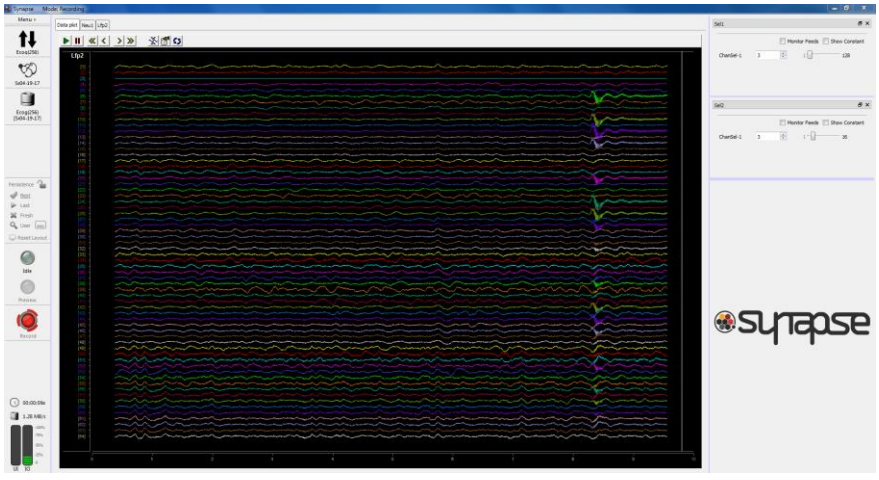


Figure 4.28: Recordings of the rat one week after surgery

It is generally seen that micromachined devices gain advantages against non-micromachined devices, especially when fabricating at 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 previous figures and signified the success of the handcrafted device. These responses were obtained after implanting the electrodes on the rat's cortical surface and confirm the stability and spatiotemporal features of the handcrafted micro device. 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 V

CONCLUSION

We have presented a high-density (256 Channel) handcrafted Electrocorticography design that has high spatial resolution and small area. Generally, this type of device was fabricated with a cleanroom facility or a micromachined fabrication technique. Micromachined techniques such as photolithography, etching, and deposition can be complicated and lengthy procedures such that each step could take several days to complete depending on the number of channels and various 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 and simultaneously recorded. Some researchers may not be able to purchase commercially available ECoG electrodes, which usually cost over $1000 per device. Whereas we have developed a handcrafted 256-channel ECoG electrode arrays without these cleanroom or micromachined techniques for recording brain signal with high spatiotemporal resolution. As this handcrafted device was constructed from commercially available material, a user can also make modifications to the design to fit onto various cortical surfaces, improving the accuracy and reducing the making time. Since handcrafting device only needs several hours to prepare, a completely functional micro-ECoG electrode can be uniquely designed and fabricated as necessary. After implementing the electrode onto a *Lewis* rat, it was confirmed that it remains stable and non-penetrative with 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 256-channel, 512-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 inter electrode 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 VI

FUTURE RESEARCH

The terms electrocorticography (ECoG) defines the technique of recording the electrical activity of the cerebral cortex by means of electrodes placed directly on it beneath the skull. Brain–computer interfaces (BCIs) convert brain signals into digital data that communicate a user's intent. In these BCI applications, the future research is a breakthrough for many kinds of disabilities.

We implanted the handcrafted, 256-channel ECoG electrode on a 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 most requirements. The device is also adjustable, minimally invasive, and quick to fabricate with a minimum expense. The size of the device can also be controlled by changing the length, diameter, and number of the wires that could be applied to investigate the puzzling concept of physical structures affecting the quality of LFPs in electrodes. 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. Since the electrode is handcrafted, users can design ECoGs with higher electrode density without more complications and the micro-fabrication limitations. A reliable performance, flexible design, and simplified fabrication are highly required for multidisciplinary biological applications. A long-term applicable device is also necessary 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 thedevice 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.

We have also 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 and higher density such as from a 512 to higher channel micro ECoG electrodes. It is preferable to acquire more information for BCI applications so to minimize the complications that might arise and to increase precision and accuracy.

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