**Design Foundation Document**

WNR

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1. **Design Context Review**

About 10% of the world’s population suffers from epilepsy, a brain function disorder that causes neurons in patients’ brain to fire at an abnormal rate with unregulated patterns. Diagnosis of this condition often involves a medical procedure called electroencephalogram (EEG), which detects the electric pulses created by the neurons.



Figure 1. A person demonstrating a particular scalp EEG device[1]

For most patients, it usually suffices to use scalp EEG to confirm diagnosis. Scalp EEG, also known as Extracranial EEG, uses non-invasive electrodes which are stuck to the surface of the patient’s scalp to detect brain wave signal. For these patients, which account for 70% of the total epilepsy patients, their illness can be controlled through therapy and drugs. However, for the rest 30% of epilepsy patients, the drugs do not work and surgical procedures must be done to remove certain problem sections of the brain to control the epilepsies. If a patient with epilepsy is being considered for epilepsy surgery, it is often necessary to localize the source of the epileptic brain activity with a resolution greater than what is provided by scalp EEG.

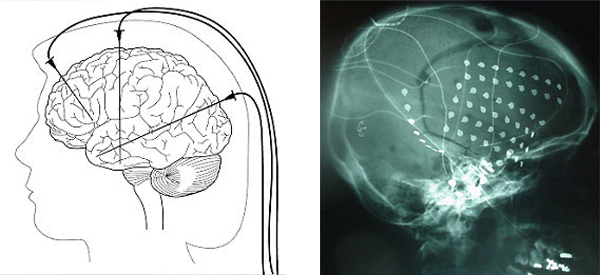


Figure 2. (left) Illustration for Intracranial EEG operation; (right) X-ray of implanted Intracranial EEG electrodes[2]

Scalp EEG does not provide the resolution of brain activity data required for neurosurgeons to operate on as the cerebrospinal fluid, skull and scalp smear the electrical potentials from the scalp electrodes. To perform the epilepsy surgery, neurosurgeons typically first implant grid of electrodes or penetrating depth electrodes under the dura (brain) mater, through either a craniotomy or a burr hole. The recording of these signals is referred to as electrocorticography (ECoG), subdural EEG (sdEEG) or intracranial EEG (icEEG)--all terms for the same thing. The signal recorded from the intracranial EEG is on a different scale of activity than the brain activity recorded from scalp EEG. Because signals are collected by directly contact with electrodes, Low voltage, high frequency components that cannot be seen easily or at all in scalp EEG can be seen clearly in EEG.

The current method of collecting intracranial EEG data from a patient’s brain is through a tethered cord to a monitoring and recording device on premise at a clinic or hospital. The intracranial EEG records the spontaneous electrical activity of the brain measuring voltage fluctuations resulting from ionic current within the neurons of the brain as recorded from multiple electrodes. This tethered EEG procedure is high invasive and disruptive to patients’ lives as they are confined to a hospital bed for several days to a week while doctors wait for very small windows of epileptic episodes to occur to gather a limited amount of useful information.

Wireless Neural Recorder’s (WNR) objective is to create a wireless monitoring solution to the problem of neural recording, allowing users the freedom and mobility to return to their normal lives at home while also enabling doctors to obtain sufficient neural data required to treat their patients’ conditions effectively.

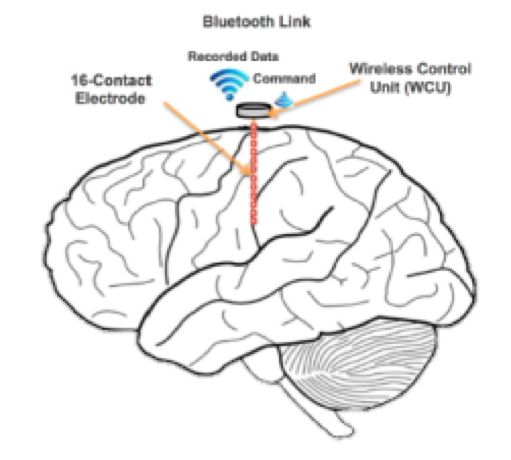


Figure 3. Illustration of a wireless neural electrode to be implanted in the brain

The figure above provides an illustration about the position of the final device in relation to the brain after it is implanted. Before we look into our proposed system for a wireless neural recording device, we will provide an overview of the components of the more common wired equivalent. The general system diagram flow of wired neural recording machines is shown below.



Figure 4. System block diagram of a wired neural recorder

Data from the electrodes (fig. 4a) is digitized by the analog front end (fig. 4b) and can be sent directly to the server (fig. 4c). Generally, the server will be running continuously from a inexhaustive power supply, and thus, will not have any power constraints. Since transmission is not through an intermediary medium, like air or water, that separates the where the data obtained and where the data needs to be transmitted, the data can be sent directly to the server for storage and analysis, without any need for preprocessing or any additional overhead.

However since the goal of our design is to provide a wireless solution to neural recording and data storage, our system design becomes more complicated.



Figure 5. System block diagram of a wireless neural recorder

The figure above shows the proposed design of our entire system. The front-end remains relatively the same. Electrode data is sampled by the analog front-end, which accounts for low-noise signal amplification and DC offset rejection that arises from the nature of brain signals and the electric potential difference that forms at the contact point between the electrode and the brain[3]. Once the data is digitized, it is passed into a CPU or microprocessor (fig. 5c) where the data is preprocessed for transmission. When the data has been processed for transmission, it is passed to the wireless transmitter (fig. 5d) and transmitted across the air medium (fig. 5e) to a server (fig. 5f), which can be a module near or on the patient’s body. In the server, the data can be stored, viewed, and analyzed for deviations from standard brain activities. It was specified by Dr. Nitin Tandon, our sponsor from UTHealth, that the device should ideally fit within a 5 x 5 x 10 mm container (maximum dimensions was specified to be 8 x 8 x 10 mm), which is an extremely aggressive size constraint and limiting factor.

Raw pulses observed from electrodes are generally in the microvolt range and require amplification to be accurately digitized[4]. Multiple problems arise because of this. Before sending the signal to be digitized in the analog to digital converter (ADC), we must send the signal through a circuit that amplifies the signal, while keeping a good signal-to-noise-ratio[4]. Proposed solutions exist in academia and in the market[3][4][5][6], so it is a matter of choosing the implementation that best suits our system’s needs. Additionally, when electrodes come in contact with the brain, an electric potential difference or DC offset is created that can be as great as a few volts[4]. Recording the signal without removing the DC offset will generally yield poor results because the DC offset is orders of magnitudes greater than the actual brain pulse[3]. Therefore, the analog circuit we create for the front end of our system must also reject as much DC offset as possible.

Beginning from the microprocessor preprocessing section of the system block diagram (fig. 5c), there are deviations from the wired neural recorder system (fig. 4). At this stage, the data will be processed based on the precision of the sampled data points as well as the limitations of the wireless transmission protocol we decide to use. For instance, one viable transmission protocol that we are considering is Bluetooth Low Energy. Bluetooth Low energy has a maximum data transfer rate of 260 kb/s[7]. If we decide to sample each contact point with a precision of eight bits, then the channel can support a data point transfer rate of 32,500 data points per second. This means if we have more than 32 channels or contact points sampled at 1 kHz, all collecting and transferring data to the same server, then the channel capacity for bluetooth low energy will be incapable of supporting the entire offered load from the electrodes, and the system will incur data loss. Then in order for the transmission rate to keep up with the sampling rate from all nodes in the array, the data coming in for transmission has to be downsampled or compressed in some other way in order to reduce the amount of bits transmitted across the channel.

Given our system design requirements, we have identified three main challenges that we will face in designing our device: wireless data transmission, power, and safety regulations. Our wireless data transmission protocol must be power efficient while having enough bandwidth and transmission speed to send 128kb/s. Five potential wireless options were considered but we decided to go with Bluetooth Low Energy as it provides adequate communication security and power efficiency[8]. It has high range, medium bandwidth and medium data transfer rate but high power efficiency. It is the best tradeoff in terms of performance to power, while also being secured via encryption and other privacy protocols. Power is another major concern as we will be sampling and sending data very frequently at the detriment of our battery life. Given our small form factor, the batteries for our application will be limited in size, hence batteries need to be high density, high efficiency batteries similar to ones found in pacemakers. Each electrode and wireless control unit should have the capability of sampling and transmitting data for at least 24 hours. However, there are very few batteries that fit within the size of 5 x 5 x 10 or 8 x 8 x 10 mm that provides significant amounts of power, so the battery will be one of the major limiting factors of the project. If power consumption goes above what the batteries can provide, then a method for reducing the system’s power, most likely by decreasing the rate at which data is transmitted to the receiver, must be implemented. Lastly our device has to conform to multiple standards and guidelines set by the FCC, FDA, and HIPPA. Our medical device has a communications link, so it not only has to conform to extensive safety testing perform by the Food and Drug Administration (FDA)[9] but also compatibility testing by the Federal Communication Commission [(FCC)[10]](http://www.fda.gov/RegulatoryInformation/Guidances/ucm077210.htm). We are working with patient data so we also have to ensure that we are HIPPA compliant and securing our data with no unauthorized access outside of patients and approved medical professionals[11].

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In order to best prepare ourselves for marketing our product to professional health-care providers, research has been done on the procedure with which hospitals purchase medical devices. Hospitals generally have a well established pipeline for acquiring new equipments[13]. First, hospitals’ directors undergo a strategic planning phase during which the they decide which type of medical devices that the hospital needs. After strategic planning, a rigorous assessment procedure is performed on multiple competing existing technologies with cost-benefit assessments. After the technology has been assessed and the final decision of purchase has been made, the technology acquisition phase of the purchasing process is engaged and final contracts are signed with medical device manufacturers.

With the knowledge of how our customers will assess our products, we look at our competitors against whom our product will compete for the final contract. For our wireless neural recorder, we found that are very few existing commercial EEGs rated for wireless human brain wave test data recording and monitoring. This is because prevalent EEG technology is generally wired and limiting in terms of the freedom and dignity of epilepsy patients, and wireless intracranial EEG recording is a very new field with very few competitors. We identified our two main competitors to be DEUTRON and NEUROPACE, but both their technologies have limitations that make their options less than ideal. We will discuss our competitors’ options more in depth in our market analysis sections.

WNR envisions a future where epilepsy patients no longer have to spend days painfully confined to a hospital bed just so a EEG electrodes can gather data to send to a computer; but, rather a future where patients can go about their daily lives at home while an implanted EEG wirelessly sends data to a mobile recording device in real time both efficiently and securely using state-of-the-art technologies allowing for more extensive real world epileptic data collection.

**Market Analysis**

The target market that our project focuses on is the 10000 health care providers and the 150 research institutions that utilizes EEG(intracranial and extracranial EEG) machines for research purposes. The market value with wireless EEG machine will be approximately $90 Million dollars with an annual projected revenue of $9 Million dollars.

The total market for EEG is divided into two market segments. Scalp EEG and Intracranial EEG operations. As discussed in Design Context Review document, scalp EEGs uses non-invasive electrodes that are stuck to the scalp of the patients. Scalp EEGs are generally for patient with less severe epilepsy symptoms and account for approximately 70% of the patients. Intracranial EEGs utilize implanted electrodes for better EEG readings, which involves a surgical procedure where the electrodes are buried underneath the scalp. The Intracranial EEG procedure is only used when the patient suffer from severe epilepsy and scalp EEG was unable to provide a clear reading of the brain pattern of the patient. Since the product that we are developing are focused on intracranial EEG applications, our target market segment is therefore the intracranial EEG market within the overall EEG market.

The Intracranial EEG market is then further divided into four components:

1. Hospitals
2. Clinics
3. Research Institutes
4. Household usages

Since our device is used for invasive medical monitoring procedure and the implantation of the probe requires surgical procedures, the product will not household usages.

As per research institutes, there are about 150 research institutes in America that engages in neuroscience research which would require intracranial EEG operations. In contrast, there are approximately 5686[13] hospitals and 4084 clinics[14] in America. Given the huge difference between sizes of the different market segments, the contribution of Research Institutes to our market size is negligible. Therefore, our main focus for market analysis is on Hospitals and Clinics.

Since EEG is a standard medical procedure for diagnosis of a spectrum of illnesses, it is reasonable to assume that each health-care provider - hospitals and clinics - will carry EEG machines. The amount of EEG machines per health-care provider is roughly estimated by the total number of EEG operations performed yearly in America. As reported, there are 10-25 Million EEG operations performed every year in the United States[15], which averages to around 17.5 Million operations/year. Given that there are around 10000 health-care providers which have the capability of performing such operations, the number of EEG operations performed per day per health care provider is simply calculated as (operations/day/provider). Given that health care providers generally purchase more EEG machines then they would normally require on a daily basis, we came to the assumption that a health-care provider, on average, has 8 EEG machines.

Some preliminary market research has shown that the average price for a medical EEG device is about $7500 dollar. Since number research institutes are comparatively small, their contribution to the total market value will be negligible as compared to the health-care providers. Finally, with the number of customers, total number of machines per customer and the unit price per EEG machine, we can calculate the total market value as follows:

The Total Market Value calculated by the above equation for our device will be $600 Million.

Research has shown that 1.1% of all EEG operations are intracranial EEGs[21]. This means each hospital will carry only 1 intracranial EEG machine. However, the previous assumption that each health-care provider will carry more devices than they absolutely require dictates that number of machine per health-care provider will be 2. Such reasoning will give us a new market value estimation of $150 Million.

Our customers, being hospitals and clinics, may be reluctant to adopt new technologies for two reasons:

1. High cost of medical devices,
2. Safety concerns.

Since medical devices are costly and updating devices usually take long review process (see Design Context Review), the willingness of our customers to purchase our products may be influenced by these factors. Nonetheless, we still expect the majority(at least 75%) of our total market to be willing to purchase our products for the following reasons:

1. Our product will be user-friendly (easy to implant and easy for data collection),
2. Our product will be wireless and therefore be convenient for patients,
3. Our product will be comparable in price with existing EEG machines.

Given that the product will provide a significant improvement over currently existing machines in terms of user friendliness, comfort and convenience and is of comparable price. The projected demand for our product is extremely promising and welcoming.

Analyzing the wireless neural recording market, we found that wireless intracranial EEG recording is a very new field with very few competitors. DEUTRON[16] is a medical device company that produces small wireless EEG recorders to medical research institutions. Their device, although much smaller than most of existing EEG recording machines, is still 24mm in length and relies on a miniSD card for data storage, meaning that the data collected will not be real-time. These two factors rendered it unsuitable for medical applications.

Another competitor currently in the field is the NEUROPACE[17]. Neuropace produces wireless EEG recording system that is implanted into the brain, similar to the purpose of our device. However, its product focuses on brain stimulation as treatment for epilepsy instead of brain monitoring which serves as a means of diagnosis. This means that the target customers of NEUROPACE will be fundamentally different from ours, as their products will be designed for patients instead of the physicians and health-care providers. More importantly, despite it being wireless, NEUROPACE’s products are still bulky and require large batteries to power, making it uncomfortable and potentially dangerous (large electricity reservoir poses considerable threat to brain functionality in the form of potential power leakage).

As shown above, the very few existing competitors in the market are either targeting different customers or are not developed enough for medical applications. Hence, we expect at least 80% of the projected customers to purchase our product, as it will be easier to use, lighter, smaller more accurate and more power efficient. Hence, the market value for our product, after accounting for competitions, will still be around $90 Million dollar. Since EEG machines have a lifespan of around 10 years on average, the projected annual revenue will be a handsome $9 Millions dollars.

1. **Customer Needs**

The Wireless Neural Recorder is special in a sense that its customers and users are likely to be two separated group of people. While health institutes, such as neuroscience research institutes, certified neurosurgery hospitals, buy WNR products, the device is installed and used on patients. The need for both groups overlaps to large extent, and can be concluded into four points below, listed in descending order of importance.

Safety is definitely the top concern for our customers, because of the invasive nature of the product. As a medical device, WNR is under US FDA medical device regulations. WNR is installed as an attachment on patient’s scalp, with its electrodes directly insert into patient’s brain. The working period lasts approximately five to six days. WNR needs to ensure the entire process to be completely safe, including external operations such as battery change and switch on/off to be stable and harmless. Further unfolding the safety requirements leads to a few more detailed technical limits: no detectable temperature raise in working device, no power surge in any case, and no feedback current leaking from electrode front end. The limit on temperature ensures no damage to skin or brain tissues; since the device will be turned on for a long period, any heat dissipated by the device will accumulate in the area, and the part that cannot be taken by humor flow will influence normal cell function. Power surge is listed as the most dangerous event, and should be prevented from the aspect of device design; that is, under any circumstance the circuit cannot possibly fall into a state that may result in power surge, such as short circuit.

Real-time, accurate, and comprehensive data collection is also required. Data read and transmitted by WNR is key for doctors and researchers to view patient’s brain activity and make judgments, thus data need to be accurate and reliable for customers to make correct, low-risk assessments. Most customers have experience with wired neural recorder, so the real-time data output should still apply to the wireless version. Real-time surveillance and danger prediction is then made available.

The next customer need is convenience, portability, and long-lasting. The currently existing human neural-activity monitor device all use wires for data transmission to the server end, which noticeably tether patients to a limited range of activity during the entire operation cycle. The greatest challenge and advantage of WNR is the riddance of wires, as well as its size dimension. Based on the feedback from doctors and patients, the top of the device, which is a chip attaching to the scalp, should be approximately 4mm by 4mm in size in order to fit on the fine scale of electrodes, and to reduce the discomfort of patients. Considering the active-time of WNR, to achieve customer convenience also means increasing its battery lifetime, which in turn reduces number of times to change battery of the device. The battery life should last at least 24 hours, because changing battery on the scalp twice a day is not reasonable for both doctors and patients.

WNR is a very useful implantable device for brain activity, and its usage should not be limited to only seizure patients’ monitoring. For most customers, especially research institutes, they want more applications to be developed on WNR platform in the future. With electrodes implanted inside the brain, they can do other operations such as brain stimulation, disease diagnosis, etc.

1. **Design Specifications**

In the previous sections, we have identified our potential markets and customer needs. Our product should ideally satisfy our customer's qualitative needs. To provide structure and a set of goals towards meeting the customer needs outlined previously, we must first translate our qualitative customer needs into quantifiable design specifications that, if achieved, will satisfy our customer needs. The rest of this section will detail our specification generation process and our final design specifications.

The general procedure we use to define our specifications for each customer need is as follows. First, we identify what constraints result on each subsystem as a result of the constraint. Next, we determine metrics we can use to measure these constraints. Finally, we determine our target measurement values based on our customer needs and specifications of competitive products.

Below, we list out a table detailing our design specifications and what customer needs they satisfy.

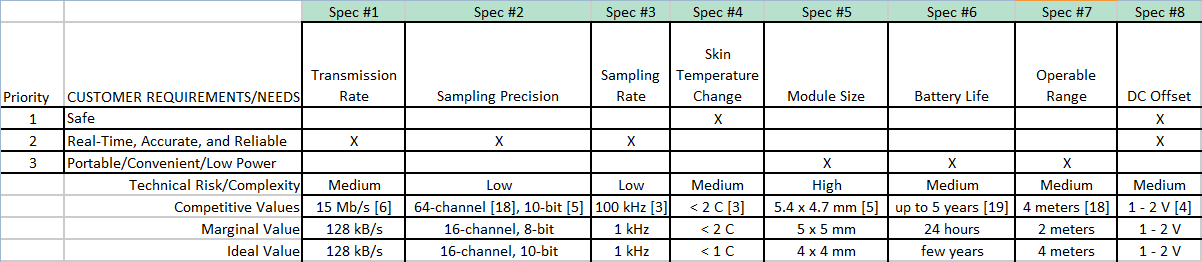


Figure 6. Design specification chart of marginal and ideal values

The first customer need listed in the table is safety. In other words, this device should not harm the user in any way to comply with FDA standards. Two issues arise because of this requirement. Since the device is battery powered and comes into direct contact with the skin, it could heat up the skin. Skin cells die after even a few degrees of temperature change, so FDA guidelines limit the maximum temperature change to two degrees Celsius[3]. The second issue that arises is that when the electrode comes into contact with the brain, an electric potential difference is formed. This potential difference, or DC offset, can be as large as two volts and can cause excess charge to leak into the brain, possibly causing adverse effects[4]. As such, our system must be able to reject up to two volts of DC offset.

Our second customer requirement is that the device must be able to transfer data in real-time. This constraint means we must be able to transfer data from each electrode to the server at a fast enough rate. 128 kb/s is our target transmission rate for each electrode in the system. If each sample is eight bits, then a 128 kb/s transmission rate can support up to 16,000 samples per second, which is more than enough samples for this device's application.

In addition to real-time capabilities, the device must also be able to obtain accurate and comprehensive data. For the data to be accurate, the precision with which we sample must be acceptable. Eight bits provides 256 different amplitude levels, which is enough to obtain a curve over a wide-range of possible amplitudes. However, since neurons have typical action potential spikes on the order of 102 microvolts, having at least one thousand different amplitude levels ensures that we have enough precision to accurately obtain every possible reading[4]. Additionally, for the data to be comprehensive, we must sample regularly. A 1 kHz sampling rate translates to one sample per millisecond, which suffices for our application.

Our last customer need is that the device should be convenient and portable. We identified three aspects to consider for satisfying this requirement. First, the module size should be small and fit on the electrodes we are working with, which have a base area of 4 x 4 mm2. However, our device can be slightly bigger than this area and still fit perfectly onto the electrode, which is why this size limitation is not one of our biggest concerns. The second aspect is the device's battery life. If the user has to replace the battery a few times every hour, then the process becomes very much a hassle. Having a battery life of one day is still not ideal, but it is a goal that is achievable for the scope of our project. The final aspect to consider is the range that the server can be placed from the electrodes and still receive accurate data. The server module will likely be on the user's body. As such, the range at which transmission between the electrode module and server can still occur needs to be about as tall as a person.

If we achieve the specifications listed above, we can deliver a competitive neural recording module with wireless capabilities to the market and facilitate the treatment and research of brain ailments.

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