WIRELESS MICRO-STIMULATOR DEVICE FOR BRAIN STIMULATION

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ISLAMABAD, PAKISTAN

JUNE,2018

Thesis Title

Author

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A thesis submitted in partial fulfilment of the requirements of the degree of MS Degree Title

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Acknowledgements

All attributes to Almighty Allah, who gave me strength for the completion and fulfillment of this work and gave me so much more than I deserve. I am very much thankful to my mother for her prayers and endless support. I am also very thankful to my brothers Umer Usman and Muhammad Nouman for their moral support throughout my way to the completion of my thesis. They have always been a major source of strength and motivation.

First and foremost, I would like to express my deepest gratitude to my advisor Dr. Muhammad Nabeel Anwar for providing me the opportunity to pursue this research and for constantly guiding and supervising me with his immense knowledge in the field of Biomedical Engineering. His mentorship ensured that I was prepared for futures in both academia and industry. I greatly appreciate the fact that he makes a large effort to be available to all his students despite his busy schedule. Also I would like to acknowledge the intellectually fertile environment that Human Systems Lab has given me for pursuing my studies. The experiences that I gathered during my stay here will stay with me forever. I would also like to express my sincere gratitude to my examination committee members Dr. Umer Ansari, Dr. Adeeb Shehzad and Dr. Syed Omer Gilani for their assistance.

I am very much thankful to my buddy brother Zaid Ahsan Shah for his continuous support. I greatly appreciate his selfless nature; despite his own large workload, he still took the time to give me significant advice and encouragement during the thesis and writing process.

I am using this opportunity to thank Human Systems Lab for providing a great, helpful and comfortable environment. My senior friends Samran Naveed, Nayyab Nawaz, Aqsa Shakeel, Hafsa Ahmad, Usman Abid Khan, Waqar Khan, Muhammad Waqas Khalid made my time in human systems lab very useful and learnable and helped me a lot during my time and especially my hostel mate Azeem ur Rehman who is more like a brother to me and his constant support made this whole journey beautiful.

I would also like to thank my awesome brother like buddies and friends Saad Habib, Atif Sultan, Hira Zahid, Maryam Shahid, Areena khan, Amnah Mahroo, Zaeem Hadi, Amna Malik, Ayesha Umbreen, Abdul Hannan Taqi and my whole class of BMES14 without them my life would be missing a wonderful experience.

Thanks to my new junior friends Azmat, Ahmed Subhani, Saroosh, Maliha, Arslan, Aftab and all other HSL members with whom I spent a great time and helped each other in a number of things.

At the end I would like to thank my buddies Zaryab Mazhar, Sultan Awais Omer, Hasan Shuja and Haseeb ur Rehman for their motivation to achieve bigger goals in life and I express my profound thanks to all those who have helped me in the realization of this work.

“And He found you lost and guided [you]”

Al Qur’an (93:8)

Dedication

Dedicated to my parents Usman Ali (Late) and Nasreen Usman, My Grand Parents, loveable Brothers, Nieces & Friends whose prayers, support and cooperation led me to this wonderful achievement

Abstract

In animal behavioral studies, transcranial Direct Current Stimulations (TDCS) & deep-brain stimulations (DBS) research has traditionally relied on the use of a cable tether, for connecting an awake animal to the stimulating hardware. Such methods can reduce animal mobility and increase stress and require a particular arena for accommodating the animal tether. The wireless stimulation system allows much more direct interaction between the animal and its environment, which could result in greatly enhanced performance. In this study a versatile, light weight, inexpensive multichannel wireless system is developed. A wireless Micro-stimulator is fabricated based on a new WIFI based module esp8266. It is a voltage controlled current simulator with the amplitude up to 350µA (0.1µA resolution), pulse per train 1-40, pulse Frequency 30-170 Hz and pulse duration approx. 0.1-0.4ms. Different waveforms can be generated by the stimulator, including monophasic, biphasic and triangular waves. Weight of the stimulator is under 20g. Lastly, a better stimulator with easily available components and better performance has been fabricated to enable detailed study of animal brains in future.

Keywords: Stimulation, Transcranial Direct Current Stimulations (TDCS), Deep Brain Stimulations (DBS), WIFI, Monophasic, biphasic.

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1 INTRODUCTION

In the recent years considerable successful research has been conducted regarding the applications of electrical neural stimulation. The avenues such as visual auditory neural stimulation, neuro-muscular stimulation for contracting disabled or otherwise paralyzed muscles ,deep brain stimulation and trans-cranial stimulation for surface stimulations have seen marked progress [1-6]. In animal behavioral studies, deep-brain stimulation (DBS) & transcranial Direct Current Stimulations (tDCS), to connect an awake animal with the hardware for stimulations research, rely on the traditional use of a cable tether. Such methods can increase stress and due to reduced mobility of the animal and require a particular arena for accommodating the animal tether. Tethered stimulation systems also Include risk of snagging or entanglement of wires, cable breakages, and have rapid deterioration disabling long term usage.

Figure 1: Tangling of wires

The wireless systems for the stimulation provides the unrestricted interaction between the animal and its environment which results in accurate behavioral studies. To avoid the issues in tethered stimulation apparatus, different portable stimulators have been developed for stimulations, including

- Head-mount systems [7-10].
- Velcro jacket, back mount systems [11-13].
- Implantable systems [14, 15].

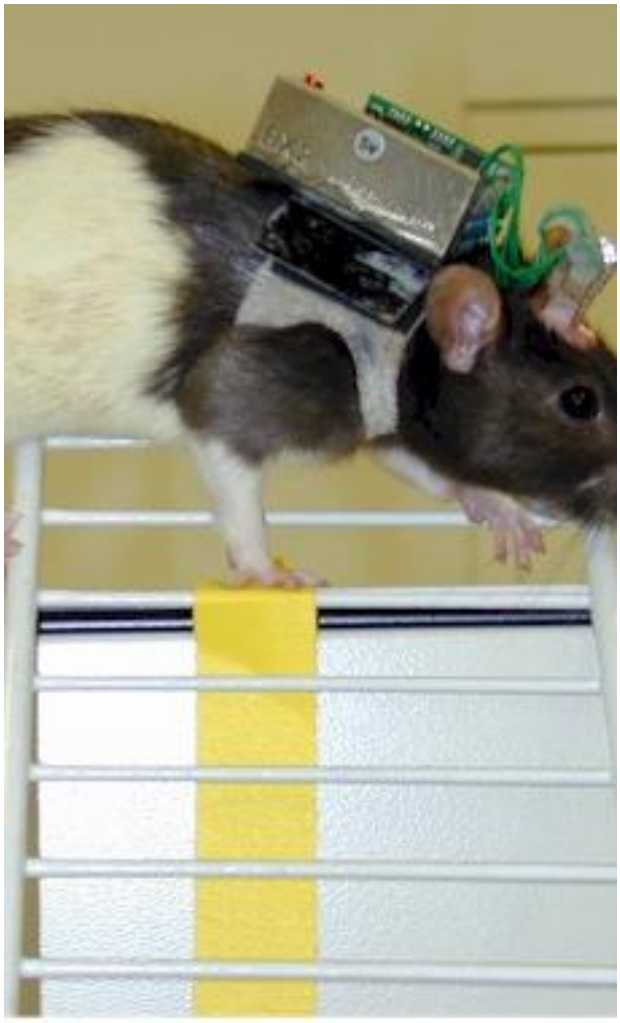

Figure 2: wireless back pack stimulator

Currently no such device is commercially available in Pakistan for animal studies. Wireless Stimulation devices are available for human beings with current range starting from 0.1mA.

This study is focused on the fabrication of a device with wide range of parameters for DBS(Deep brain Stimulations and tDCS (Transcranial Direct current stimulations).

1.1 Neural Stimulation Theory

The nervous system facilitates communication between different regions of the body through the transmission of electrochemical signals. Neuron is the main functional unit of Nervous System. The main functional unit of the nervous system is the neuron, it is a specialized cell that is electrically excitable. The nervous system is composed of large, complex networks of interconnected neurons that communicate with each other in the form of action potentials. From a high-level perspective, the nervous system is responsible for controlling the

body: sensing of external stimuli, processing stimuli to determine an appropriate response, and coordination of muscle groups to enact the response [16].

Although multiple types of neurons exist, a typical neuron cell is composed of three structures: the soma or cell body, an axon and dendrites. Dendrites and axons are extrusions from the soma, which houses the nucleus of the cell. Axons serve as the output to other neurons while dendrites serve as the inputs. The connection between the axon of one neuron and the dendrite or soma of another is known as the synapse. When referring to the synapses, the neuron that is sending information through its axon is known as the presynaptic cell, while the neuron receiving the information through its dendrite is known as the postsynaptic cell [17].

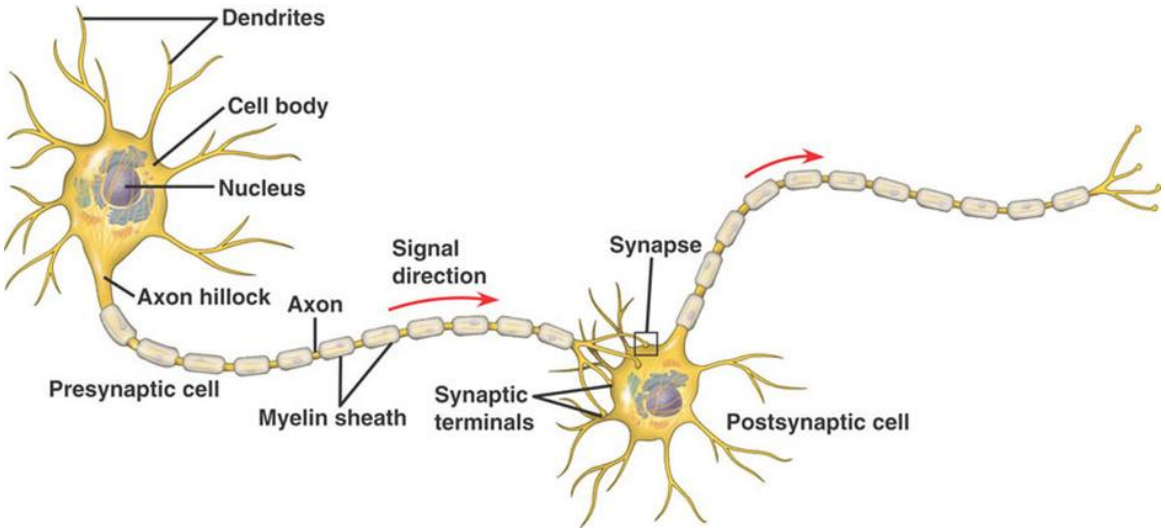

Figure 3: A diagram of the neuron highlighting the chain structure between the axon and dendrite [18].

The structure of a typical neuron and its interface with a neighboring neuron is shown in Figure 3.The Information came to nervous system is encoded in the form of action potentials, which are events during which a neuron's transmembrane potential rises and falls in a predetermined manner. The transmembrane potential of a cell is the difference in the voltage between its interior and exterior. A plot of transmembrane potential during an action potential with respect to time shown in Figure 4.

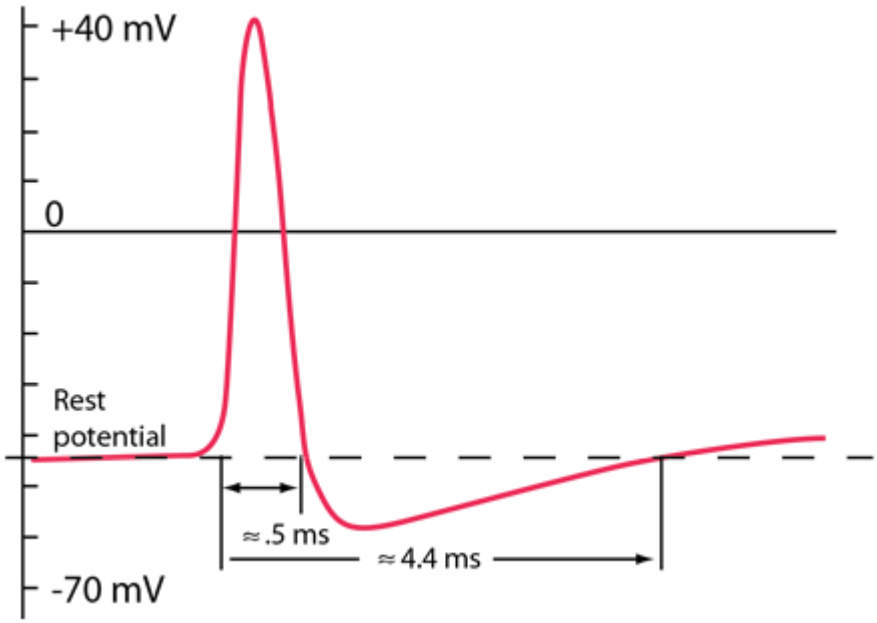

Figure 4: Action potential [19].

In event of sufficient excitation of the soma or dendrites, this transmembrane potential can change, causing it to deviate from its resting potential (typically -70 mV). Action potential is generated when the potential across the membranes reaches a threshold of approximately -55 mV, Action potential begins with an initial period of rapid depolarization, which is followed by a period of rapid repolarization. The repolarization period causes the membrane potential to drop below the resting potential. This refractory period reduces the likelihood of any additional stimulation to evoke an additional action potential within a short period after the action potential is initiated. The transmembrane potential then returns to its resting potential of -70 mV [20].

The transmembrane potential of a neuron is not uniform but varies between regions of the cell. Action potentials do not affect an entire neuron at once, but the depolarization of one region causes the depolarization of neighboring region, allowing the action potential to propagate from one region to another. Typically, action potential propagation begins at the soma of the neuron and propagates outwards along the axon. When the action potential reaches the synaptic terminals at the end of the axon, the axon of the presynaptic neuron releases neurotransmitters. The uptake of neurotransmitter of the postsynaptic neuron results in either hyperpolarization or depolarization of the soma of the postsynaptic neuron [21].

Sufficient depolarization results in action potential which is being generated in postsynaptic neuron. In networks of neurons, action potentials can be chained until the signal is ultimately

received at the intended cell. One of the primary characteristics of an action potential is its “all or nothing” nature. Changes in transmembrane potential that fail to reach the threshold level do not induce an action potential. Similarly, stimulation far past the threshold potential will yield the same amplitude action potential as stimulation that just reaches the threshold. This property allows the system to be robust to noise, while also discretizing the information sent by neurons and simplifying information transfer between neurons [22].

Although neurons typically fire action potentials in response to the presence of neurotransmitter, action potential firing can also be induced through electrical stimulation.

1.2 Areas of Application

tDCS (Trans-cranial Direct Current Stimulations)

For the modulation of cortical excitability popular method these days is a non-invasive method called transcranial direct stimulation. Direct current is found very effective in modulation of spontaneous firing of neurons. Weak direct current can even influence activity of human brain [23].

With the understanding of advance pathology and function of central nervous system, new techniques like TMS facilitates a more detailed understanding of tDCS effects which supports the making of new applications for the clinical testing. Currently used protocols shown no significant adverse effects and more novel applications and powerful protocols are also emerging. tDCS is a versatile and effective neuromodulation tool [24].

DBS (Deep Brain stimulations)

Deep Brain Stimulation (DBS) is another application of neuromodulation that developed in the late 20th century. After Alim Benabid of the University of Grenoble discovered higher frequency stimulations of the ventral intermediate thalamic nucleus had similar results to lesioning regions of the brain for the treatment of movement disorders, DBS became the preferred method of treatment for Parkinson’s disease [25]. Benabid’s research in 1987 prompted further exploration of the modality for the treatment of other diseases. Currently, DBS is used to treat conditions such as chronic pain, obsessive-compulsive disorder, and depression but is officially approved by the FDA for the treatment of essential tremor, Parkinson’s disease, obsessive-compulsive disorder and dystonia. While currently exact mechanisms of action behind DBS are not understood fully, the benefits, at least for Parkinson’s disease and dystonia, are undisputed [26]. Deep Brain Stimulators are like

pacemakers in that they possess electrodes that stimulate a certain region of neural tissue which varies depending on the intended treatment. The device is composed of similar components: an implantable pulse generator, a battery and the electrode with corresponding extension wire. The electrodes are placed deep within the brain through drilling a small hole in the skull, while pulse generator is generally implanted below the collarbone. The implantable pulse generator generates a charge balanced biphasic pulsatile waveform (typically between 120-180 Hz with 60-200 μs pulse duration) that is delivered to the electrodes to stimulate the areas of interest [25].The stimulation is thought to replace the inhibitory function of the substantia nigra to the subthalamic nucleus and globus pallidus interna in case of Parkinson's disease [26]. An example a DBS waveform is shown in Figure 5. As with the other neural prostheses presented, the charge balanced nature of the waveform is necessary to avoid tissue death and premature electrode corrosion.

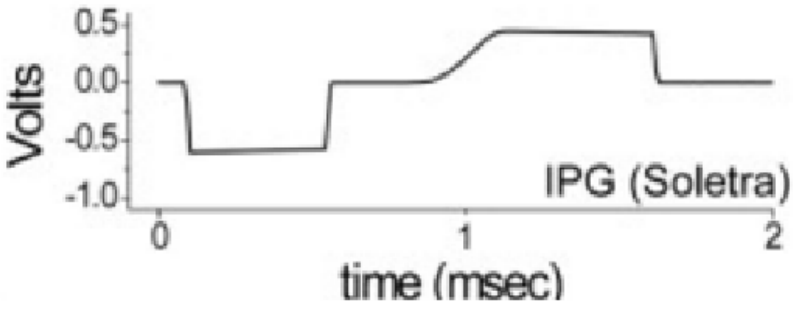

Figure 5: Charge balanced biphasic stimulation waveform of a Soletra implantable pulse generator used for deep brain stimulation. Adapted from [27].

2 LITERATURE REVIEW

2.1 Stimulation parameters and physiological impact

the stimulation parameters applied will condition the respective physiological response, so it is necessary to adapt those parameters to the therapeutic objectives. The cause-effect relation of all the parameters and respective physiological consequences should be known for the correct application of the stimulation.

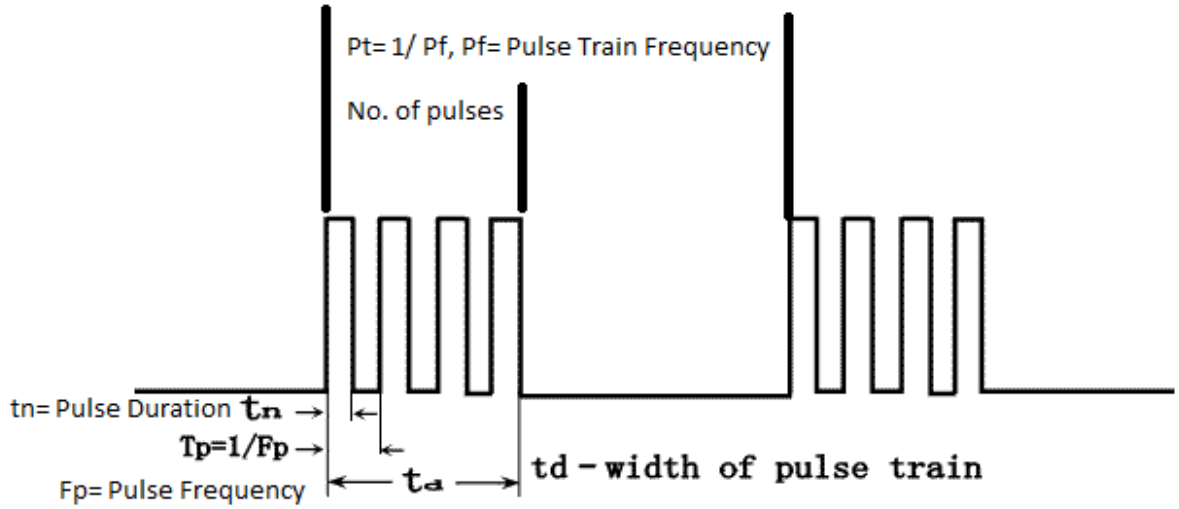

Figure 6: Temporal construction of a signal

2.1.1 Amplitude

The amplitude of the stimulation pulse (Figure 7) can be measured in current or voltage, depending on the modulation type. The amplitude determines the stimulation intensity, which consequently determines the total number of nervous fibers that are recruited and activated. As the intensity increases, the depolarizing effect become stronger in the structures which are underlying the electrodes [28]. Increase intensities enable hypertrophy process and contraction strength also increases [29-32].

Stimulation amplitude will also influence patient comfort, higher intensities makes stimulations less tolerated. However, quality of muscle contraction produced will be inevitably determined by the intensity and frequency [33, 34].

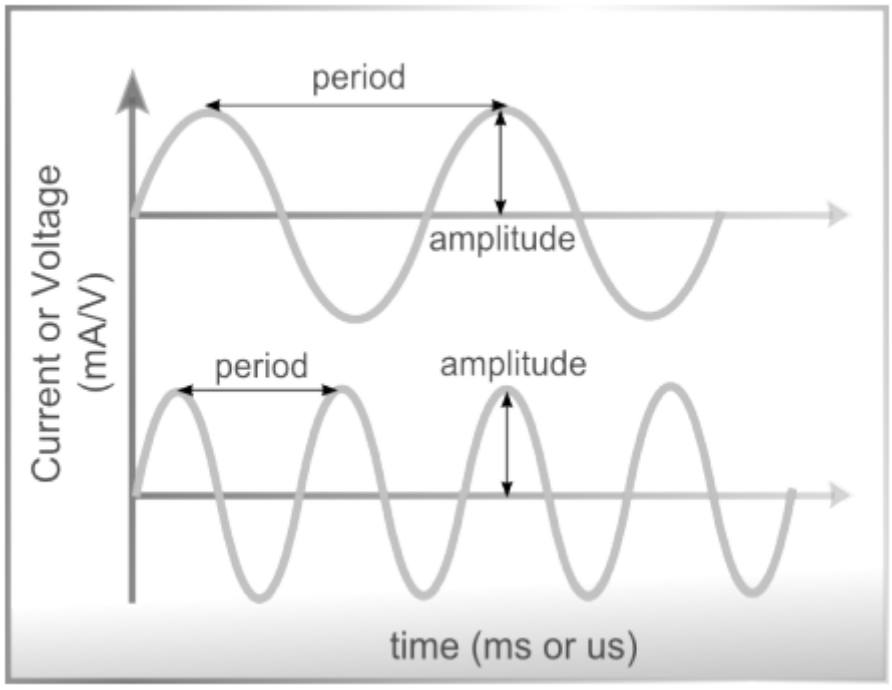

Figure 7: Amplitude and period of a wave.

2.1.2 Pulse-Width:

Pulse duration or pulse-width is time span of a single pulse. It is the duration of the wave at 50 % of the maximum amplitude and is expressed usually in microseconds (µs). Research has shown that patients exhibited a strong preference for phase durations of between 200-400 µs which are also capable of producing reliable muscle contractions while minimizing the possibility of skin irritation beneath the electrodes [34]. In a Recent work, 50 µs, 200 µs, 500 µs, and 1000 µs pulse-widths were compared with a stimulation frequency of 20 Hz to sole muscle. It is found that stronger contractions of plantar-flexion were produced by wider pulse-widths and additionally overall contractile properties were augmented. In addition, deep penetration into the subcutaneous tissues will be achieved by the longer pulse durations, so when trying to impact secondary tissue layers these widths should be used [35]. The pulse-width affects the current amplitude which is necessary to trigger the action potential and also determines the sensitivity of sensory, motor or pain stimulation. Pulsed currents with lower pulse-width are less uncomfortable. As illustrated in Figure 8, the sensory, motor and pain sensitivity to stimulation amplitudes is maximal when applying pulses with low duration.

However, in this section, it is important to refer an accommodation phenomenon [36], which makes the excitability threshold of the nervous tissue adaptive and not absolute. Because of this effect, if the current transfer ratio, which is related to the rise time of the electrical pulse,

is longer than several hundreds of µs, the current amplitude required to reach the action potential will be superior (Figure 9).

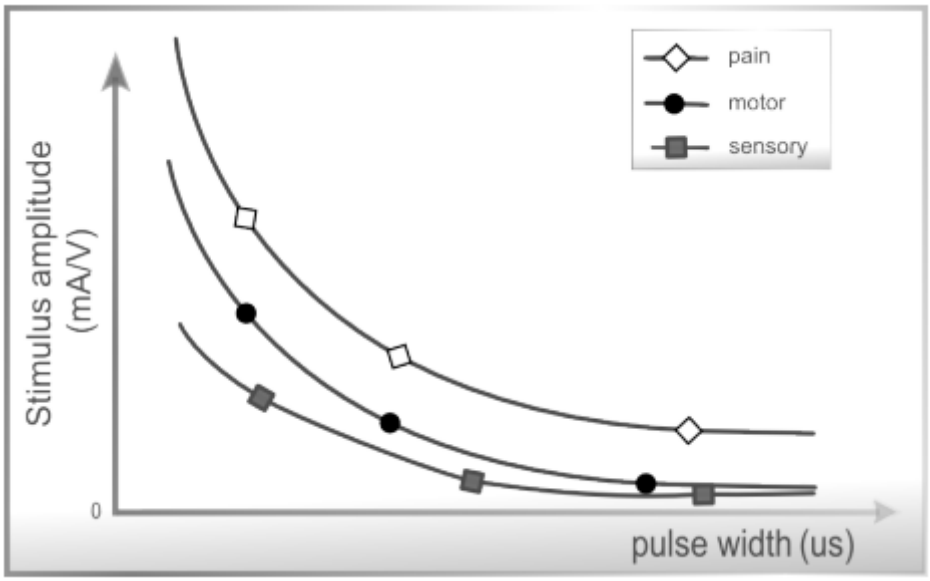

Figure 8: Strength-Duration curves: Relation between amplitude and pulse-width when relating with the influence on excitability thresholds: sensorial, motor and pain tolerance. Adapted from [37].

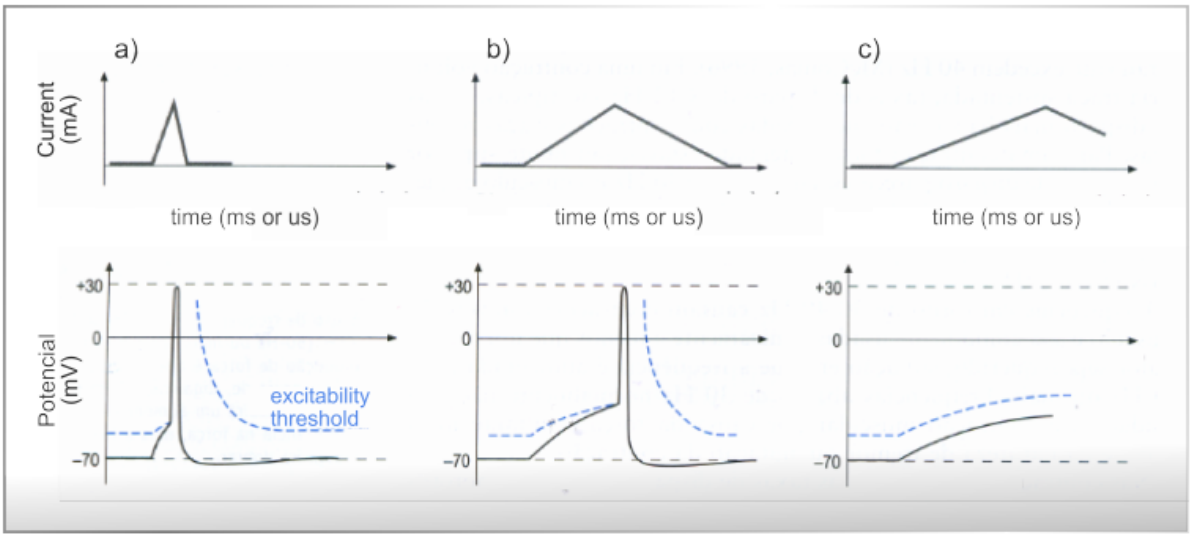

Figure 9: Relation between the pulse-width applied and the accommodation of the nervous fiber: a) the small current transfer ratio triggers the action potential; b) a bigger current transfer ratio triggers the action potential but showing threshold accommodation c) the transfer ratio is very high and never surpasses the excitability threshold.

2.1.3 Frequency

The pulses produced per second during stimulations are called as frequency. The frequency of a stimulus affects the clinical response as it influences the muscular contraction which can be isolated or tetanic. A tetanized state or tetanic contraction (also called as tetanus) occurs when a motor neuron maximally stimulates its motor unit. This occurs when multiple impulses which are sufficiently at a higher frequency stimulates a motor unit of muscle. Every stimulus will cause a twitch. The tension present in the muscle will relax in between successive twitches if pulses are delivered slowly enough, the twitches will run together if pulses are delivered at high frequency, which results in tetanic contraction. Stimulation frequencies above approximately 30 Hz produce a tetanic contraction [38]. In Most clinical applications 20-50 Hz patterns are used for optimal results [39, 40]. Increasing the stimulus frequency leads to much stronger contractions. However the rate of muscle fatigue also increases due to increase in contractions [33, 41]. Constant low frequency stimulation is used to optimize fatigue, due to which a smooth contraction is produced at low force levels [42]. However, the muscle fatigue index induced by artificial stimulation is always higher than the voluntary contractions in which the motor neurons activation is triggered asynchronously.

The contraction strength is defined by the frequency of the action potentials and number of motor units recruited. In terms of patient comfort, typical NMES stimulator frequencies in the range of 30-60Hz are found to be optimum [34].

Figure 10 shows the variation of the fiber strength with the stimulus frequency, for intensities above of the motor limit. A stimulation frequency above 30Hz is indicated for the production of maximum force.

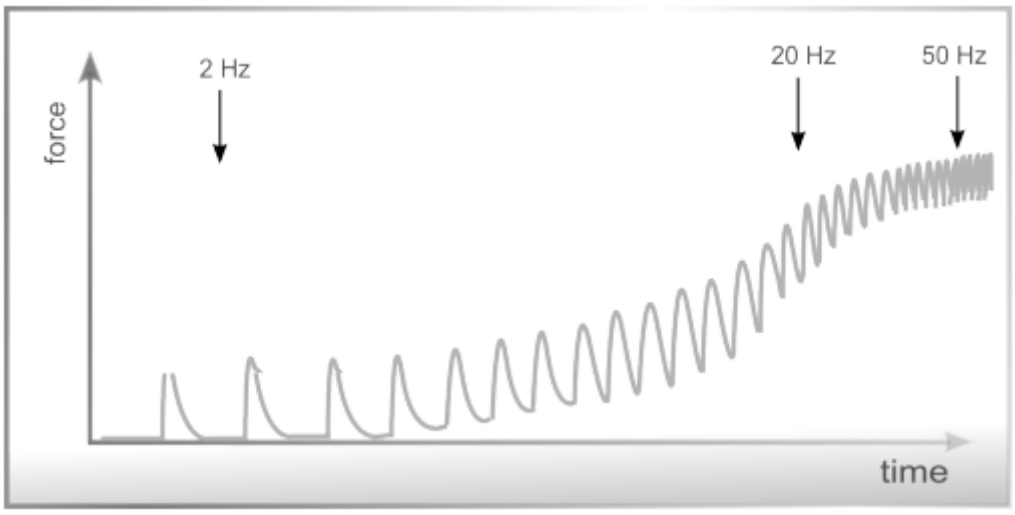

Figure 10: Muscular strength variation with the stimulus frequency, for stimulation intensities above the motor limit. Adapted from [43].

2.1.4 Waveform

In surface electrical stimulation the waveform is the representation of the variation, over time, of the current or voltage that is injected into the biological tissue. The polarity, in the context of electrical current, refers to the charge way. The pulse may be monophasic (unidirectional / continuous polarity) or biphasic (bidirectional / alternating polarity), as it is represented in Figure 11 [44]. The power of the two kinds of current pulses is equal, but if the wave is symmetrical the charge compensation avoids the deposition of ions above the electrodes surface which may cause lesions on the tissue level [45] .

A typical biphasic stimulus pulse consists of two phases: a stimulating phase and an adjacent phase of opposite polarity. The simple monophasic stimulus is a periodic unidirectional pulse, where current passes in only one direction. This type of stimulus is not used for prolonged periods, as such irreversible faradaic reactions may cause tissue damage. These negative reactions due to prolonged periods of negative (or positive) potentials associated with monophasic stimulation is minimized by the use of a biphasic waveform pulse [46-52].

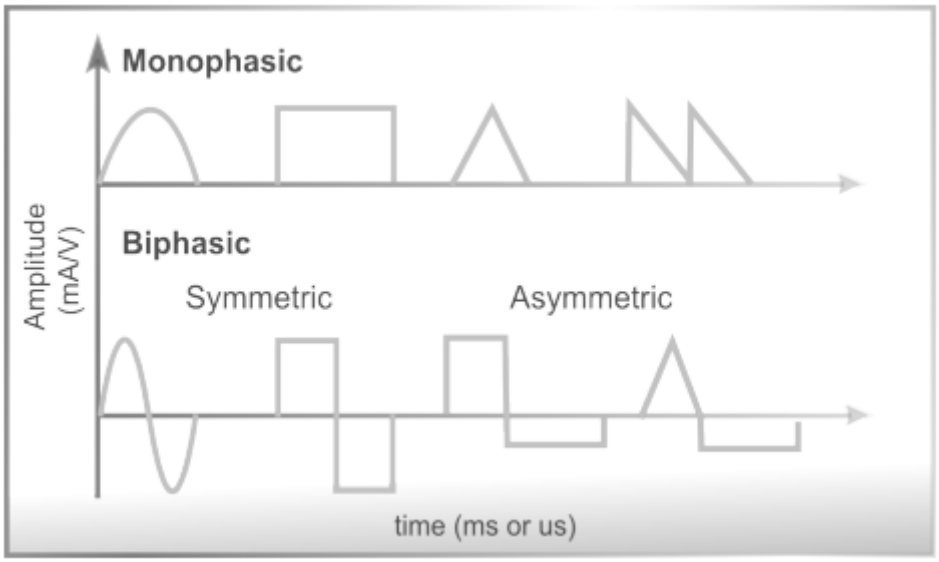

Figure 11: Examples of electric pulses with different polarities and waveforms.

Contemporary devices generate pulses of voltage/current with predefined geometric shapes, traditionally the square wave. Figure 9 shows a comparison of stimulation waveforms. It shows the ability of wave forms to generate low threshold stimulation, low tissue damage and low corrosion.

There are a very few studies on the practical effect of the waveform on the physiology response. Durand [53], evaluated the standard waveforms and those studies enabled the compilation of the information present in Figure 12. However, there are still various waveforms for which the correspondent biological effect is still unknown. The evaluated parameters by Durand - threshold, corrosion and tissue damage - represent only part of the information about the effect of the waveform on the excitable tissue.

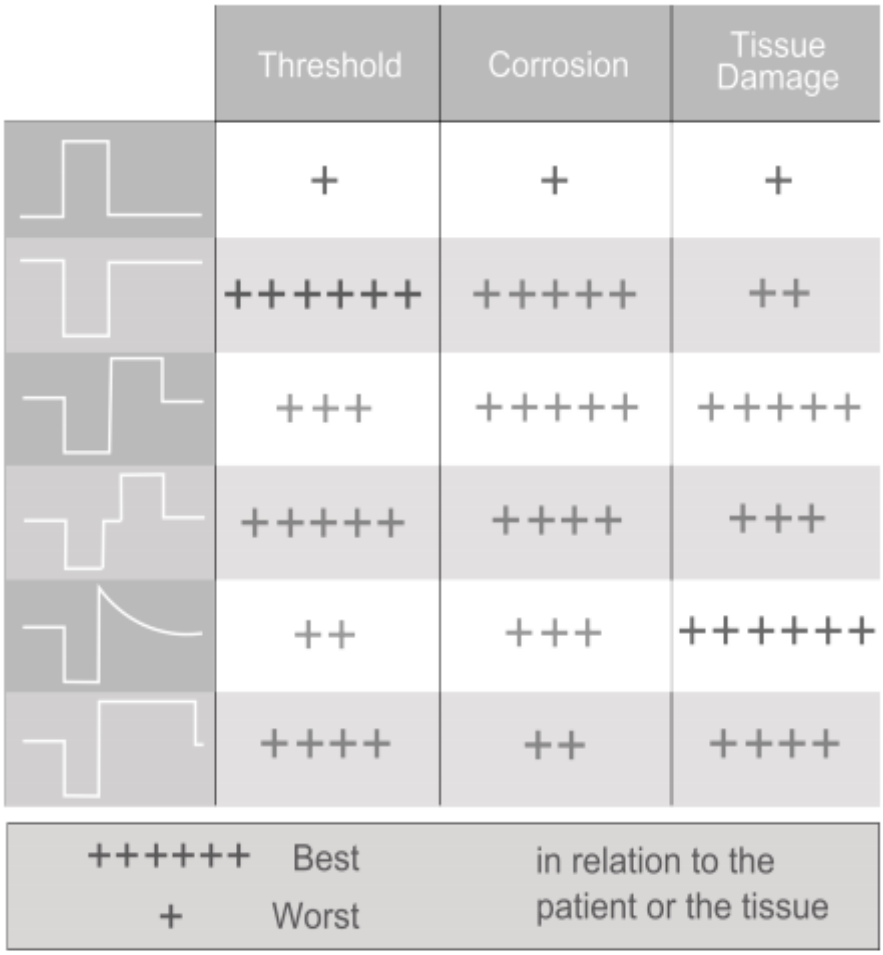

Figure 12: Comparison of stimulation waveforms. the ability of wave forms to generate low threshold stimulation, low tissue damage and low corrosion. Adapted from Durand [53].

2.2 Stimulation Devices

Nerves are stimulated by the help of neuromodulation devices with electrical signals, pharmaceutical agents or energy of other forms. This can be done by modulating abnormal neural pathway being caused by the disease process. Profound effects can occur that include pain relief, function restoration or bladder control or normal bowel, tremors control, Parkinson's and many others [54].

Professor Iaso Shimoyama, University of Tokyo, developed the roach by implanting a micro-robotic backpack for movement control. The robo-roach had the ability of carrying mini-camera and sensory devices for sensitive and crucial missions [55].

For training of the laboratory animals, State University of New York Procedures developed a robo-rat Animals were taught to give responses to the cues for obtaining rewards

such as food. It showed that the physical constraints, learning paradigms having basis on micro-stimulation of brain was used for transcending traditional boundaries regarding animal learning that had been used for the behavioural model [56].

For electrical stimulation for multiple brain locations in free rats, a system was designed which allow the experimenter to deliver pulse train. It consisted of a transmitter-based station and a receiver consist of a microprocessor pack placed on back of the animal. The pack was small and light for the easiness of the animal. The backpack had been configured with specified parameters to provide biphasic pulse trains. It used constant-voltage TTL backpack output microprocessor. A new behavioural model had been developed regarding this system [57].

For a navigation-based technique of BCI, a remote stimulator was developed. This also based on constant current or constant voltages modes with a transmitter and receiver. It weighted 20g and consisted of five channels connected with implanted micro electrodes. The stimulations that offered to diPAG (dorsolateral periaqueductal gray area) were for the improvement of effect regarding stimulations on the behaviour of rat [58].

A rat navigation based, new and intelligent control system was presented with state machine techniques and video tracking. A pre-set course automatic navigation was also demonstrated. The system consisted, a rat movement capturing video camera device, a wireless backpack stimulator and an automatic navigation generated by a control program that is state machine based. Main control system was the intelligent control system for rat navigation that showed the system to be practical and stable [59].

A new motion scheme for the guidance of the rat had been developed as a bio-robot navigation operation. The rat tried itself to reach from one start point to the goal point in a room. The points are randomly given. In the experiments a telemetry micro-stimulation platform was provided for the rat to move with and without obstacles. A CC2431 module was used for determining the operant rat position. Biphasic pulses were generated by the controller which is mounted on back of the rat [60].

A non-invasive rat behaviour navigation control system had been designed using LED, epidermal and ultrasonic stimulators. The system delivered specified stimulations to the visual, pain and hearing senses of rat. The results showed the working of stimulations for the navigation of rat. The rat can be controlled easily and turned easily and efficiently. The

experiment verified the reach of the reach to a certain destination with the assistance of the coordination of the three stimuli [61].

Neural prosthesis and other therapies are based on the recorded neural activity and electrically stimulated nerve tissue. Same as every system regarding experiments for roaming subjects, conventional stimulation system also has its limitations. The main objective and approach was designed for the development of versatile, inexpensive and modular wireless system and overcoming of the constraints, using the commercial components. The system was light weight and small and can be carried easily. Small in vivo experiments and bench tests were conducted for validation, testing and reliability of the system. The results included the accuracy, comparable stimulation sequences and regular transmission changes allowing the overall stimulation control and real time parameters. The system was flexible and reliable and can be tailored regarding experimental needs [62].

For experimentation of the animal behaviour, wireless neural stimulation devices were offered as a significant advantage. An extremely light weight cost effective and simple device was made of the off-shelf components that had a low powered consumption. Mostly stimulation was carried out in either of the two sources mode; voltage or current. The stimulation was applied inside the premotor area of brain HVC of a songbird that demonstrated the stimulations to be causing rapid perturbations of the acoustic song structure [63].

A new remote-control system had been designed for delivering stimulation in the brain of rat using a micro-stimulator for training of animal's behaviour. The system consisted of an integrated control program with a receiver and a transmitter. The C8051 microprocessor had a changeable pulse output for constant current and constant voltage modes. Behaviour had been monitored and recorded in the operant chamber. It had also been tested with and without obstacles. The animals had been able to take desired turns between the reward and cue stimulation in the MFB (Medial Forebrain Bundle) [12].

2.3 Challenges of wireless stimulation devices

Wireless stimulation devices find many applications in various fields such as prognosis of disorders, animal behavior study etc. A few salient features of practical wireless stimulation devices are:

- The device must be **light weight** to facilitate unobstructed movement of animal in the study arena.

- The device must be **power efficient** so as to allow extended operation.
- The device should contain **multiple stimulation channels** to excite multiple areas of the brain.
- The device must be **compact in size** such that it is negligible compare to size of the animal.
- The device must provide a range of **tunable operational parameters** for different applications and allow multiple modes of excitation (monophasic, sawtooth etc.).
- The device must provide **reliable wireless communication** for remote operations.

2.4 Objectives of study

The objective of this study is;

"To design an inexpensive, lightweight, compact, multichannel, power efficient wireless stimulation system with tunable operational parameters."

3 METHODOLOGY

3.1 Research overview

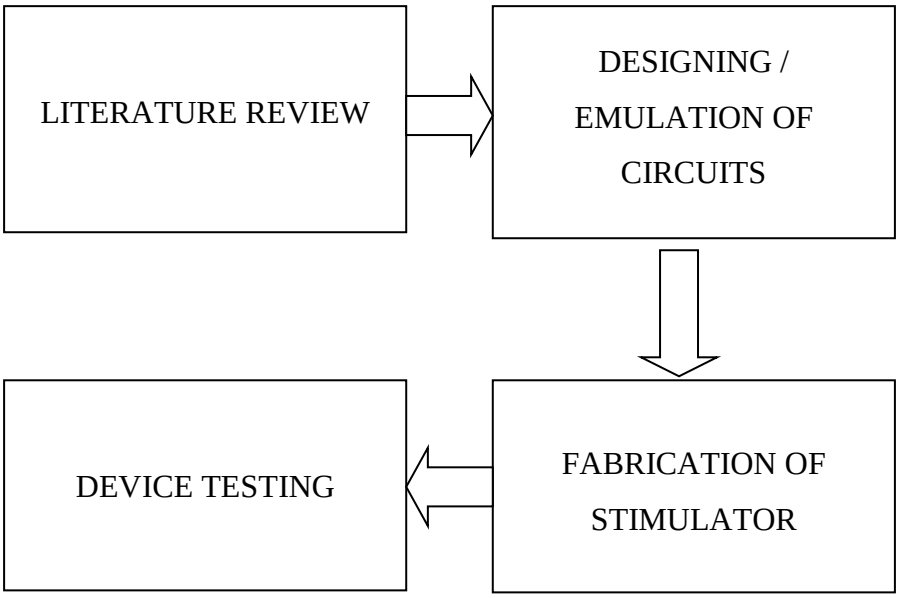

Figure 13: Research strategy block diagram

3.1.1 Application overview

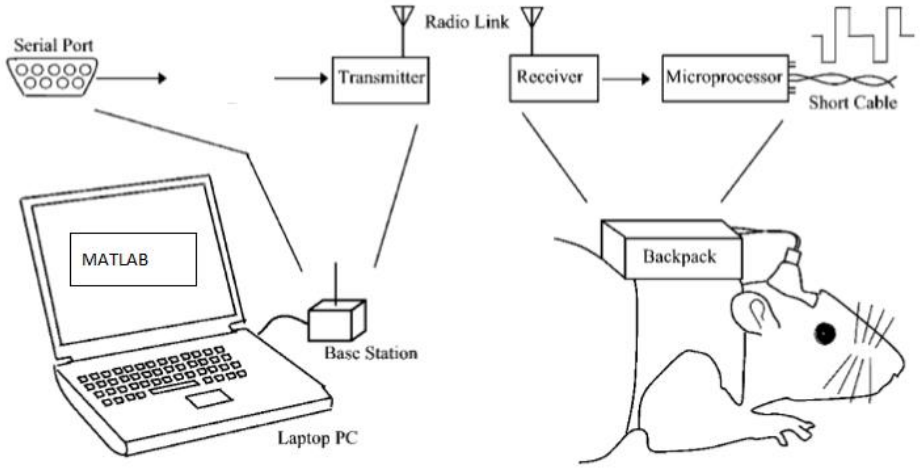

Figure 14: Application Overview

3.1.2 Target Parameters

Literature review was done for the selection of variable parameters. Following parameters were finalized according to the wide range of application.

PARAMETER	RANGE
Amplitude current(A)	0-350 µA
Pulse per Train	1-40
Pulse Frequency	30-170 Hz
Pulse Duration	0.1-0.4 ms
Frequency of trains	0.5-3 Hz

Figure 15: Stimulator Parameters

3.1.3 Design /Emulation of Circuit

Designing was planned considering the parameters and applications according to the objectives. Following different designs were emulated and tested on breadboard.

3.2 Design 1: Communication using AT Mega 8 and RF module

3.2.1 Transmitter

Figure 16 shows flow chart for the transmitter. Data is transferred serially from the computer. The MAX232 is a dual receiver / dual transmitter that is used typically to convert the TX, RX, RTS, CTS signals. It was used for voltage leveling / shifting. A high performance, low power 8-bit microcontroller ATmega8 was used. HT12E encoder was used which is a 2^{12} series of encoder for remote control system application. Tx433 low power high performance FM transmitter was used to transmit the required signals. Figure 17 and 18 shows the ED layout of to and bottom view of transmitter pcb. Figure 19 shows the Tx 433 transmitter.

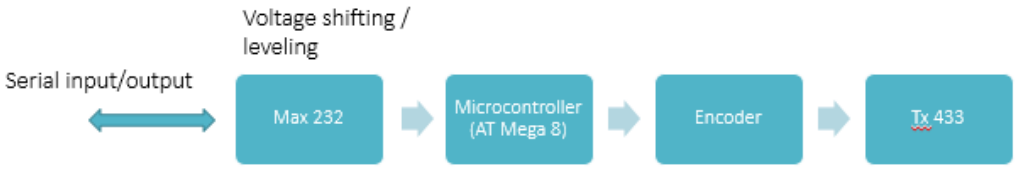

Figure 16: Transmitter

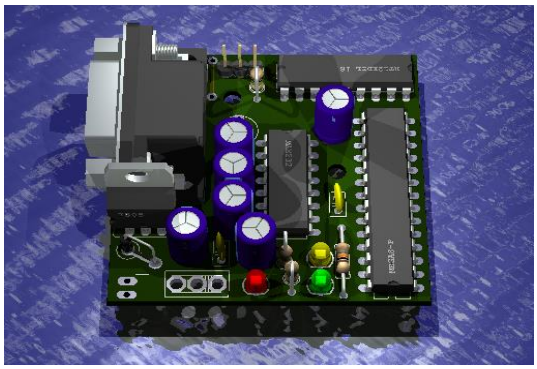

Figure 17: Transmitter pcb Top View

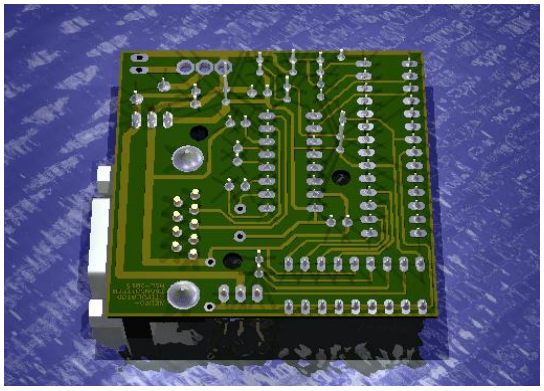

Figure 18: Transmitter pcb bottom View

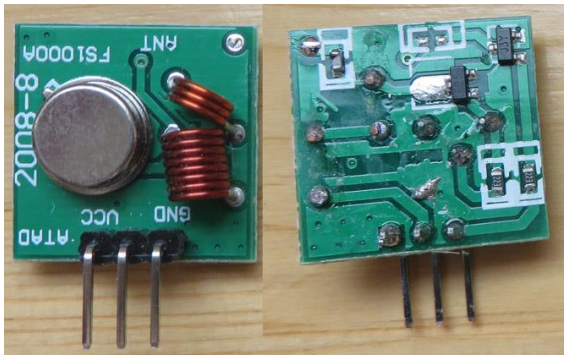

Figure 19: Tx433 Transmitter

3.2.2 Receiver

Figure 20 shows the flow chart of the receiver side of the wireless stimulator. Rx433 was used to receive the signals from transmitter. HT12D is used to as a decoder. A double layer pcb was designing to accommodate the components on a compact size. ATmega8 microcontroller was again used . DAC0800 was used to convert digital signals to analogue , which converts voltages into current. At the end MUX is used for the channel selection which is controlled by ATmega8 to control the selection of channel for different electrodes. Figure 21 shows the 3D layout of top and bottom view of 1st layer of receiver while figure 22 shows the Ed layout of top and bottom view of 2nd layer of receiver.

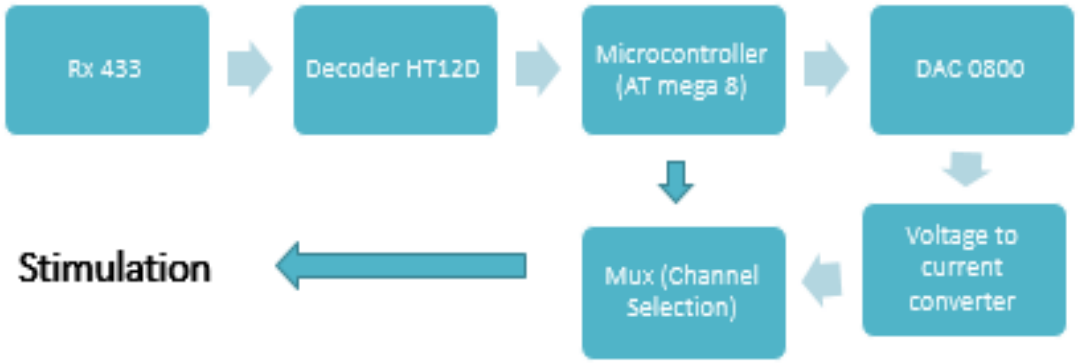

Figure 20: Receiver

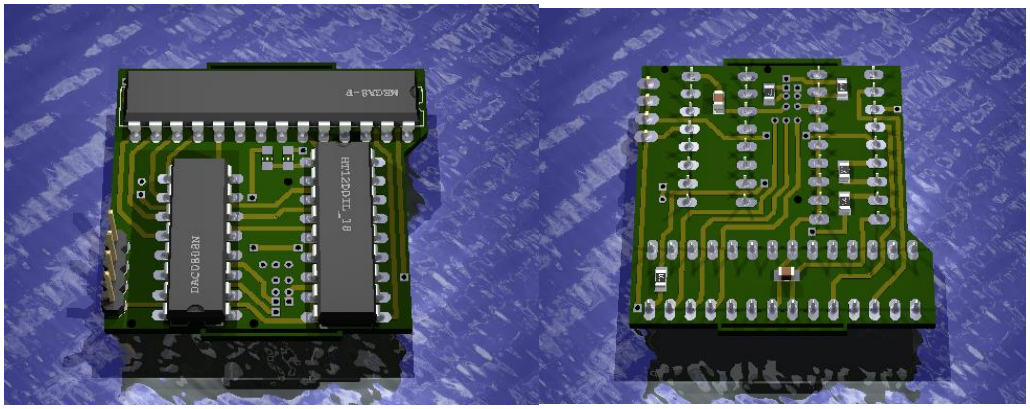

Figure 21: Receiver Layer 1 top and bottom

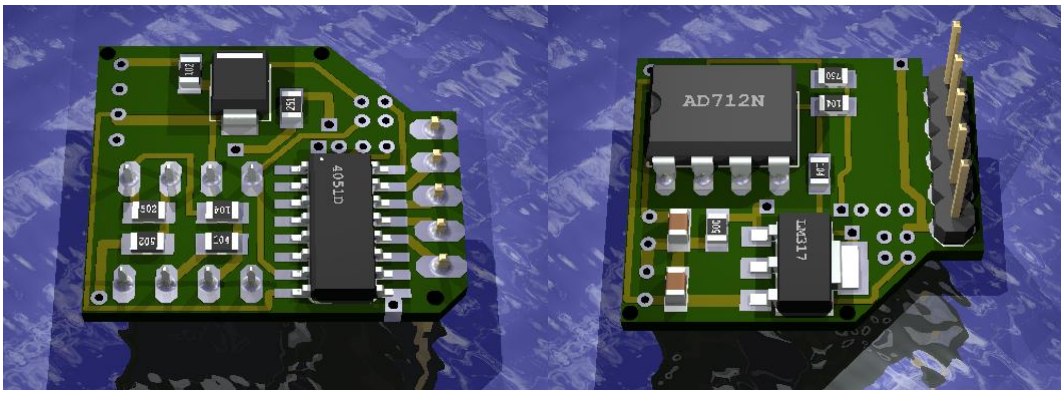

Figure 22: Receiver Layer2 top and bottom

3.2.3 Dimensions

The dimensions of the transmitter are as follows:

- Transmitter 5x5 cm
- Receiver upper board 2.3x2.0 cm
- Receiver lower board 3.8x3.5 cm

3.2.4 Limitations

Design was rejected due to following reasons:

- Availability of components
- Circuit complexity
- Serial Communication frequency mismatch
- Noise in output wave

3.3 Design 2: Communication using Arduino mini and RF module

To cater the problems of components availability, circuit complexity and noise in the output AT mega 8 and some components were replaced by **Arduino pro mini 328** with same RF Module.

3.3.1 Limitation:

- Size and weight due to Arduino and RF Module
- RF module availability issues

3.4 Final design Communication using ESP8266 WIFI Module

The final prototype contains all the components which were described in the previous sections. The individual components and their designs are discussed in their respective sub-sections. The overall block diagram of the final design is shown below;

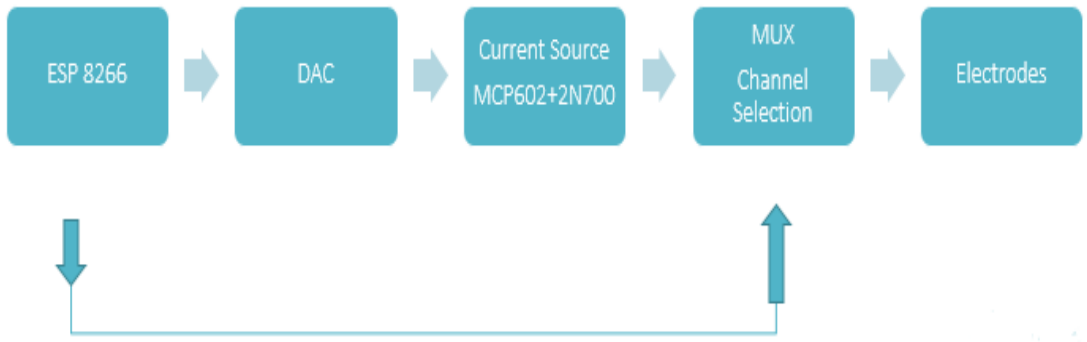

Figure 23: Flowchart for receiver

3.4.1 Design Criteria

The final prototype has all the desired features for a wireless stimulator as discussed in the previous chapter. The design had to meet following specifications;

- It must contain easily available components.
- It must be light weight and compact in size.
- Provide seamless WiFi connectivity for practical applications.
- It must be power efficient.
- It should have multiple channels for excitation.
- And it should contain variable parameters for task performance, i-e it should support multiple modes of stimulation with multiple waveforms.

The design sub-systems are described in the following sections;

3.4.2 Main Processor

The main onboard processor for the final prototype is ESP8266 based Wemos® D1 mini, board. It is a compact and lightweight processor with enabled WiFi connectivity. The D1 mini is shown in the figure below.

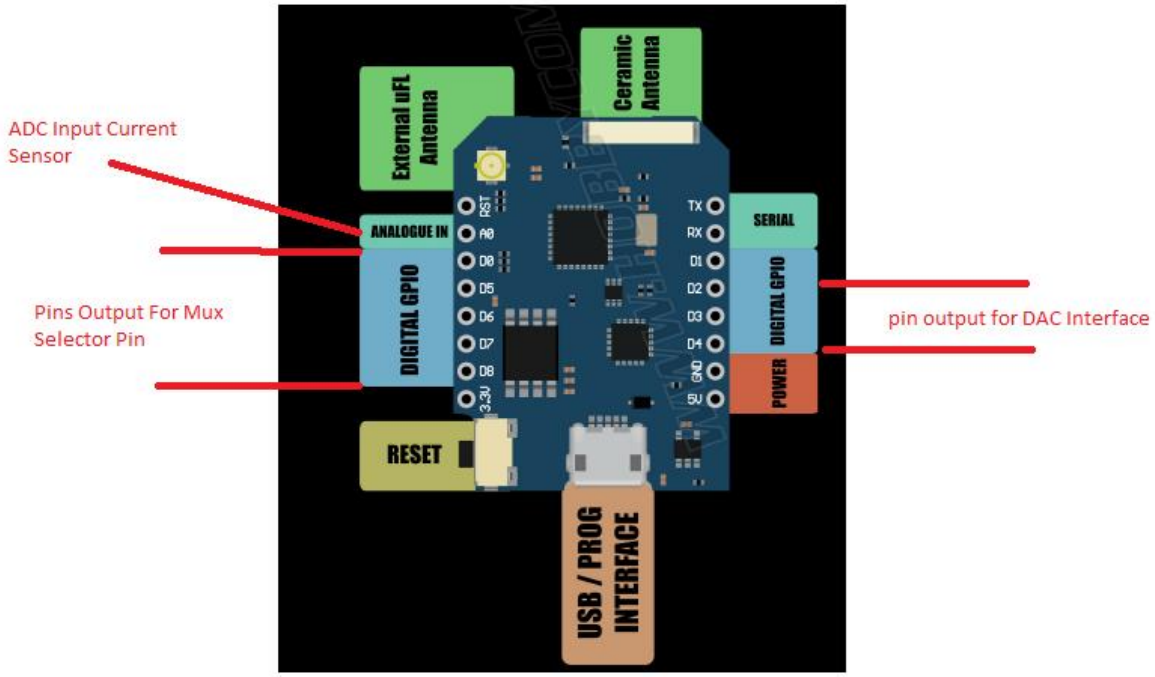

Figure 24: ESP8266 layout

3.4.3 Digital to Analog Convertor (DAC)

In order to convert digital input from the main processor, to an analog output voltage a 12 bit Digital to Analog Convertor is used. The MCP4725 based DAC comes in a small SOT-23-6 package. It has an I^2C interface with communication bandwidth of 400MHz. For the prototype the commercially available breakout board GY4725 was used, shown in the figure below.

Figure 25: DAC MCP4725

3.4.4 Current Source

The voltage output from the DAC is given as input to the regulated current source. The current source is designed with a Rail-to-Rail non-linear OP-AMP based negative feedback integrator, with the integrator output controlling the current flowing through the load.

The OP-AMP used is MCP 602 which comes in a small 8-pin package. The capacitor of the integrator is the gate to source capacitance of the MOSTFET 2N7000. The current source is biased with a biasing resistor of 2.8 kΩ. The Biasing resistor controls the current and limits the feedback system to ensure over-current condition is never met and also regulate the voltage of the integrator. The CMRR of the OP-AMP used is 90dB.

As an added feature of the system an accuracy vs range trimming potentiometer is also used which provides adjustable flexibility of operation if it needs to be adjusted, however in the final design this is replaced by a pair of SMD resistors. The schematics design of the isolated voltage controller current source is shown in the figure below.

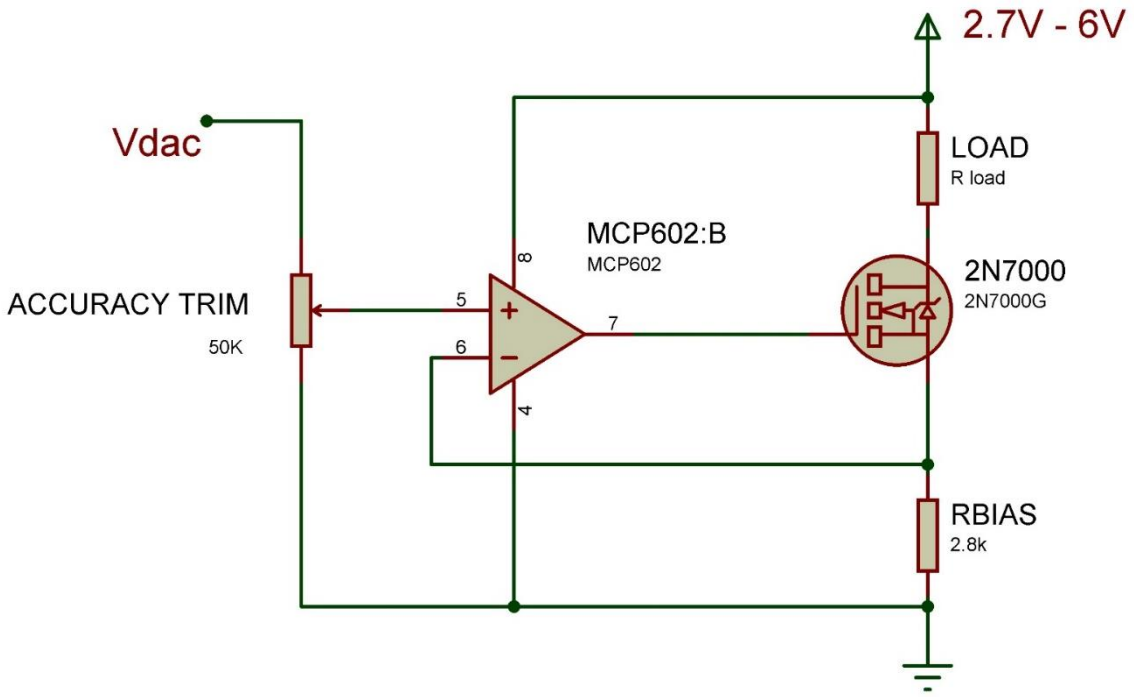

Figure 26: Isolated voltage controlled current source

This design allows a maximum load resistance of 10 kΩ, beyond which the peak current value reduces to ensure smooth operation. This is taken as a good approximate for the tissue model observed from studied literature. If a load larger than 10 kΩ must be connected, then the system can be altered slightly by adding a 6V regulator for the OP-AMP and connecting the load

resistance to a higher voltage. However, the ratio is calibrated for animal brain tissues and need not be changed. With a 12-bit DAC, the system supports a current resolution of 0.1 µA.

3.4.5 Multi-Channel Switching

In order to provide multi-channel functionality a CD4052 Analog Multiplexer is used. This allows the single current source to be used to stimulation of up to 3 electrode pairs. As discussed in literature regarding neural stimulation the simultaneous stimulation of multiple channels is not needed thus a multiplexer-based approach is feasible.

The fastest switching of MUX for biphasic signaling is 0.5 µs without spike and 60 ns with a sharp negative voltage spike, the spike is needed to ensure the current value is maintained at the set point of the system. The MUX has a very high switching speed and can toggle between various states in under 12.5 ns. The system is designed for Electrode pairs to have the following channel states;

Serial No.	Select Channel State	Electrode Pair Status
1	00	Floating
2	01	A+ B- Polarity
3	10	B+ A- Polarity
4	11	Short Circuited (Pair Bypassed)

3.4.6 PCB Layout and Designs

All the components are readily available in the SMD packages which reduce their weights and sizes significantly. The weights of all the components used is as following;

Serial No.	Component	Weight (g)
1	ESP 8266 module	11
2	3V – 750 mAh Battery (x2)	1.416
3	Optional 1N4007 Diodes (x2)	0.336
4	2n7000 MOSFET	0.205
5	MCPMCP 602 OP-AMP	0.063
6	Trim Pot SMD	0.283
7	DAC GY4725 (MCP4725 = 0.043g)	5
8	MUX CD4052 (x2)	0.083
9	Additional Parts (PCB + Resistors etc.)	0.5
	Total	**18.836**

With the choice of components, the total weight falls just under 20g, which adheres to the design constraints.

3.4.7 USER INTERFACE

The Wi-Fi processor used (ESP8266) was given an online webpage with the following interface to show the diverse functionality of the system. The GUI can be accessed through an html webpage and it shows the variable tunable parameters of the wireless simulator.

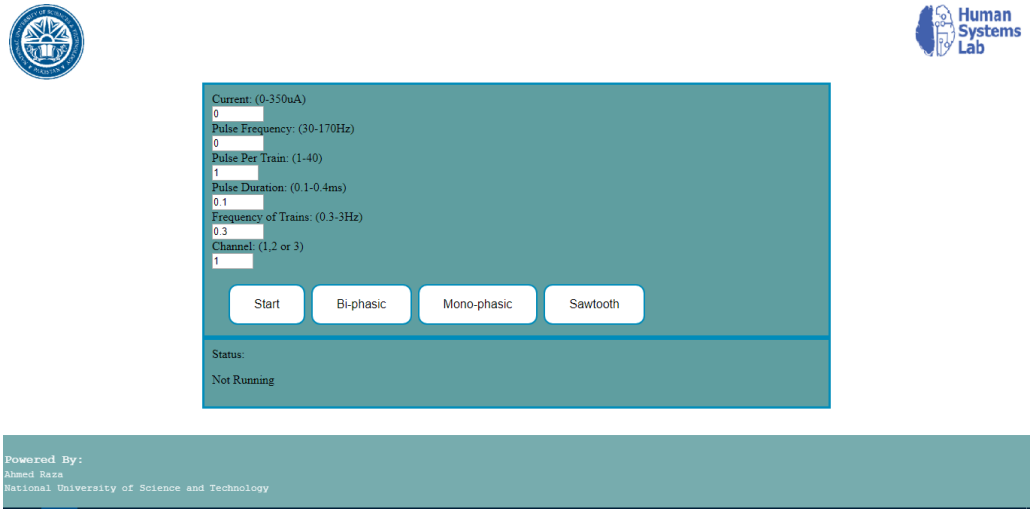

Figure 27: User interface

3.4.8 Complete Schematics

The following figure shows the complete system schematics with all the components connected as described in the previous sections

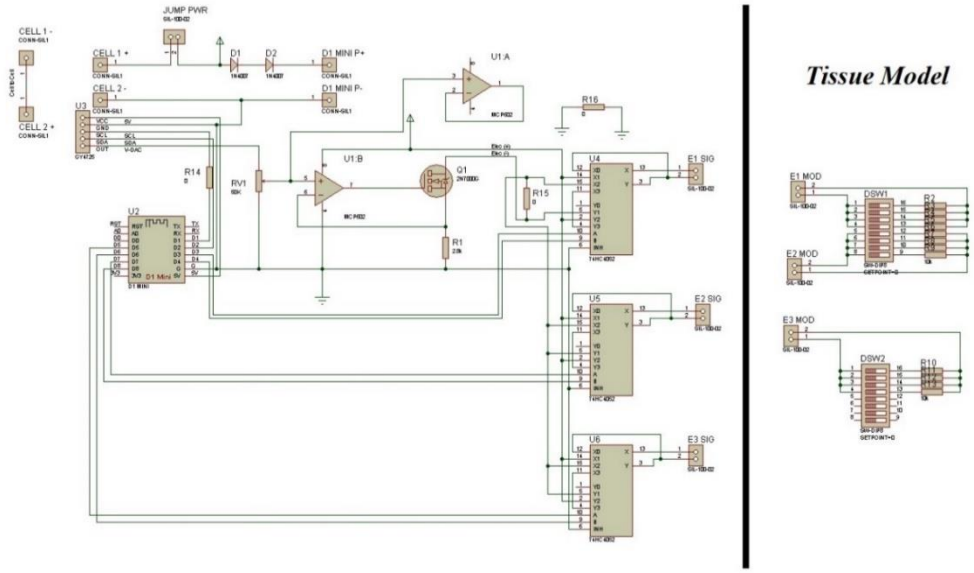

Figure 28: Schematic of final Design

3.4.9 PCB Layout

The PCB Layout of the final prototype is shown in the figures below;

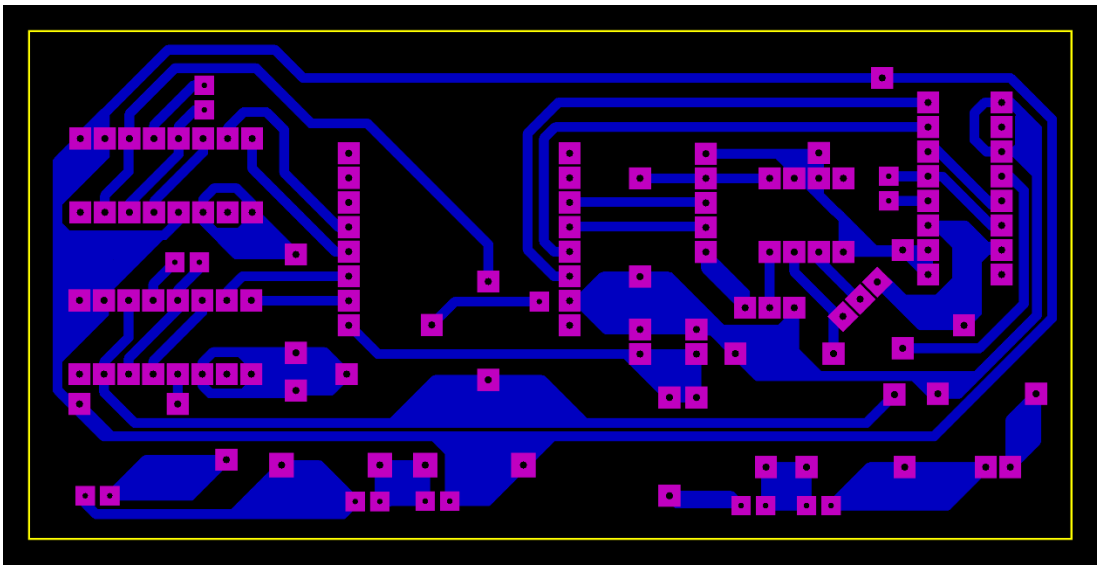

Figure 29: Pcb Layout

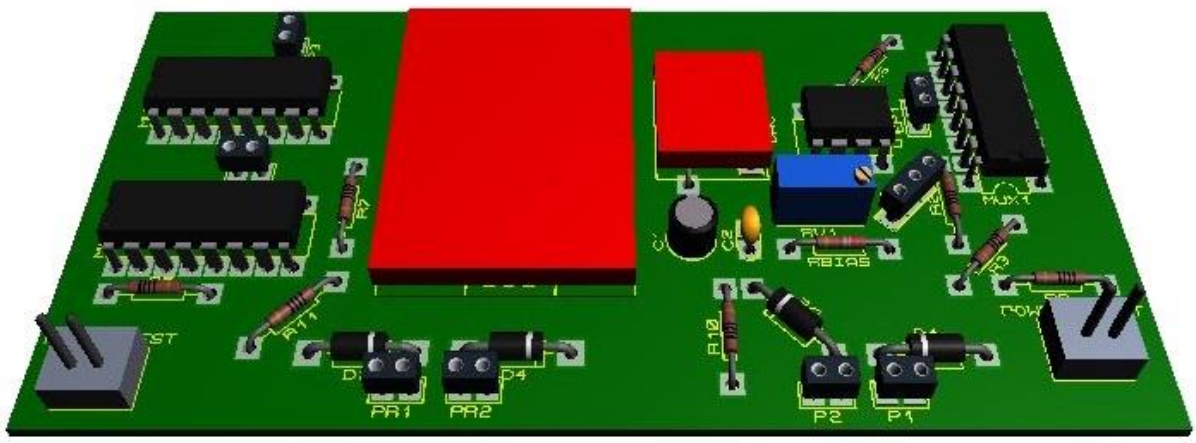

Figure 30: 3D layout

The layout was reworked to contain only SMD components and the actual product was designed with the size equal to ESP-8266. The entire system was mounted underneath the ESP-8266 Wi-Fi module.

4 RESULTS

Data was acquired using power lab through lab chart at sampling rate of 100k/s.

4.1 Monophasic waveform

Monophasic waveform of following parameters:

- Pulse width 0.4msec
- Peak current 258µA
- Pulse frequency =30Hz
- Train frequency =0.5Hz

A single pulse is shown in figure 24 & monophasic pulse train is shown in Figure 25

Figure 31: Monophasic wave

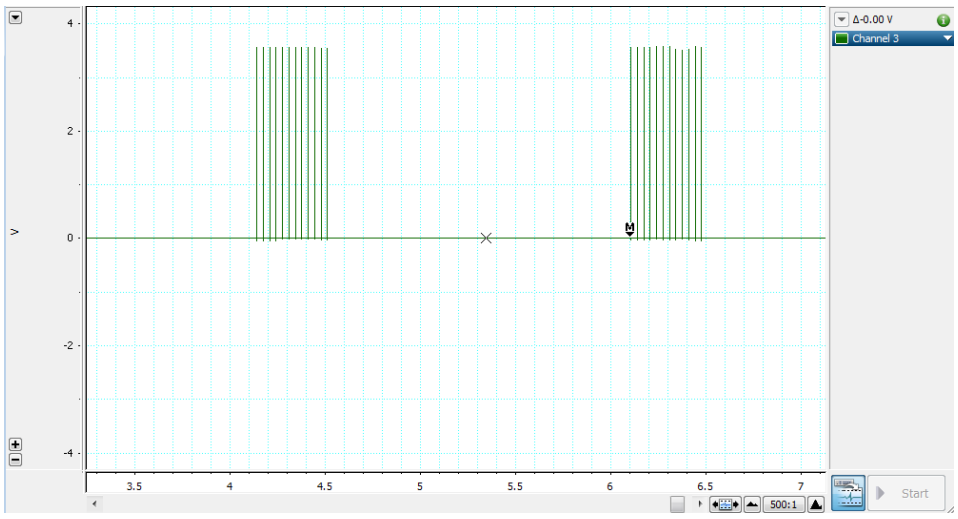

Figure 32: Monophasic pulse train

Monophasic pulse train in opposite polarity is shown in figure 26

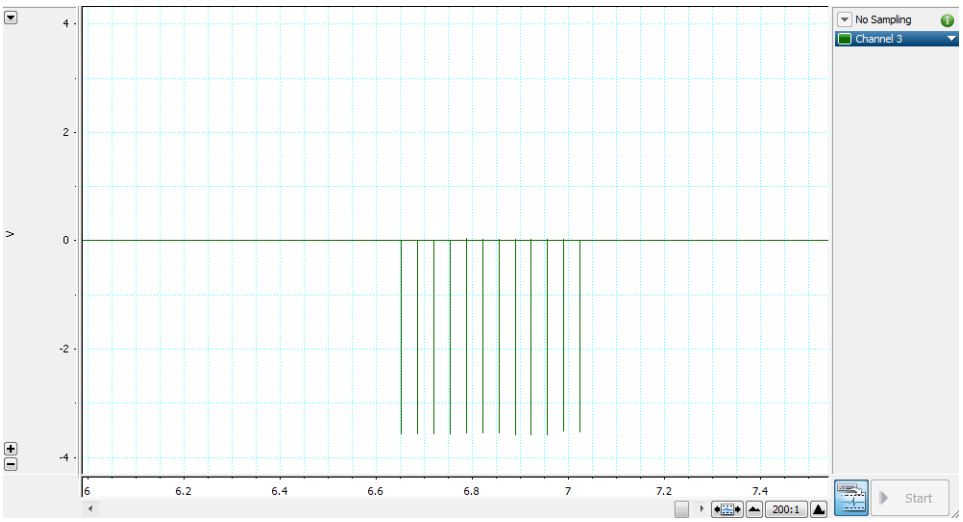

Figure 33: Monophasic pulse train in opposite polarity

4.2 Biphasic waveform

Biphasic waveform of following parameters:

- Pulse width 0.4msec
- Peak current 258µA
- Pulse frequency =30Hz
- Train frequency =0.5Hz

A single biphasic pulse is shown in figure 27 & biphasic pulse train is shown in Figure 28

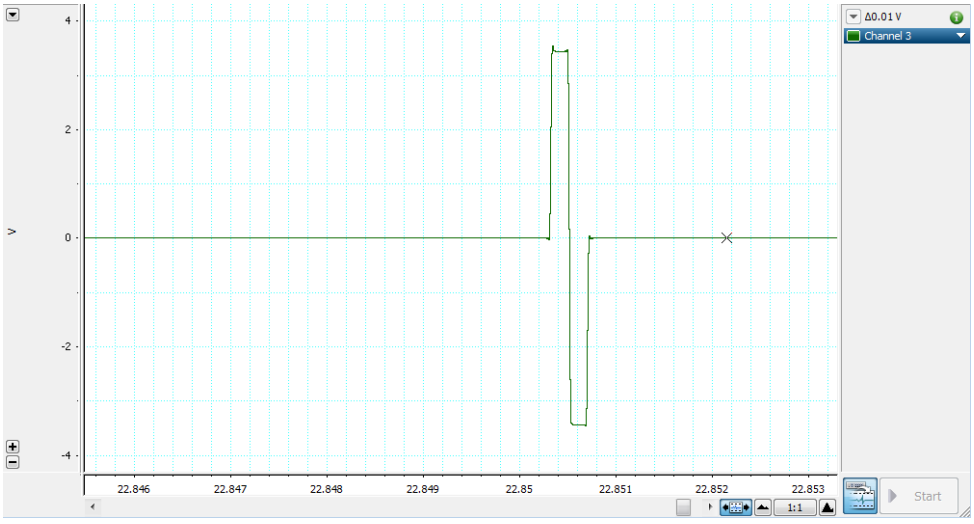

Figure 34: Biphasic pulse

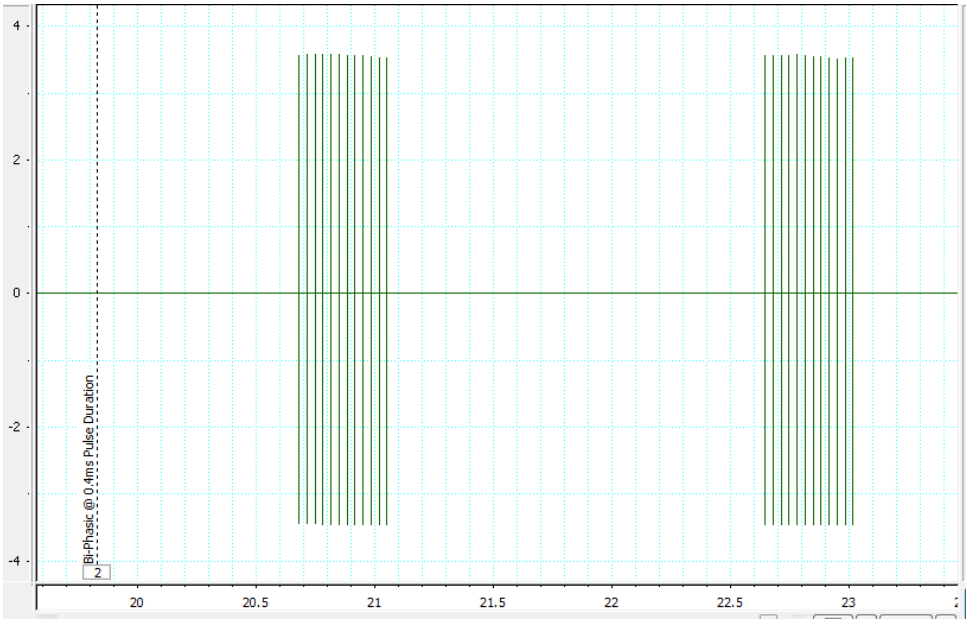

Figure 35: Biphasic pulse train

4.3 Biphasic waveform with Varying Current

A continuous, varying magnitude, Biphasic waveform was generated with the following parameters:

- Peak magnitude of 125µA
- Minimum magnitude of 75µA
- No of steps 10
- Frequency 1Hz

A continuous, varying magnitude, Biphasic waveform is shown in figure 29

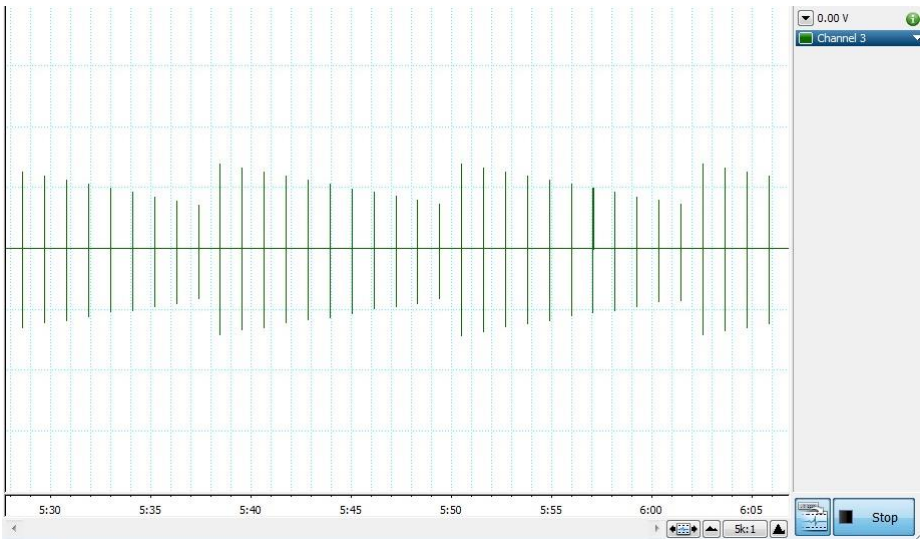

Figure 36: A continuous, varying magnitude, Biphasic waveform

4.4 DAC performance

The DAC was given digital input and its voltage output was given as input to the voltage controlled current source. The figure 30 shows the output voltage of the DAC versus the digital input digital value and figure 31 shows the output current generated by the current source against the digital input value. The current output from the current source was measured against a load resistance (R_{load})of 9758 Ω.

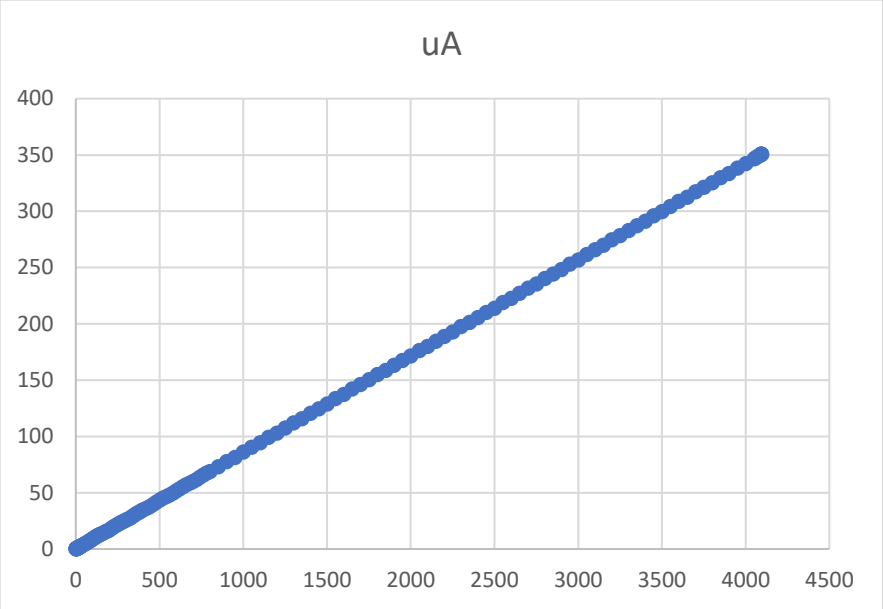

Figure 37: output voltage of the DAC versus the digital input digital value

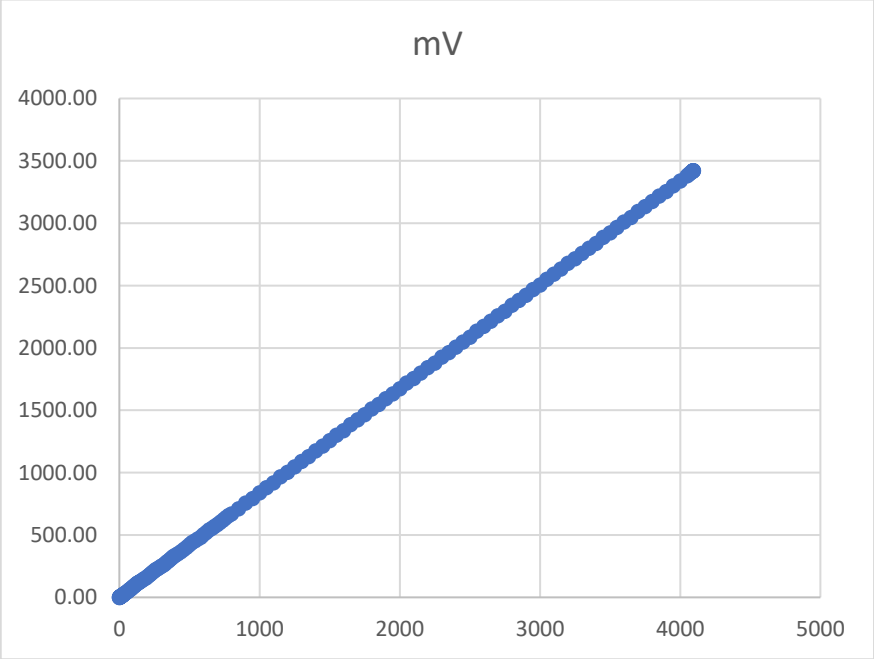

Figure 38: output current generated by the current source against the digital input value

4.5 SNR (SIGNAL TO NOISE RATIO)

To examine the efficacy of the stimulator below is the calculated SNR. SNR was calculated with equation $SNR_{dB} = 20\log_{10}(\frac{\sigma}{\mu})$ where σ = peak noise variance & μ = mean signal amplitude:

- SNR for Biphasic Signal at maximum and minimum frequency.

  SNR at 30 Hz = 71.13dB

  SNR at 170 Hz = 68.0dB

- SNR for Monophasic Signal at maximum and minimum frequency.

  SNR at 30 Hz = 67.2dB

  SNR at 170 Hz = 65.1dB

4.6 CMRR(Common Mode Rejection Ratio)

High CMRR is desired for all medical devices. CMRR for stimulator was calculated by 20xlog $\frac{Peak\ noise\ amplitude}{Noise\ amplitude\ at\ base\ line}$. Below is the CMRR for biphasic and monophasic signals.

- CMRR Biphasic Signal @ 0.4ms = 153.45dB
- CMRR Monophasic Signal @0.4ms= 121.27dB

5 CONCLUSION AND DISCUSSION

5.1 Wireless Stimulation Device

The wireless stimulation device developed through this study meets all the mentioned design specifications. The device was developed using easily available components without increasing the complexity of design too much. The final prototype was tested, and the behavior was found comparative to the other wired stimulation devices commercially available.

The wireless connectivity over Wi-Fi instead of Bluetooth or RF has added advantage of universal availability and ease of access. Bluetooth has considerably less range than Wi-Fi whereas RF is more susceptible to environmental noise. The device was tested, and the current waveform generated as the output was observed though Power Lab® using Lab Chart® by AD Instruments™.

Such a device can find many applications in biomedical and neural engineering systems, such as tDCS for the treatment of Parkinson's disease, behavioral studies of animals in their natural resting states, deep brain stimulation for animal movement control and reinforced feedback behavior training.

5.2 Future Work and Recommendations

The final model designed using SMD components can be used as a readily available alternative to commercially available high-end devices. The system can also be enhanced further by introducing further features which facilitate the applications of the device such as;

- Extension of a backpack or jacket for mounting the complete apparatus on the animal under study. This will also ensure that the battery can be replaced with relative ease between trials.
- Performing in-vitro testing on animals will yield better performance analysis and it can be used for product life-cycle testing.
- An analog input slot has been left to incorporate an analog feedback current sensor for monitoring the current provided. Effectively the voltage across the R_{BIAS} resistance of the current sensor is also a direct feedback of the current generated by the current source.
- Adding a 3rd MUX and an instrumentational amplifier to the design will allow the model to be converted from an active stimulation to a passive sensing device. Thus, also allowing the user to acquire EEG information directly by measuring the electrical activity inside the brain. This extends the range of applications of the device considerably.

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