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Transcranial Electric Field Stimulation

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Transcranial Electric Field Stimulation

A dissertation submitted in partial satisfaction of the
requirements for the degree of Doctor of Philosophy

in

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by

Arash Arfaee

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Co-Chair

Chair

University of California, San Diego

2015

DEDICATION

This thesis is dedicated to whoever felt punished for their capabilities and disabilities in an education system.

EPIGRAPH

The saddest aspect of life right now is
that science gathers knowledge faster
than society gathers wisdom.

Isaac Asimov

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VITA

1998-2001	B.S. in Computer Hardware, Azad University of Southern Tehran, Tehran, Iran
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ABSTRACT OF THE DISSERTATION

Transcranial Electric Field Stimulation

by

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Doctor of Philosophy in Computer Science (Computer Engineering)

University of California, San Diego, 2015

Professor Vilayanur Subramanian Ramachandran, Chair
Professor Patrick Mercier, Co-Chair

Nervous stimulation with electric methods not only has a long history in the treatment of many conditions but also in the last two decades has been used increasingly as a powerful functional brain mapping tool alongside other imaging techniques. This technology has been used to record the stimulation-evoked activity of the stimulated location.

This research describes work surrounding a novel technique for brain and nervous stimulation using the electric field as the medium; particularly transcranial brain stimulation by an electric field and its possible advantages compared to relatively similar

techniques.

This thesis discusses our knowledge regarding brain electrical activities as they relate to this project. We will present discoveries concerning the role of electric fields in the brain and the effects of external electric fields on neuronal function. Then we discuss our new prototype, its design, and some results from simulations. Our device aims at introducing the use of electric fields in modifying the functional activity of the brain in a precise and accurate manner, one that surpasses that of other current methods, minimizing some of the side effects, and maximizing effectiveness in altering desired brain function.

The goal in this thesis is to demonstrate the potential that this technology can provide us. We show that in theory this device could be used as a very high-resolution brain stimulation device. we leave the speculation about impacts of this device in the medical world to the readers imagination.

Chapter 1

Current Methods in Transcranial Electrical Brain Stimulation

For centuries, scientists have been experimenting with electricity and its effect on the brain and the nervous system. A Roman physician reported the use of transcutaneous electrical nerve stimulation (TENS) using torpedo fish electrical discharge for treatment of medical conditions such as gout, headaches, and general pain [1]. We have come a long way from there. Nowadays, advances in science and technology allow us to introduce miniature devices inside the brain [2] to control mood [3], treat psychological disorders [4], and reduce symptoms of neurological diseases such as Parkinsons disease [4]. The use of magnetic fields also allows us change our brain function temporarily or permanently [5] and can help us to discover more about the human brain and treat many neurological conditions.

Herein, we will summarize some of the best-known electrical brain transcranial stimulation methods. Although brain stimulation can be done more efficiently and accurately with invasive Deep Brain Stimulation, DBS [2], the focus here is on noninvasive methods, which by changing the neurons' membrane electric potentials, stimulate the brain. Three methods will be discussed. Electroconvulsive therapy (ECT) and Transcranial Direct-Current Stimulation (TDCS) and its variations stimulate the brain by passing massive (ECT) or minimal (TDCS) current through the brain. Transcranial magnetic stimulation (TMS) achieves this goal by affecting brain function through magnetic fields.

1.1 Electroconvulsive Therapy (ECT)

Electroconvulsive therapy (ECT), a much evolved procedure from its original crude version, is a short treatment done under general anesthesia or, with the administration of muscle relaxants, as an outpatient procedure. The treatment includes stimulating the brain with enough electric current which causes transient brain seizures, which is much more than the current level that causes stimulation, and consequently changes the functioning of the brain, reducing or eliminating signs of severe mental illness such as depression or bipolar disorder. Some research suggests that brain seizures are sufficient to generate an effective treatment. Currently, brain seizures can also be induced with chemicals [6].

The mechanism of action for ECT is hypothesized to be by flattening the electroencephalogram (EEG) signal over the course of multiple treatments, suggesting a resetting of the brain signals. ECT also seems to change the concentration of various neurotransmitters in certain regions of the brain and not others. In some areas neurotransmitters including seratonin and glutamate are increased or receptors have an increased sensitivity to the molecule. As a consequence, the dopaminergic pathways are activated. These pathways are associated with positive feelings or the reward center of the brain, which can explain the change from the depressive state of the patient [7, 8]. According to Karamustafalioglu et al. [9], ECT decreases the nerve growth factor brain-derived neurotrophic factor (BDNF), an increase in which is associated with a wide array of mental illness. Microarray studies reveal which genes are active. These studies have been done by Kaneko et al,and currently demonstrate genes and pathways activated.

This suggests that ECT activates neurogenesis (formation of neurons) [10]. While the complete mechanism of action is not known, there is a body of evidence that indicates both a change in the electrical and the chemical state of the brain as a result of ECT. The induced brain seizures are responsible for the healing effects of ECT for mental illnesses such as depression.

Many side effects are observed after ECT treatment. In almost all cases, ECT recipients suffer from retrograde amnesia.

1.2 Transcranial Direct-Current Stimulation (TDCS)

TDCS is technologically the simplest transcranial stimulation device than can be built. It is as simple as connecting a battery to the brain through two electrodes. This method injects a low and constant current into the brain, which causes an increase in the neuronal excitability and more spontaneous cell firing [11, 12]. More advanced and medical versions of TDCS devices often have additional circuits to control the exact amount of the current. Some studies show improvement of cognitive function, memory, and mathematical abilities. In the 1960s, there was a short period of time when TDCS was the subject of multiple studies [13, 14] however, it is not the subject of much research today. TDCS recently has become more popular among gamers in hope to improve their reaction-time and focus during the game (see Figure 1.1 Right side) [15].

Figure 1.1. Left: A homemade TDCS device made for personal use [16]. Right: A gamer using TDCS to increase his focus [15].

Multiple variations of the TDCS device with more control over the shape and level of the stimulation current, like Transcranial Alternating Current Stimulation (tACS) [17], have been developed. At the moment there is not active research on this device. It showed some effect on the Alpha (8 - 13 Hz) to Beta (1 - 4 Hz) frequency bands, but no effect in Theta (4 - 8 Hz) or Gamma (30 - 70 Hz) frequency bands has been observed [18, 19].

Since devices in this category are relatively cheap and can be purchased or easily made and used without a physician's prescription [15] (see Figure 1.1 Left side), they are one of the most commonly used brain transcranial stimulation devices in the market.

1.3 Transcranial Magnetic Stimulation (TMS)

In 1910, lack of technology stopped Silvanus P. Thompson from a successful implementation of his version of TMS (Figure 1.2). 75 years after Thompson's attempt, in 1985, Anthony Barker and his colleagues made a functional TMS and performed the first successful TMS study (Figure 1.3).

Since then TMS design has improved significantly, and it is now a primary tool in many studies [20, 21, 22, 23]. Moreover, many studies explore the use of TMS as a treatment for various psychiatric conditions[24, 25, 26]. In 2008, the FDA approved the use of TMS for treatment-resistant major depressive disorder [27]. TMS also received approval from the FDA for treatment of migraines in 2013 [28].

Alongside approved TMS treatments, TMS is used frequently in Brain mapping [20, 21, 22]. In the last couple of years there has been a rise in many neurofeedback and neuropsychotherapy practices all around the US, offering a variety of unapproved treatments that involve repetitive TMS (rTMS) sessions. Among these treatments, we can find treatments for ADHD [25], addiction [24], pain management [23] and depression [26].

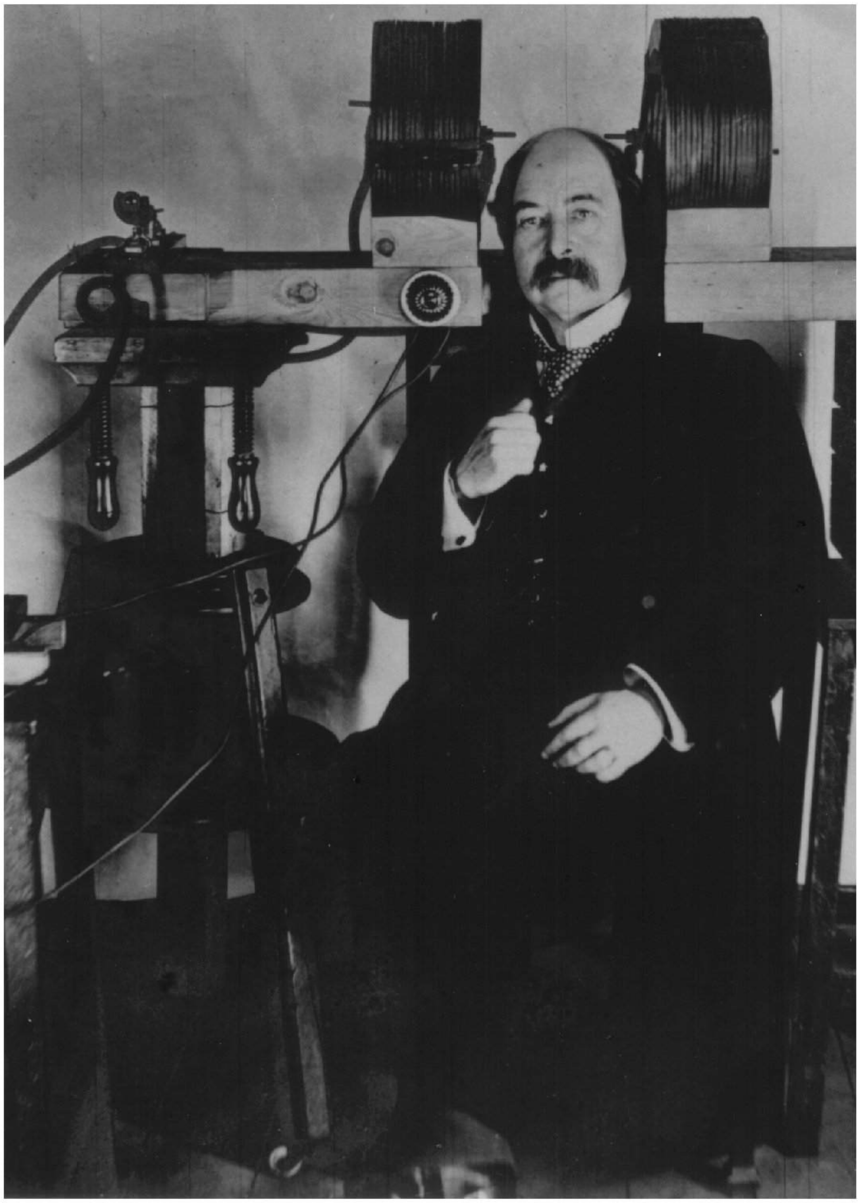


Figure 1.2. Silvanus P. Thompson with his unsuccessful TMS machine, London 1910 [29]

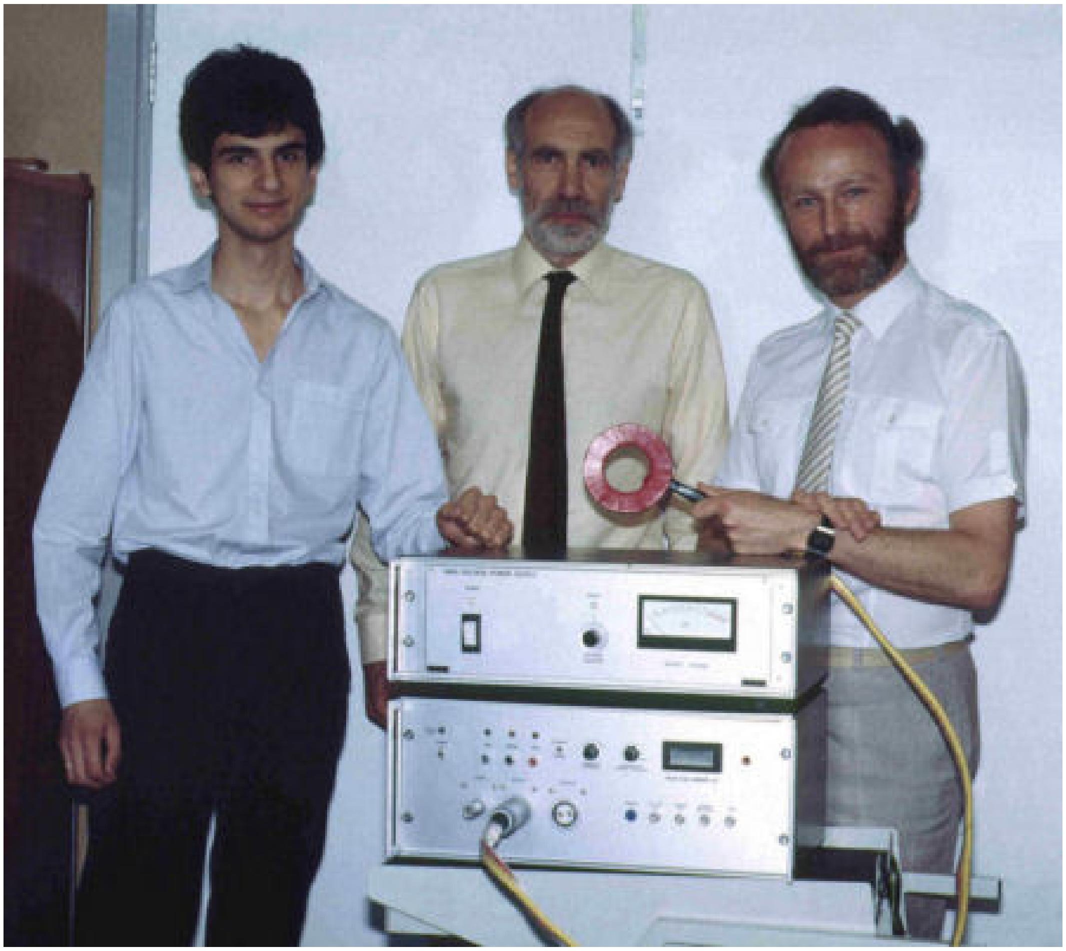


Figure 1.3. The Sheffield group with the their first successful TMS, February 1985 [29]

1.3.1 How TMS Works

TMS stimulates the brain by generating magnetic field pulses (see Figure 1.4). During the procedure, a coil is placed near a subject's head close to the targeted region. The discharge of a capacitor array pumps a massive current into the coil(s) that produce(s) a magnetic field pulse. Part of the field enters the brain and affects the targeted tissues.

The change of the magnetic field inside the brain tissue generates an electric field. The change of the electric field causes a change in the transmembrane current of the neuron, which results in the depolarization or hyperpolarization of the neuron and finally causes an action potential.

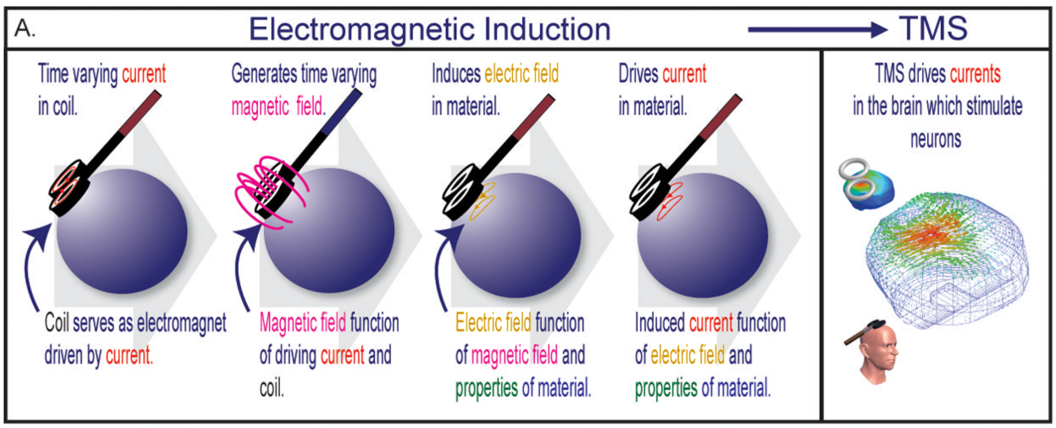


Figure 1.4. the mechanism of stimulation with TMS. A current pulse inside the coil generates magnetic fields. Change of magnetic fields induces electric fields inside the brain. Change of electric fields induces electrical current which results in brain stimulation. [30]

Repetitive Transcranial Magnetic Stimulation, rTMS (see Figure 1.6 Part D for pulse shape), is known to have a longer effect than the effect of single or paired pulses. rTMS is a series of magnetic pulses that is applied to a subject. Since it has a more lasting effect, it has more potential to be used in many therapeutic procedures.

In rTMS, low frequencies, particularly less than 1 Hz (in less commonly used definition, up to 5 Hz), are known to reduce brain activity (inhibitory) in the part the brain that has been stimulated. Higher frequencies, $(10-20)$ Hz, tend to increase the brain activity (facilitatory) in the stimulated region [31].

Although in most TMS devices, the maximum frequency is in the range of 20 Hz, some new devices, mainly produced for research purposes, can generate pulses with full intensity up to 30 Hz and with less than full intensity up to around 100 Hz [31].

Typical TMS coils can only stimulate cortical areas of the brain. For deep brain stimulation [32] with TMS, the H-Coil has been used (Figure 1.5). The H-coil is a combination of multiple coils in the shape of a helmet. The field generated by these coils in any place of the head can be less than harmful (over-stimulation) and at the same time, the summation of field vectors in the deeper area can be sufficient for the stimulation.

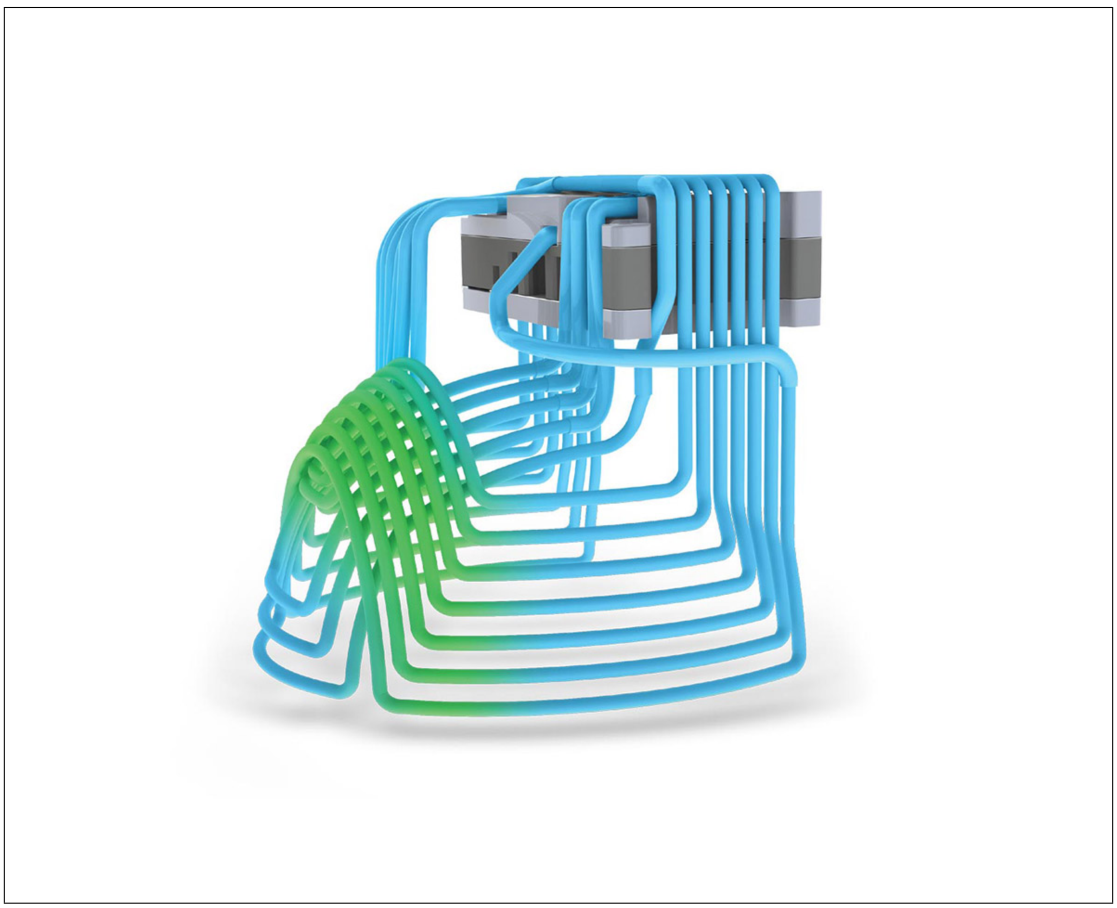


Figure 1.5. Deep Brain stimulation is possible with an over the head special coil called an H-Coil [33, 32]

New TMS devices have added more control/protocols over the shape of the stimulation signal [34]. These protocols are used in functional brain research and are not approved by the FDA for any treatments yet. These new TMS devices can be programmed to generate a train of pulses (Figure 1.6 Part C). The Theta Burst protocol, consists of bursts of 3-5 pulses at 50 Hz that are repeated at 5 Hz (theta rhythm) (Figure 1.6 Part E) [35]. new devices also can generate Paired-Pulse TMS (Figure 1.6 Part B), ppTMS, which consist of two pulses each with their own distinct magnitude and with specified timing between them. The Ramps protocol is a series of pulses. Their magnitude is gradually increased in the beginning of the series and decreased at the end of it (Figure 1.6 Part F).

Some TMS devices can also be used to stimulate peripheral muscles without the pain experienced by electrical stimulation. Devices capable of such stimulation are called Peripheral Magnetic Stimulation (PMS) or TMS with PMS capability (Figure 1.6 Part F).

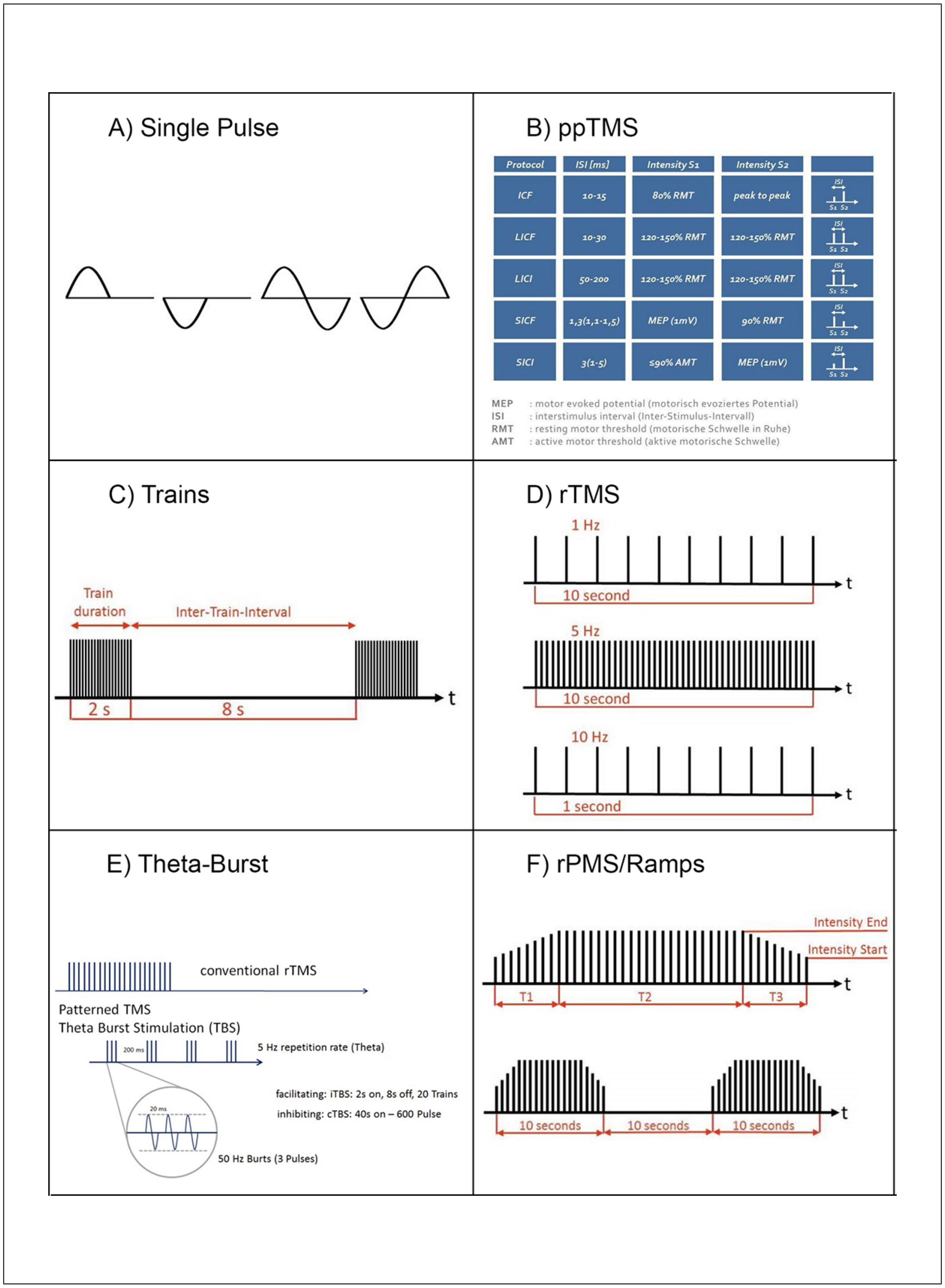


Figure 1.6. Some TMS Protocols implemented in Mag & More GmbH Co. TMS devices [34]

1.4 Conclusion

There are multiple electrical devices out in the market that can be used on patients to treat or control their conditions transcranially. Each has their own benefits and limitations, which we discuss in more detail in Chapter 3. As it has been discussed in this section, one of the most commonly used devices in both research and treatment is TMS. There is a great deal of recent research studies using TMS, and its applications. We presented the most advanced protocols to show how far TMS have come from its early days. As useful as TMS has proven to be, it has some limitations that our current advances in science and technology cannot overcome. We discuss these issues in more detail in Chapter 3.

We presented functional aspects of TMS devices in more detail in this chapter, since this thesis is presenting a device that is most similar to TMS versus the others, and we hope that it will be the next step in brain stimulation devices. Thus, it is essential that, at least, our device should be capable of being programmed with the known TMS devices' capabilities.

Chapter 2

Electric Fields and the Brain

In this section, we discuss some facts about brain electrical activity. First we discuss the electrical activity of individual neurons, and then some recent findings about the function of electric fields in the brain, and on the effect of external electric fields on the brain. Here, we will try to show that not only are electric fields an essential part of brain activity, but that external electric fields can also easily manipulate the functions of the brain.

2.1 Some Facts About Brain Electrical Activity and Characteristics

In 2011, a group of scientists [36] at Allen Institute for Brain Science/California Institute of Technology made a high-resolution measurement of the electrical field activity of rat brain cells. Their findings indicated that electric fields generated by a neuron's action potential can feedback to adjacent neurons and modify their behavior. This suggests that another form of communication in the brain is through electric fields. Although scientists use electric fields generated by neurons useful to monitor brain activity (EEG, ERP), before these findings, the only well-known phenomena associated with the function of electric fields in the brain was the neural activity during severe pathological conditions such as epileptic seizures.

A brief review of a few known facts and definitions about neural mechanisms of activity from an electrical point of view seems helpful in this chapter.

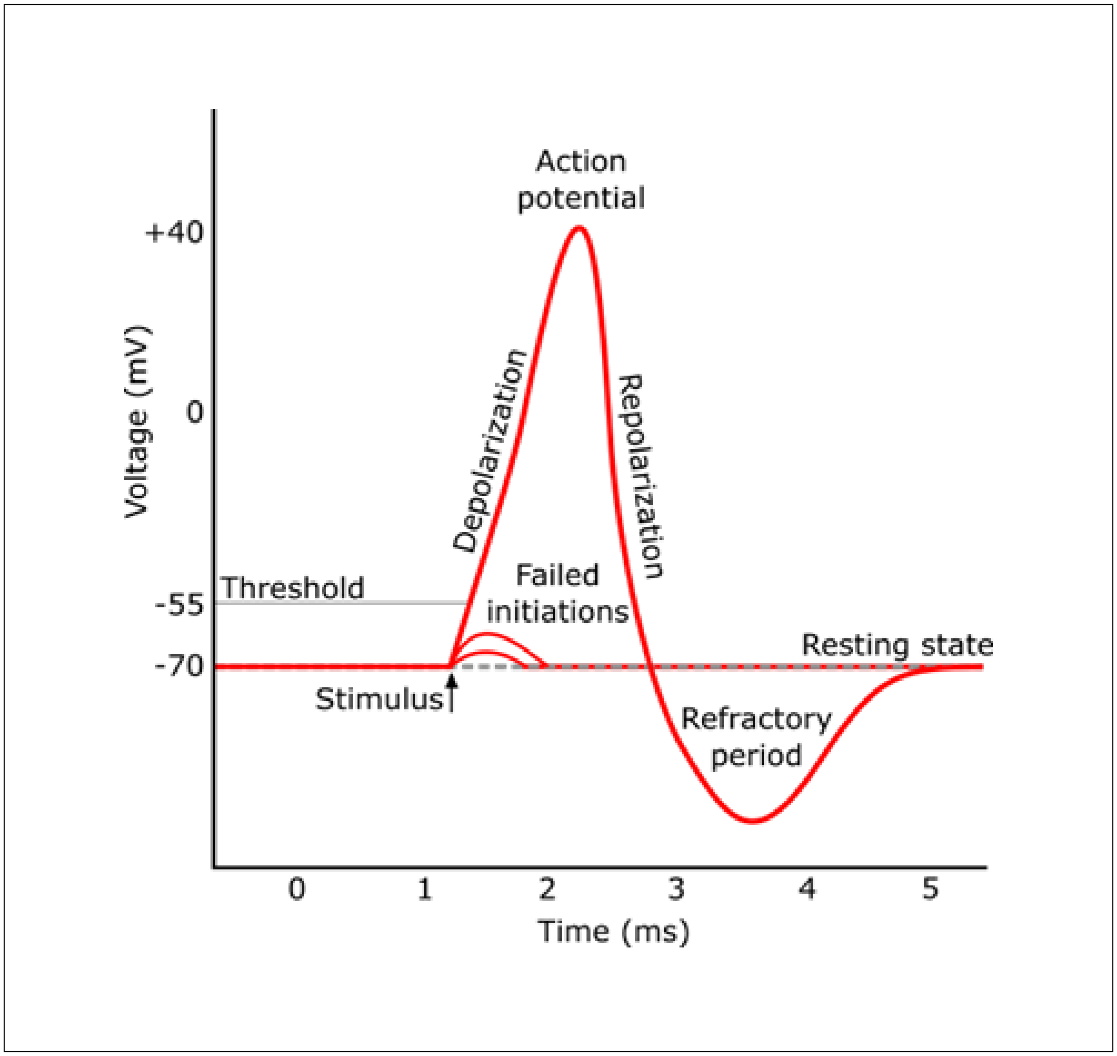


Figure 2.1. Approximate plot of a typical action potential shows its various phases as the action potential passes a point on a cell membrane. The membrane potential starts out at $-70\ mV$ at time zero. A stimulus is applied at $time = 1\ ms$, which raises the membrane potential above $-55\ mV$ (the threshold potential). After the stimulus is applied, the membrane potential rapidly rises to a peak potential of $+40\ mV$ at $time = 2\ ms$. Just as quickly, the potential then drops and overshoots to $-90\ mV$ at $time = 3\ ms$, and finally the resting potential of $-70\ mV$ is reestablished at $time = 5\ ms$ [36, 37] .[38]

Action potential or nerve impulse :

When a stimulus, or a set of them, increases the typical neuron cell membrane voltage from $-70\ mV$ to $-55\ mV$ (threshold) it causes the neurons to generate an electrical pulse. Simply, if the voltage of a typical neuron cell membrane increases $15\ mV$ when the cell membrane voltage is in its resting state, the neuron will fire. So, any external stimulation device needs to increase cell membrane potential by $15\ mV$ to evoke an action potential at a point and hence cause simulation. If we look at the brain cell membrane as a capacitor, the increase in electrical potential of the cell membrane would be a function of intensity of stimulation and time. In other words, to know how to appropriately charge this capacitor to the desired level (increase cell membrane potential by $15\ mV$) we need to know electrical characteristics of brain cells. The so-called strength-duration curve could answer some of these questions.

Rheobase and strength-duration Curve :

> Rheobase is a measure of membrane excitability. In neuroscience, it is the minimal current amplitude of infinite duration (in a practical sense, about 300 milliseconds) that results in the depolarization threshold of the cell membranes being reached, such as an action potential or the contraction of a muscle.
>
> Rheobase can be best understood in the context of the strength-duration relationship. The ease with which a membrane can be stimulated depends on two variables: the strength of the stimulus, and the duration for which the stimulus is applied. These variables are inversely related: as the strength of the applied current increases, the time required to stimulate the membrane decreases (and vice versa) to maintain a constant effect. [38]

This curve shows how the duration and amplitude of a stimulation can be adjusted to ensure that the desired effect is applied to the brain (see Figure 2.2 and Figure 2.3). Although this curve is originally defined based on the current value and stimulation time, different varieties of it have been used. In general the curve is based on a stimulus quantity and the stimulation time. Figure 2.3 shows an example based on a particular TMS maximum pulse amplitude and stimulation time.

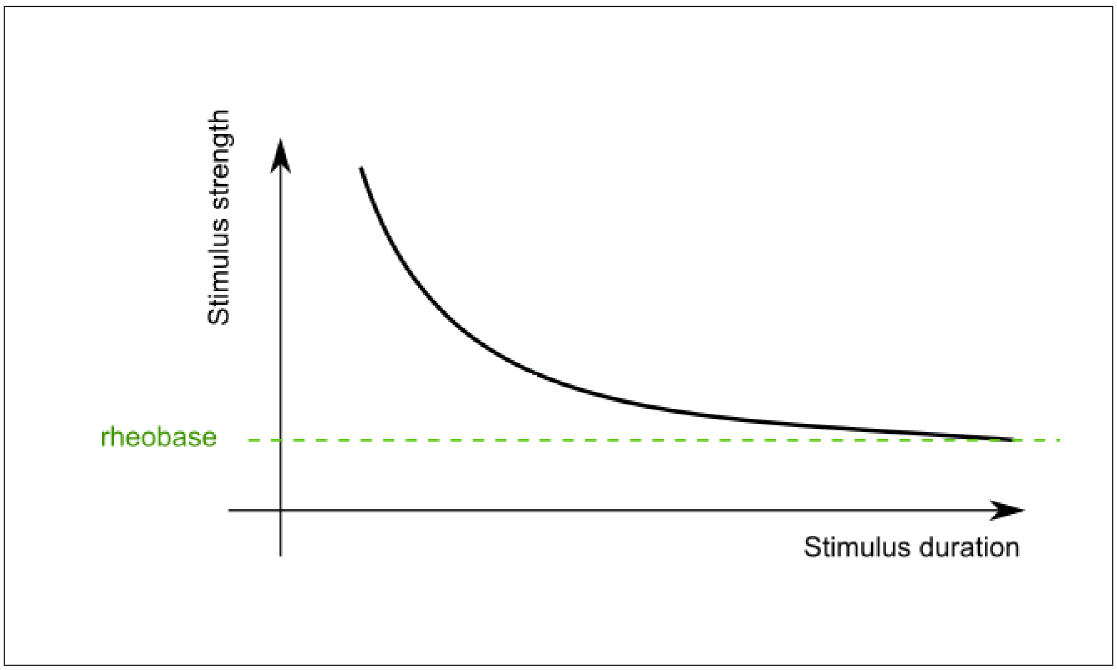


Figure 2.2. A typical Strength-duration Curve[39]

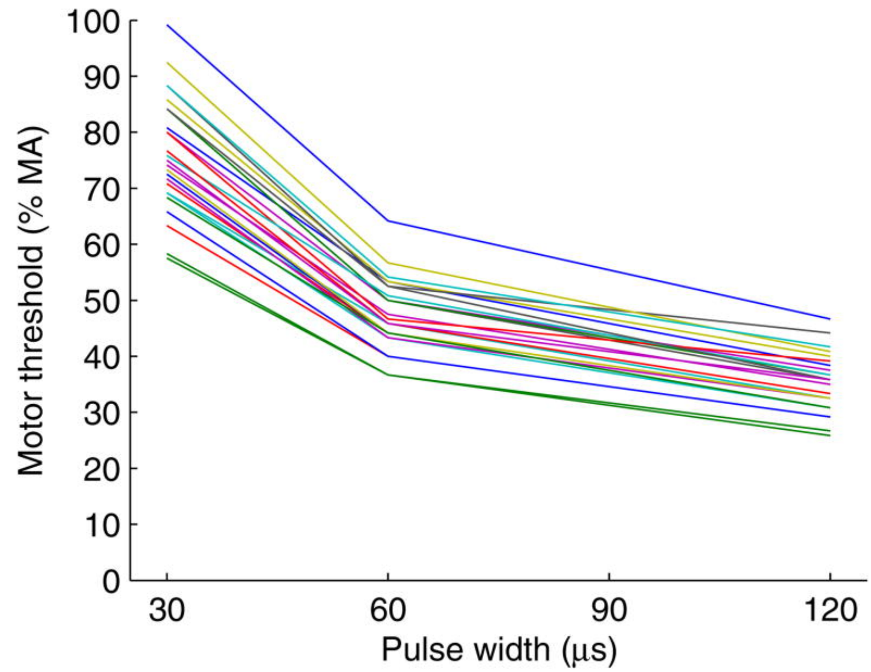


Figure 2.3. Strength duration Curve calculated by measuring motor threshold of 26 subjects measured as percentage of TMS maximum pulse amplitude (% MA) at pulse widths of 30, 60, and 120 μs [39]

Ephaptic coupling :

> Ephaptic coupling is a form of communication within the nervous system and is distinct from direct communication systems like electrical synapses and chemical synapses. It may refer to the coupling of adjacent (touching) nerve fibers caused by the exchange of ions between the cells, or it may refer to coupling of nerve fibers as a result of local electric fields. In either case ephaptic coupling can influence the synchronization and timing of action potential firing in neurons [40].

Ephaptic coupling is a phenomenon associated with the effect on the adjacent nerves, and has been known for more than a century. This phenomena suggest the possibility of affecting the nervous system through an external electric field from outside the head which we will discuss in section 2.3.

2.2 History and Previous Works

There is not much research on the effect of the electric fields on the brain. Although there are multiple publications on the safety of electric fields emitted from power transmission lines, they are not addressing any information relevant to this project. However, there are two published papers from 1986 and 1975 available about exposing the human brain to external sources of electric fields and its effect on subjects.

In 1986 [41] Blackwell conducted an experiment to evaluate the effect of electric fields on the rat brain. In this experiment rats were put between two plates and they were exposed to an electric field of maximum 100 V/m in frequencies from 5 – 100 Hz. For low frequencies i.e., 15 Hz and 30 Hz (Figure 2.4 and 2.5) the electric field was enough to modulate (synchronize) the neural activities with the frequency of the external electric field. However, we now know, based on the strength-duration curve, that to stimulate at the higher frequencies we need much higher field magnitude to cause any effect. As can be seen in Figure 2.4 and Figure 2.5, a field with similar magnitude, as was used for the lower frequencies, was not enough to create synchronization at 50 Hz. However, their effects are obvious at 15 Hz and 30 Hz (see Figure 2.5).

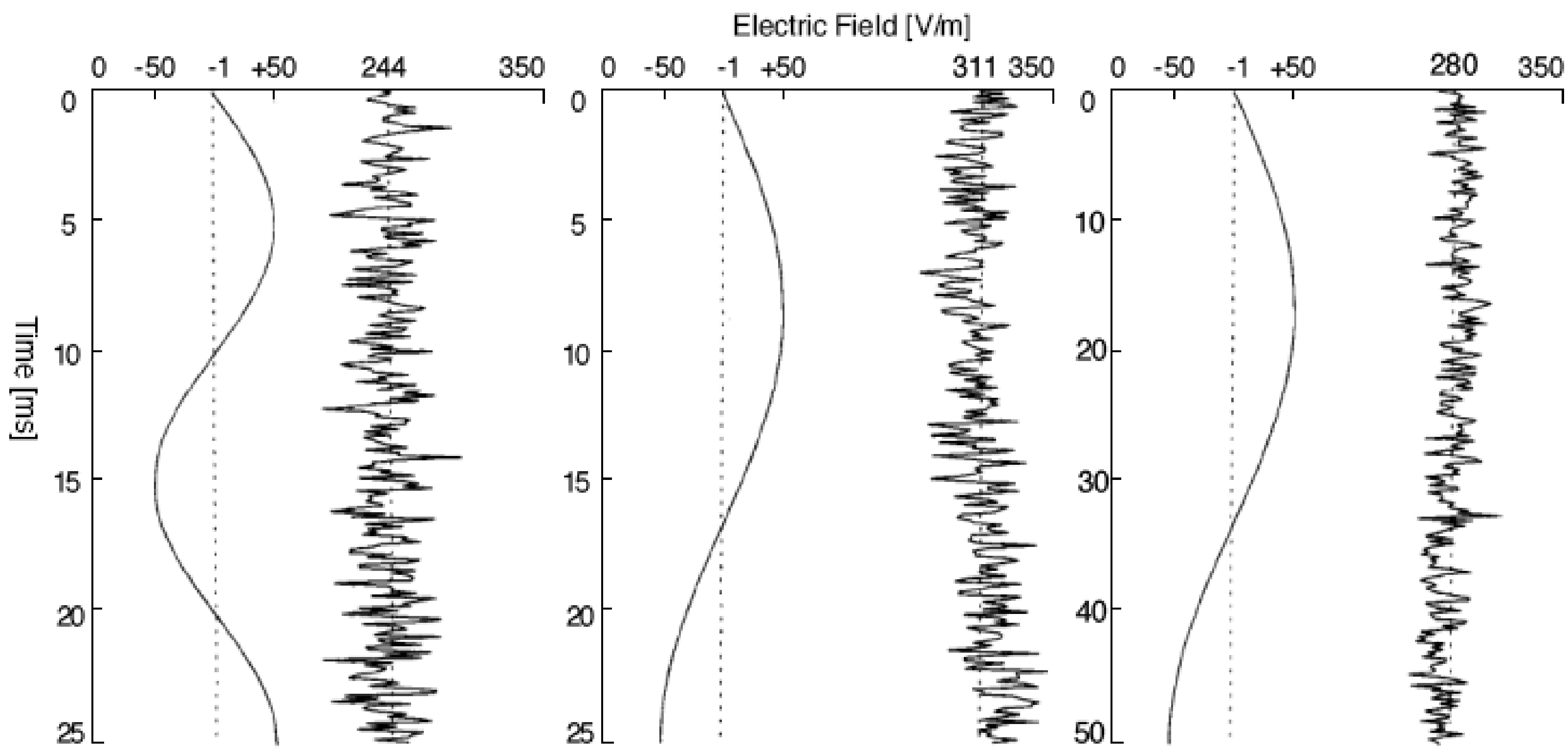


Figure 2.4. Results of the effect of exposure on time of arrival of spikes for 15 *Hz*(upper), 30 *Hz* (middle), and 50 *Hz*(lower) exposures. The upper portion of each trace shows the total number of spikes recorded from all exposures. The lower portion of each trace shows the amplitude of the exposure waveform. Dotted lines show the mean values of both the total spike count and the exposure waveform. [41]

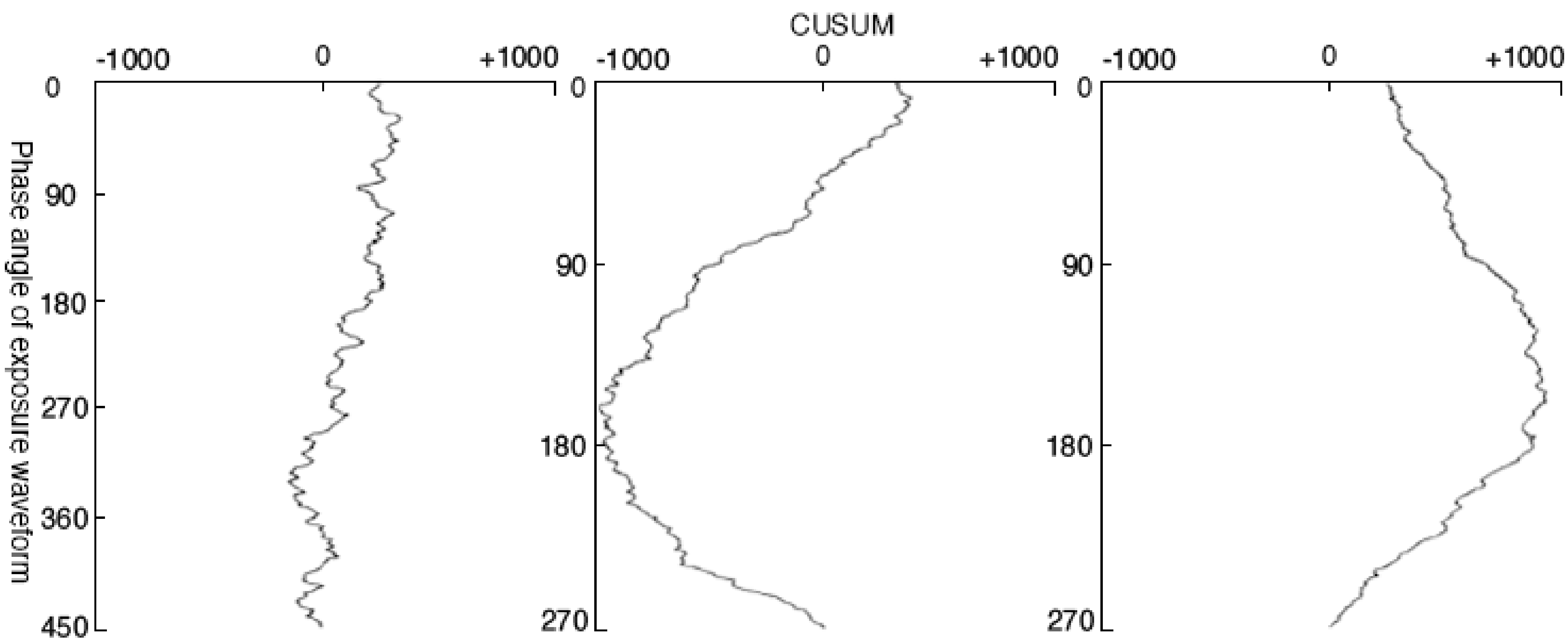


Figure 2.5. The data expressed as a cumulative sum of deviations from the mean value as a function of the exposing waveform phase, for 15*Hz*(upper), 30 *Hz*(middle), and 50 *Hz*(lower) experiments. [41]

A decade earlier in 1975, Persinger and et al. [42] explored the effect of a weak electric field at 3 Hz and 10 Hz on human reaction time. Here is how the condition of the experiment was described in [42]:

> The electric fields were produced by applying electrical potentials horizontally from a Heath-Schlumberger (model EU-81A) function generator (sine-wave mode) across two 12-gauge steel plates ($0.8\ m \times\ 0.8\ m$), separated by 0.8 m. The plates were held vertically on their 0.4 cm edges in a wooden reinforced frame $1.1\ m \times 0.9\ m \times 2.0\ m$. A single layer of galvanized-steel fly screen was wrapped and stapled around the frame. One end of the cage was made into a door so that when closed the cage was sealed by wire screen (Faraday cage). The steel plates, Faraday cage, and signal generator were connected to the standard 110 V ground cable.

The subjects were exposed to 3 different magnitudes of electric fields: 0 V/m, 0.3 V/m and 3 V/m in 3 Hz and 10 Hz frequencies. Once again the results showed high dependence on frequency and magnitude of the field. The only noticeable changes accrued when subjects were exposed to the strongest level of electric field, 3 V/m, and the results were more noticeable in the 3 Hz frequency. As expected, with our current knowledge about brain stimulation, subjects exposed to the electric field stimulation had slower reaction times with Delta wave (3 Hz) and faster reaction times with Alpha wave (10 Hz) stimulation. These results not only confirm the possibility of using weak electric fields for transcranial stimulation, but also show importance of adjusting the field magnitude in different frequencies based on the strength-duration curve to achieve the preferred level of stimulation. Later in Chapter 4 we show it is also highly dependent on the shape of the field as well.

2.3 Effects of Electric Fields on Neurons Generated by an External Source

In this thesis, we use an expanded definition of ephaptic coupling. The original definition refers to the voltage change of adjacent neurons cell membrane through electric field induction, where the neuron activity itself generates the electric field. Here ephaptic coupling refers to a voltage change of the cell membrane through electric field induction from any electric field in general [36].

Research on ephaptic coupling phenomena shows that a relatively small external field can affect the neuron action potential timing, and at higher amplitudes, can force them to have action potential. The effective amplitude in both conditions based on the strength-duration curve is related to the duration of the stimulus or, in a repetitive stimulation, to its frequency.

The most recent notable study on the effect of external electric fields, as mentioned above, has been done at the Allen Institute for Brain Science in 2011 [36]. This experiment was performed on rat cortical neurons. Here is how they summarized their results regarding neurons stimulated with an external electric field [36]:

> We found that extracellular fields induced ephaptically mediated changes in the somatic membrane potential that were less than 0.5 mV under subthreshold conditions. Despite their small size, these fields could strongly entrain action potentials, particularly for slow (<8 Hz) fluctuations of the extracellular field.

Their findings once again not only show potential for synchronization of brain cells with an electric field below the action potential threshold, which our device (described in the next chapter) can also provide, but also once again demonstrates the relation between stimulation frequency and the stimulation magnitude.

Granting this research evidently points to the effectiveness of transcranial electric field stimulation, it also shows our relative lack of knowledge in this field. This leaves us with many unanswered questions that demand much more prolonged and in-depth research before a clear picture of the possibilities with transcranial electric field stimulation can be drawn.

2.4 Summary

Electric fields play a critical role in our brain. Although the importance of electric fields in the brain is often undermined, there would be no flow of current without the presence of at least one electric field source. For example, when we connect a circuit to a battery, the voltage difference between positive and negative poles is considered to be the cause for the current to flow from the battery through the circuit. Although it is a true statement, it is not the whole truth. We need a force behind any actions, and the force that moves the electrons in a circuit is the electric field. In fact the electric field definition is the electric force per unit charge. When a circuit is connected to a source of voltage, i.e. a battery, electric fields on the poles of the battery attract and repel the electrons in and out of the battery to flow out of it and injects current into the attached circuit.

The same process and facts are in action in our brains. In this chapter, we discussed recent discoveries which suggest that electric fields generated in our brain are not only byproducts of our neurons' activity, but they are also an essential type of communication in our brain, which has been neglected until recently. One of these new discovered functions is their importance in modulation of nearby neurons. In a very simplified and abstract way, for a computer scientist, we can assume that they are a type of synchronization mechanism or are local clock signals.

Strong external electric fields are not the only source that can evoke an action potential(s) in the brain, or in other words create a current (stimulation) in brain circuits.

Much weaker electric fields can affect normal brain circuitry in a very different way and synchronize activity with the frequency of the weak external electric field.

We presented some very limited research and experiments that have shown some success with weak electric field brain stimulation in the 60s and 70s. With the expansion of our understanding of the effects of eclectic fields on the brain, we can now see reasons behind their results and reevaluate them under a new light.

Unfortunately, for almost half a century there has not been much research interest or publication on the effect(s) of electric fields in our brain, except on the safety of the high frequency electric fields emitted from power transmission lines and their health risk, which are not useful in our particular application. Fortunately, in the beginning of this decade new research has shed light on some interesting and fundamental roles that electric fields play in our brain activity. This recent research has clearly demonstrated the effects of external electric fields on neuronal function.

Chapter 3

Transcranial Electric Field Stimulation

In the last chapter, the effect of electric fields and their function in the brain were reviewed. It was discussed that, not only external electric fields can affect the neurons' functions, but a series of weak external electric pulses can manipulate their rhythm and synchronize them with the field. In this chapter, we show how those facts can be used to stimulate the brain transcranially with an external TEFS device. Also, we will speak to the differences between the TEFS and TMS, the possible benefits of using TEFS vs. TMS and the limitations that must be assessed before TEFS can be used as a TMS substitute device.

3.1 How TEFS Works

Transcranial Electric Field Stimulation, or TEFS, stimulates the brain by generating electric fields and affecting nerves through ephaptic coupling. During the procedure, a plate is placed near a subject's head close to the targeted region. The switching mechanism connects the plate to a high voltage source that makes the plate produce an electric field pulse. A portion of the field enters the brain and affects the targeted tissues. The change of the electric field causes a shift in the transmembrane current of the neuron, which results in the depolarization or hyperpolarization of neurons and finally causes an action potential.

To discuss the working mechanism of TEFS, a comparison between our novel TEFS device and the well-known TMS device can be helpful to better clarify not only our purposed device characteristics, but also to elaborate its possible drawbacks and benefits.

3.1.1 TEFS vs TMS

Electromagnetic fields are a combination of an electric field and a magnetic field. The magnetic field is generated by moving charges (current) and the electric field is generated by stationary charges (voltage). While existence of a magnetic field produced by electricity implies current and thus power consumption, the existence of an electric field does not necessarily imply any power consumption. In any electrical device the power consumption happens, if and only if, when there is a current in the system. Any battery or anything with an electric potential, like a charged capacitor, emits electric fields without being connected to any circuits. To be clear, just existence of a charge, negative or positive, creates electric fields. Thus, after connecting TEFS's plates to a high voltage source they emit electric fields without any power consumption. The only noticeable power consumption happens during the period that the plates charge or discharge. This power consumption is caused by the circuit's resistance between the high voltage source and the plates and not for electric fields emitting form the plates.

TMS and TEFS both use the electromagnetic field to create the stimulation. However, they use different parts of it as the stimulation's delivery medium. Where TMS uses the magnetic fields, TEFS uses the electric fields. Each device's characteristics and limitations are defined by the difference in the ways that the magnetic fields and the electric fields can be generated and controlled. Table 3.1 shows some facts about these different type of fields and Table 3.2 shows differences between TMS and TEFS in practice.

At its core, TMS is a machine that generates controlled magnetic field pulses. The magnitude of the magnetic field generated by TMS is directly proportional to the current running through its coil(s). Hence, major challenges in designing a TMS system are the circuits for generating and controlling the current on the coil(s) and also coil design itself.

Table 3.1. Electric Fields VS Magnetic Fields

	Electric fields (TEFS)	Magnetic fields (TMS)
Nature	Created around electric charge / time varying magnetic fields	Created around moving electric charge
Produced by	Stationary charges	Moving charges
Strength proportional to	The electric charge	Proportional to charge and speed of electric charge
Directly proportional to	Voltage	Current
Unit	Volts per meter	Tesla
Polarity	Monopole or Dipole	Dipole

Table 3.2. Functional difference between TEFS and TMS. Brainsway and Neuronetics are two FDA approved TMS Devices

	TEFS	TMS
Spatial Accuracy	relative to the plate size	limited by the coil size
Max frequency and Train duration	125 KHz and Unlimited	Brainsway: 18 Hz and train duration of 2 s Neuronetics: 10 Hz and train duration of 4 s
Overall Session Duration	Unlimited	Brainsway: 20.2 minutes Neuronetics: 37.5 minutes
# Concurrent Stimulation	Unlimited	Two set of coils
Location	Area close to upper head and some parts of skull base	Area close to upper head
Size and Weight	Small and light	Heavy and large
Portability	Portable	Somewhat portable for very limited use
Heat generation	No	Yes
Noise Generation	No	Yes
Sensitivity to connection of the body and the ground	Yes	No
Price	Very Cheap	Very expensive
Stimulation Direction	Perpendicular to the plate	Parallel to the coil

In contrast, TEFS is a machine that generates controlled electric field pulses. The magnitude of the electric field generated by TEFS is directly proportional to the voltage on its plate(s). Hence, the major challenges in designing TEFS are the circuits for generating and controlling the voltage pulse level and timing on the plate(s).

A typical TMS needs to generate around a 10 *KA* current pulse. Heat generated by this current in the coil(s) is a general issue when there is continuous use of the device. To reduce the heat the coil's resistance needs to be as low as possible. This makes designing smaller coils an engineering challenge. By minimizing the resistance in the coils to reduce the generated heat, the voltage connected to the coil(s) has to be also around several thousand kilovolts. The high current/high voltage power supply in TMS commonly consists of a large array of capacitors which contributes to the TMS devices' size. Additionally, the switching mechanism in TMS generates a loud and unpleasant noise.

The engineering issues in the designing of TEFS are quite different. The goal of the device is to generate an electric field by putting a very high voltage on its plate(s). Here, the value of the output's current does not affect the magnitude of the electric fields. Thus, the machine needs to generate and control high voltage/low current pulse.

The circuits for generating and controlling the high voltage/low current pulse in TEFS are cheaper, smaller and consume less power than the high current/high voltage circuits in TMS. Furthermore, the switching mechanism in TEFS does not generate any noise.

Here is a list of some of the differences between TEFS and TMS in more detail than what was summarized in Table 3.2:

Spatial Accuracy :

The size and shape of the plates are not bound by TMS coil design limitations. The shape and strength of electric field pulse can be controlled by the shape, size and voltage on the plate(s). Therefore, TEFS can provide more refined and accurate stimulation for a smaller target area than TMS.

Continuous Use :

A repetitive stimulation can be lengthened indefinitely in theory while heat generated in TMS confines the stimulation timing to seconds in each rTMS application.

Multiple Concurrent Stimulation :

In TEFS multiple plates can stimulate multiple targets simultaneously. In TMS the size of coils and size of the brain area that each stimulate limits the amount of simultaneous stimulation. In practice not more than two coils have been used simultaneously. TEFS is not confined by its plate(s) size.

Stimulation Location :

TEFS can access certain parts of the brain that are not easy or possible to target with TMS. For example brain parts close to the base of the skull , th most inferior area of the skull [43], cannot be stimulated by TMS, whereas a small plate can stimulate some of those areas transnasally by putting the small plate close to those areas through the nasal cavity. Clearly no TMS coil is small enough to fit inside a nasal cavity.

Device Size and Weight :

The TMS device size is about that of a large desktop case, where the TEFS size is about the size of a small cell phone. Portable versions of TMS use large batteries while TEFS can run on small batteries.

Portability :

TEFS's low power consumption and small circuits makes TEFS more portable than any portable version of TMS (Figure 3.1). TMS portable devices are relatively large and their battery supports a very limited number of pulses.

Heat :

TEFS consumes much less power than TMS, and therefore does not suffer from the heat issue in the TMS's coil.

Noise :

Unlike TMS, does not switch massive level of current and does not have arrays of capacitors, so TEFS works in complete silence.

Sensitivity to connection of the body and the ground :

Unlike magnetic fields, electric fields can be disturbed by conductive material connected to other sources of voltages. If the user's body is connected to the ground, the skin surface becomes conductive with almost $0V$ on it. This can prevent most of the electric fields generated by TEFS from penetrating the skull. This issue can be solved by isolating the body from the ground. Most shoes create this isolation. Moreover, there could be an electric spark between the user's body and any conductive surface connected to the ground that can be unpleasant.

Price :

The lack of necessity for creating and controlling high currents in a TEFS device makes its cost, with functionality limited to a TMS device level, just a small fraction of the cost of a TMS device.

Stimulation direction :

Electric fields and magnetic fields are perpendicular to each other. Hence the induced current with the TMS stimulation appear in planes parallel to the coil(s) whereas the induced current with the TEFS stimulation appears in planes perpendicular to the surface of the plate(s).

3.2 Possible TEFS Modes/Usages

static electric fields :

Although the change of electric fields is the cause of generating current in the stimulation of the brain, static electric fields can cause a constant shift in magnitude of the cell membranes' electric potential. Hence, an static electric field can potentially change brain function and inhibit or activate brain cells. Further experiments *in vivo* are needed to examine this hypothesis.

strong low frequency alternating electric fields $<100\ Hz$:

It's been shown that alternating electric fields in the range of normal brain activity can force brain cells into generating an action potential [36]. It is known that magnetic fields generated by TMS cause electric fields and stimulation in the brain. Similar magnitude electric fields generated by TEFS can cause a similar magnitude of stimulation in the brain. Although electric fields generated by TEFS are perpendicular to those generated by TMS directionality, the change in the magnitude of electric field is the source of the brain stimulation and not its direction. The difference in direction certainly can cause some differences in the way that we use these devices and appropriate ways to achieve desired stimulation in TEFS. Although it is possible that we could explore TMS protocols in the use of TEFS devices, and possibly they can be similar to the TMS's protocols, these protocols must be evaluated via *in vivo* experiments.

Weak low frequency alternating electric fields $<100\ Hz$:

It's been shown that alternating electric fields in the range of normal brain activity with magnitude less than the magnitude needed to force brain cells to the action potential state, can synchronize brain cells with the external electric field's frequency. Again, the TEFS's signal shapes and magnitudes in each application need to be investigated *in vivo*. This mode is potentially more suitable for much longer sessions than TMS protocols.

Other usages :

Alternating Electric Field Therapy or Tumor Treating Fields [44], TTF or TTFields, is an approved method of treating some type of cancers in Europe and the USA. This therapy uses $1-3\ V/cm$ electric fields at $100-300\ KHz$ to stop cancer cells replication by hyper-depolarization of the cell membrane. Also, it has been shown that electric fields with intensity of $1-100\ mV/cm$ at frequencies of $20-$

200 kHz can increase bone fraction healing [45]. We can expect that, like TMS, TEFS can be used for the stimulation of the peripheral nervous system [46]. Some new drug delivery systems use disruption of electric field in the targeted tissue through minimally invasive electrodes [47, 48], which can be adapted with TEFS in a way that the same electric fields can be applied to the targeted tissue in a non-invasive way. The current TEFS prototype circuitry is capable of generating such electric fields and most of the frequency range for all the above applications. Clearly for each application the device needs to be adjusted with appropriate settings and the plates needs to be adapted with the site and the application.

Figure 3.1. Portable TMS [49]

3.3 Summary

In this chapter, first we discussed the basic working principles of our novel device, the Transcranial Electric Field Stimulation (TEFS). In plain words, TEFS works by generating electric field pulses. Then we had an in-depth comparison with Transcranial Magnetic Stimulation (TMS), the most similar device on the market to our device. We discussed this both based on different physical phenomena behind their working mechanism, and then the consequences of these differences in their design, production and utility. For instance, our device is much smaller, affordable, and unlike TMS does not generate heat or noise.

We also discussed possible applications of this device. Some of these uses are based on existing and proven applications of electric fields in medicine, e.g., the effect of electric fields on cancer cells or broken bones, and for some we hypothesize based on the similarity and difference of our device with other stimulation devices (i.e. TMS and TDCS).

Although TEFS has a long road ahead and many research experiments need to be done before we come to a clear picture of its limitations and capabilities, it is not so difficult, based on our limited knowledge about our brain and some established physics phenomena, to consider it the very first step towards developing a game changing device in the field of brain stimulation.

Chapter 4

Simulation Results

Two electromagnetic field simulation software packages have been used to predict the effect of TEFS on the human brain. For each program, a model of the human head and TEFS output have been developed. Since neither of the human head models is well detailed, the results should not be considered to be a very close approximation of reality. Nevertheless, they explore the possible effects of exposing the human brain to the external electric field(s). Due to budget restrictions, results are limited to the resources available for experimentation; however, the accuracy can be immensely improved by using a more detailed head model and full version simulator packages. Future *in vivo* studies or better simulations could clarify the validity of these results and their proximity to reality.

Although there are various EM field simulator packages available on the market, there are only small number of them that support low-frequency analysis. Maxwell from ANSYS Inc. and SEMCAD X from Schmid and Partner Engineering AG (SPEAG) are two simulators, each of which has some options for low frequency simulation.

A typical TMS pulse is 100 ms. In SEMCAD X we performed the simulation with a similar pulse, however in ANSYS Maxwell we reduced the pulse timing to 100 μs to be able to perform the simulation with available computational power. It must be noted that the actual effect of TMS on the brain of a live specimen is not well studied, and hence there is not enough data available to use to calibrate these results. By comparison, the standard TMS response in many articles are either theoretical or are driven from simplified simulations.

4.1 ANSYS Maxwell

The ANSYS site [50] introduces this product as follows:

> ANSYS Maxwell is the premier electromagnetic field simulation software for engineers tasked with designing and analyzing 3-D and 2-D electromagnetic and electromechanical devices, including motors, actuators, transformers, sensors, and coils. Maxwell uses the accurate finite element method to solve static, frequency-domain, and time-varying electromagnetic and electric fields.

In comparison with other possible choices, this software comes with more options and capabilities than any other tested options. It has more flexible simulation and reporting capabilities. On the other hand, it uses much more memory than SEMCAD X over a geometrically simpler head model. Although this should not be a factor in an ideal situation, memory usage plus hardware limitations in this project prevented us from using a detailed head model. After implementation and testing of seven, five and three layer head models, it became apparent that the only practical model for the available hardware on hand was a one layer head model.

4.1.1 ANSYS Maxwell Simulation Results

Figure 4.1 demonstrates the general model for all simulations presented here. The electrical characteristics for the brain model were selected based on the electrical characteristics of the gray matter, and at the switching-time frequency of the TEFS prototype. The model represents the top half of the human head [51]. This hemisphere has two layers. The outer shell has a diameter of 85 *mm* and a thickness of 4 *mm*. The inner layer, with 81 *mm* diameter, represent the brain. A copper plate on top of the head model represents the TEFS output plate. This plate is isolated electrically from the head model with a 1 *mm* layer of polyethylene. The copper plate and its isolation layer, polyethylene, has a radius of 28 *mm*, which creates a surface area of 25 cm^2. Our TEFS prototype's plate currently has the exact same surface area.

In Figures 4.2-4.4, measurements for the notation of Ez in the simulation figures represent the scalar value of electric fields in the z direction, which is perpendicular to the surface of the copper plate on the top of the hemisphere. The d represents the distance of the measurement position from the outer shell of the model on the z axis. For example, $d = 0$ represents the 0 *mm* distance from the outer shell, the closest part of the brain to the plate, and $d = 20$ represents 20 *mm* inside the brain in our model.

To be able to perform the simulations with our limited computational power, simulations were done in the range of $0 - 10$ *ms*. Although this period is much less than a typical TMS pulse period, our TEFS prototype is capable of making pulses within this timing range. In all of these simulations the magnitude of the high voltage is set to 10 KV, which is the maximum voltage output of our current prototype.

Figure 4.2, Figure 4.3 and Figure 4.4 show the magnitude of the electric field vector in z direction at various depths under the shell and to three different types of voltage pulses. The speed at which the high voltage on the plate is activated (on) or deactivated (off) can generate a different shape of the electric field inside the brain. This is generated from the high voltage plate as a result of the stimulus. This shape is a major factor in the shape, magnitude, duration, and the polarity of generated electric fields. Any change in the high voltage signal will change the field shape in the brain.

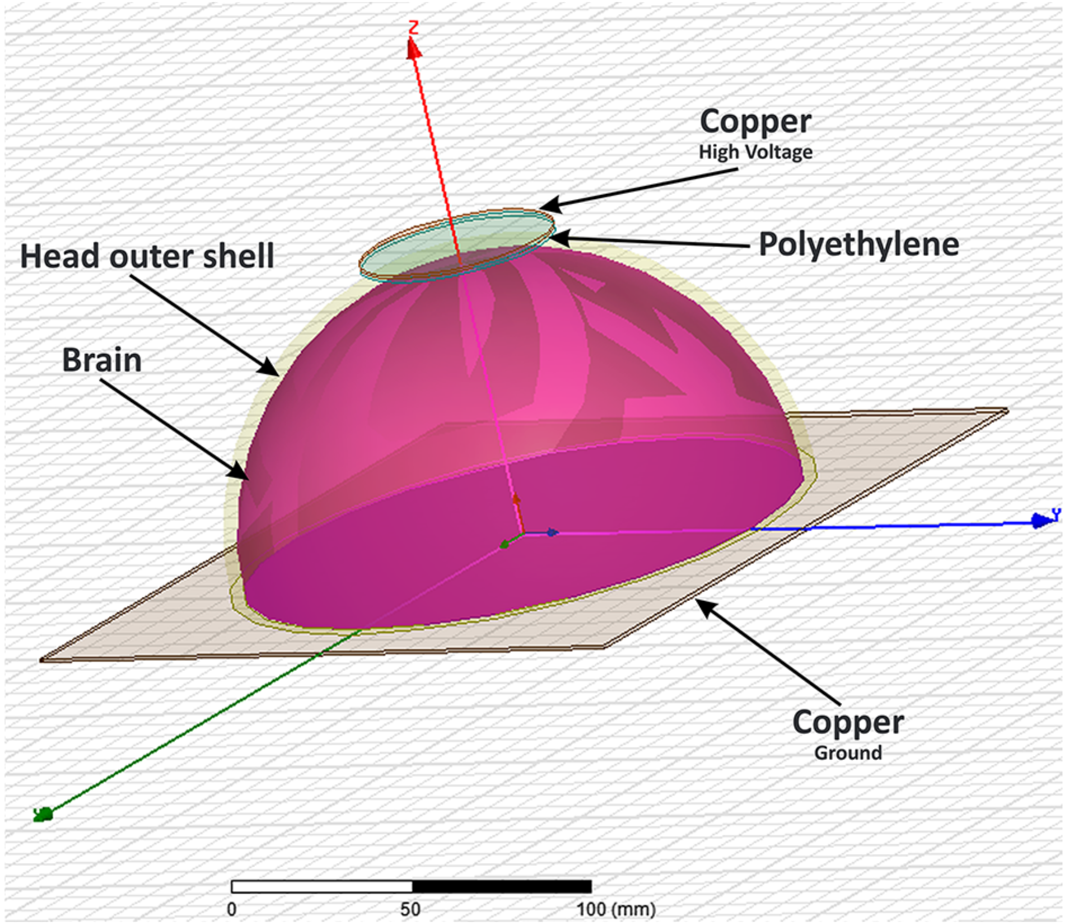


Figure 4.1. Ansys Maxwell's Head and TEFS model

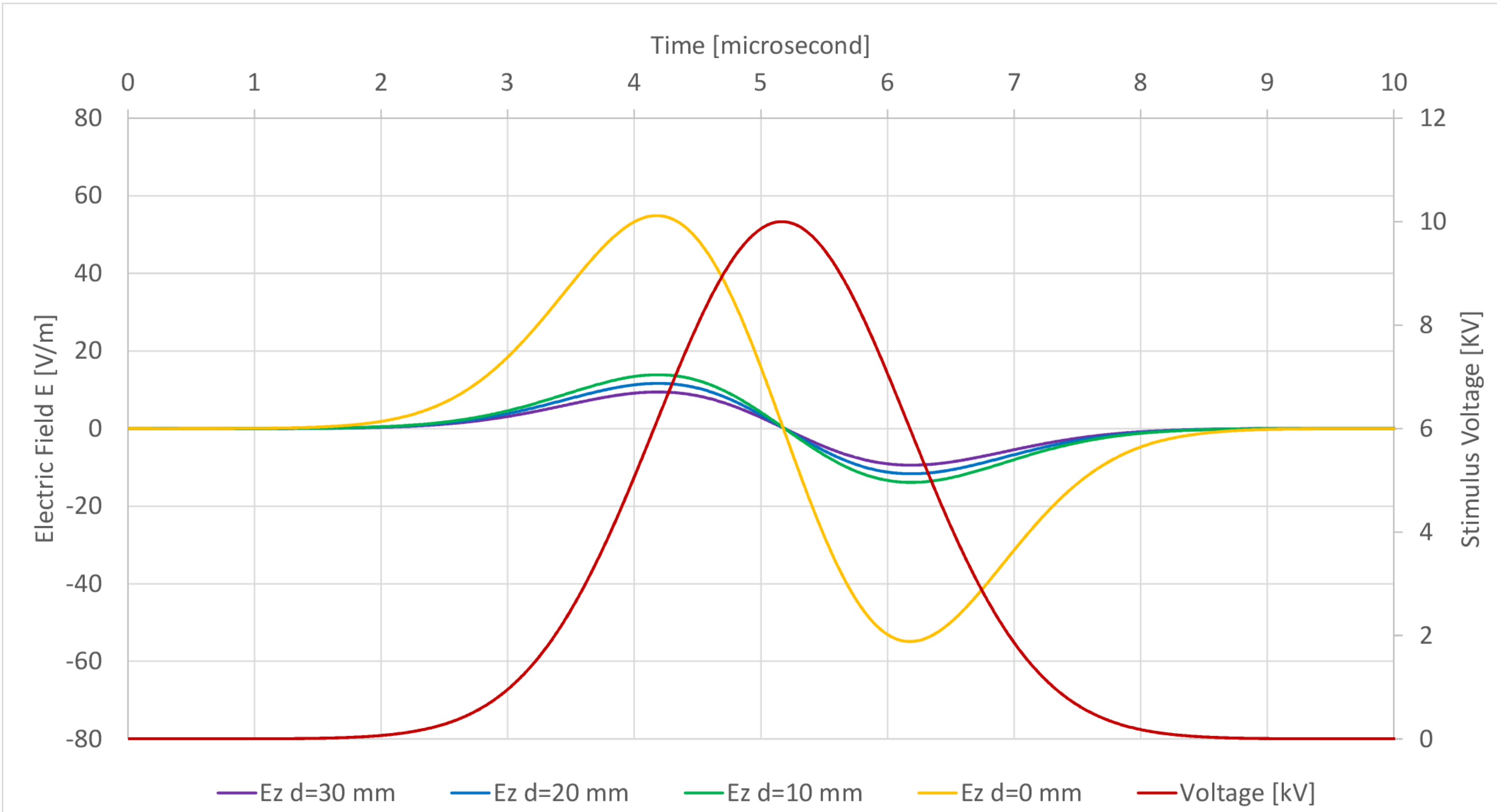


Figure 4.2. Ansys Maxwell's simulation with standard normal distribution shape pulse as the stimulus. The right vertical axis represents the voltage on the late. The left vertical axis represents the value of electric fields in the *z* direction. This simulation shows a smooth rise and fall of electric fields where maximum magnitude of the field is less and the duration of the generated electric fields is longer than other simulations.

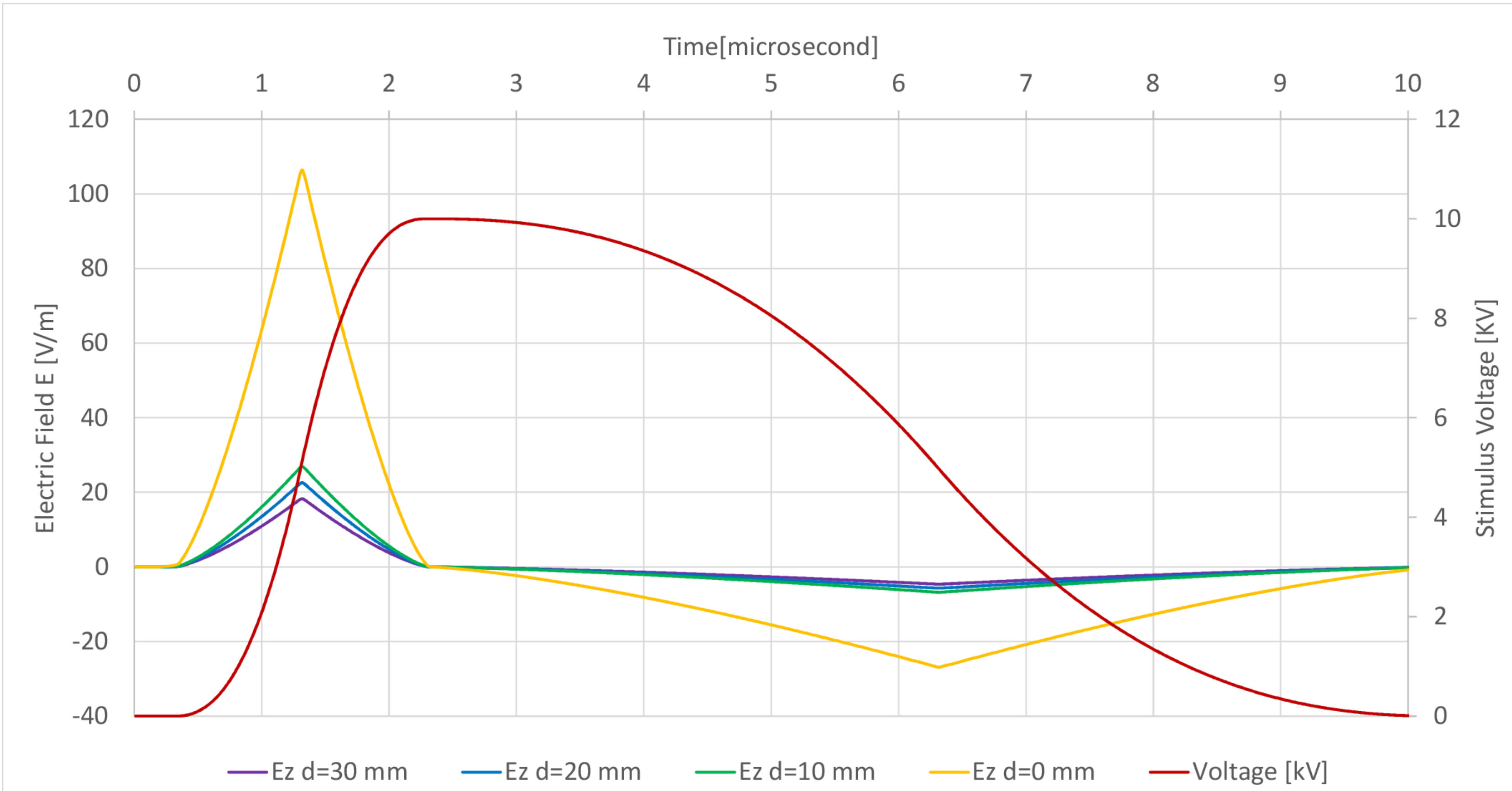


Figure 4.3. Ansys Maxwell's simulation with fast rise and slow fall stimulus pulse. The right vertical axis represents the voltage on the late. The left vertical axis represents the value of electric fields in the *z* direction. The fast rise of the stimulus increases the magnitude of the generated positive electric field and the slow fall makes the negative electric field magnitude less than simulation in Figure 4.2

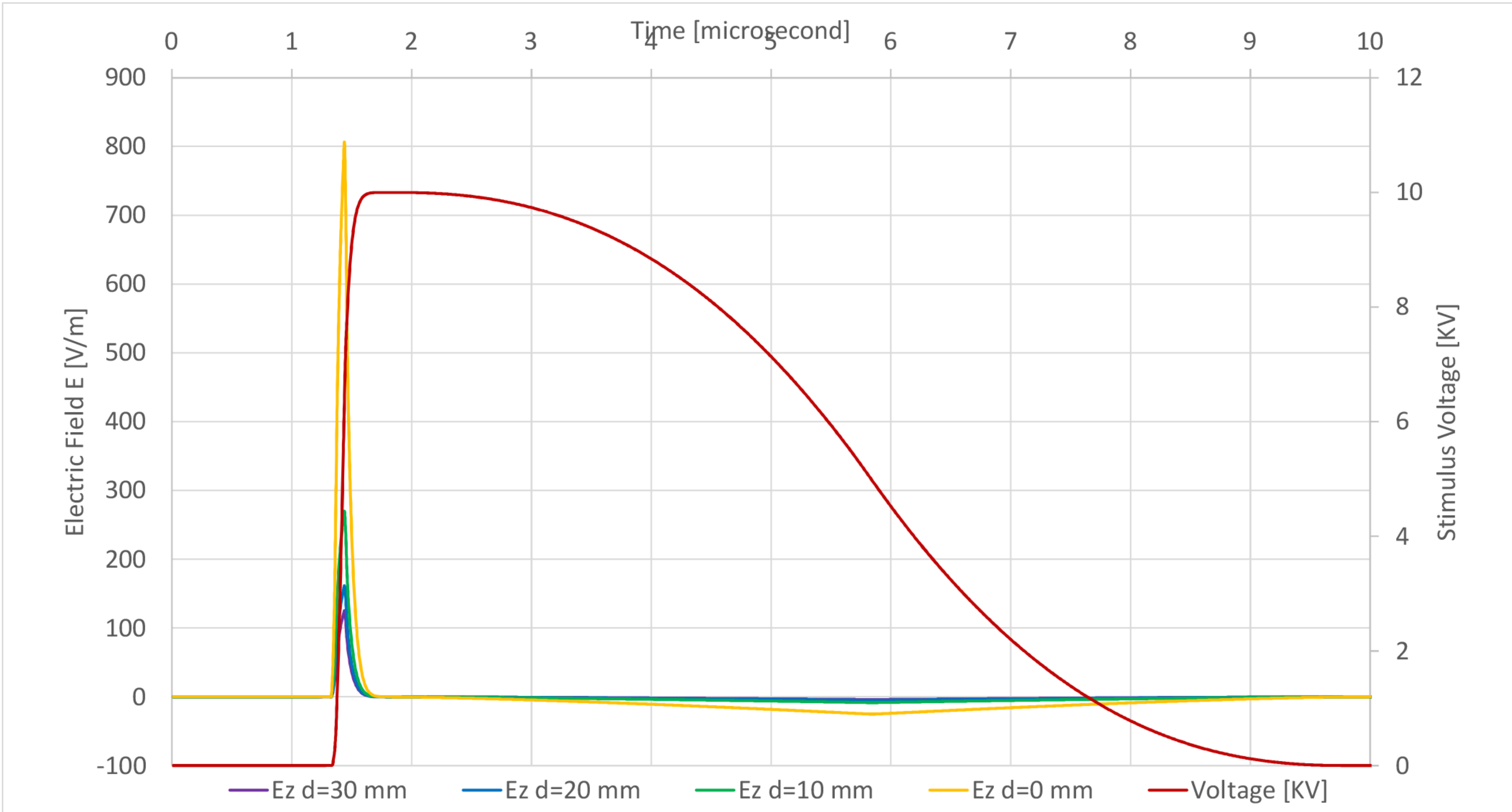


Figure 4.4. Ansys Maxwell's simulation with very fast rise and slow fall stimulus pulse. The right vertical axis represents the voltage on the late. The left vertical axis represents the value of electric fields in the *z* direction. The very fast rise of the stimulus increases the magnitude of the positive electric field and decreases it's duration. the slow fall makes the negative electric field magnitude less than simulation in Figure 4.2 and Figure 4.3

From these simulations we can accurately calculate the current density. The current density is defined as electric current per unit area [52]. To calculate this value we can use the following equation:

$$E = \sigma J$$

Where E represents the electric field and σ is the electrical conductivity and J represents the current density. In our head model $\sigma = 0.14311\ S/m$ and relative permittivity is equal to 1749.3.

4.2 SEMCAD X

The SPEAG website [53] describes their ELF solution as follows:

> SEMCAD X Matterhorn ELF Solution comprises a family of quasi-static solvers to model low frequency, static applications and movements in static fields. The novel implementation of electro/magneto static and electro/magneto quasi-static approximations of Maxwell's equation on a rectangular grid significantly extend the performance of SEMCAD X Matterhorn.
>
> Each solver is optimized for a different approximation of Maxwell's equations, offering improved speed, convergence, and accuracy for a wide range of scenarios.

SEMCAD X comes with a head model that is not internally detailed in its trial version, which was the limitation of working with this package in this project. The simulation speed is much faster than Maxwell while the head model is much more detailed than our Maxwell's hemisphere model. Although this provides better visualization of the results, generating output charts, i.e. electric field / time, is relatively complex.

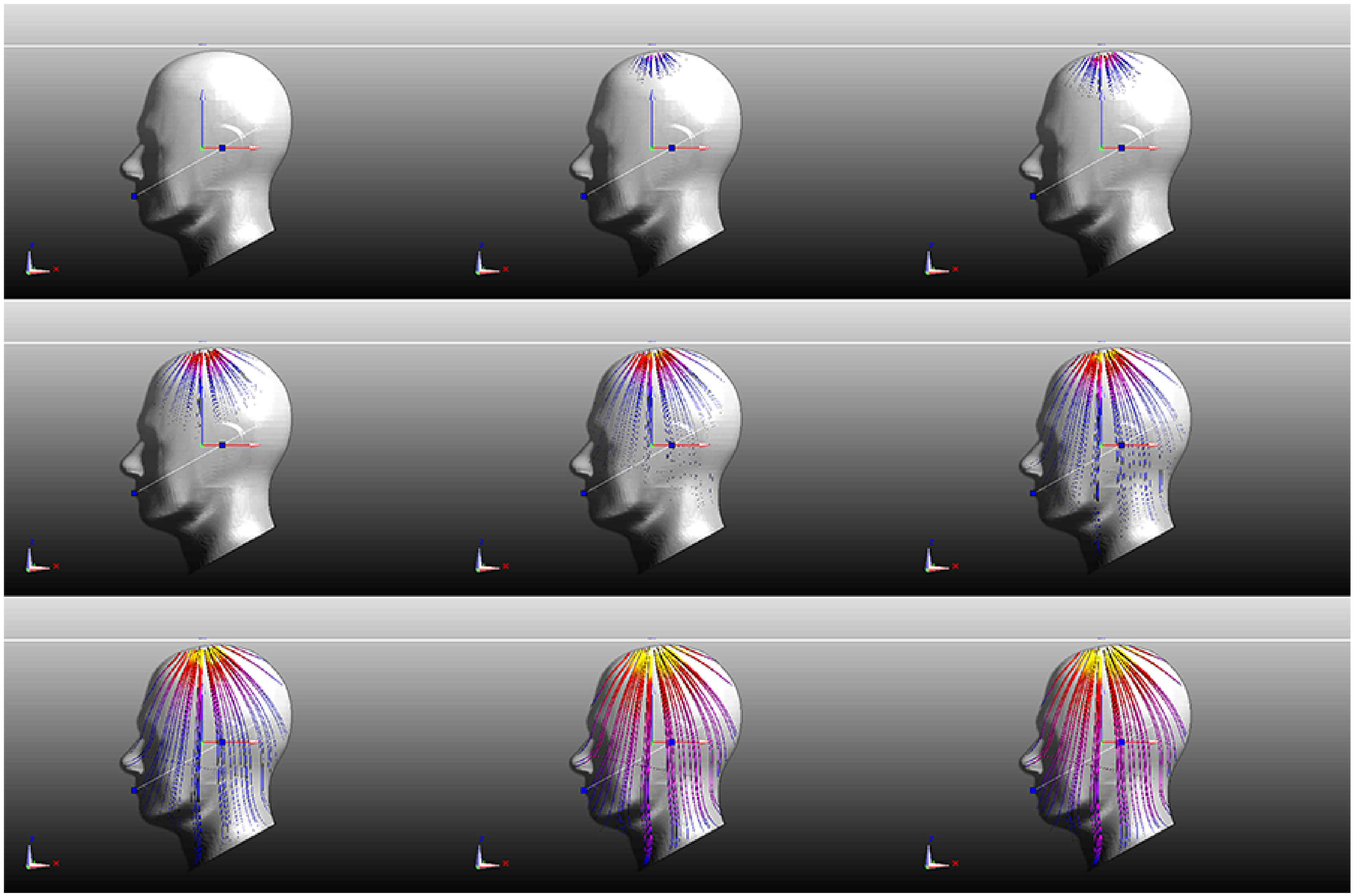


Figure 4.5. SEMCAD X simulation results of distribution of the electric field during a 100 *ms* 1 *KV* pulse on the plate on top of the head model

4.2.1 SEMCAD X Simulation Results

In the SEMCAD X we used a plate on top of the head model with the radius of 1 *cm* and 5 *mm* distance from it. Figure 4.5 shows distribution of electric fields inside the head model when a 100 *ms*, 1 *KV* pulse is on the plate.

4.3 Discussion

Our limited time with the SEMCAD X stopped us from generating more detailed results. However, despite our budget and computational power limitations that stopped us from having reliable and accurate simulations, simulations with these two packages provided two essential answers. First, from the SEMCAD X simulation we can see how electric fields generated from a source close to a human head can go inside the head and generate a stimulation current, and second, based on the results from ANSYS Maxwell package, 10 *KV* is sufficient to generate a field strong enough to cause a stimulation. Unfortunately limited research on the effect of external source of electric fields on human neurons does not give us an exact value and timing for rising an action potential based on the electric fields. However, we showed that slight variation on the shape of the stimulus can lead to a completely different field and stimulation, and thus strength duration curve is useful for calculating stimulus duration and time for a known and studied source of stimulation.

A great deal of time had been spent on trying to adapt available data to the simulation results. We can calculate current or current density to use a strength duration curve based on the current or current density, estimate the progress of the curve on the high frequency range of the simulations, and try to adapt the shape of the stimulus in the simulation with those curves. However, there are too many variables and adaptions and assumptions involved in order to observe and conclude something meaningful from simulations which can only estimate the outcome. At this point the simulation results, beside showing the extent to which the outcome is sensitive to any minor changes in the stimulus shape, are only useful to show that the method has a potential to stimulate the brain with a source of electric fields stimulus.

The logical next step in the development of TEFS would be using the device on a cadaver observe response to our unique stimulus type and shape and use the results to adjust and update the prototype.

Chapter 5

TEFS Prototype Implementation

In this chapter the design and implementation of the hardware and the software of the new TEFS prototype are presented. We describe how by using optodiodes (optocouplers), our prototype generates high voltage pulses quietly for frequencies up to 125 KHz.

Our latest TEFS device prototype is equipped with a high voltage source and switching parts with maximum $+10\ KV$ or $-10\ KV$ outputs. Our current prototype hardware is not only capable of being programmed to provide stimulation equivalent to the most advanced TMS protocols (Figure 1.6) [34] but it can also be programmed with protocols that TMS devices cannot provide. In our prototype, we can create pulses as short as 4 μs and each individual pulse can be programmed to have any intensity from 0 V to maximum of (in this prototype) up to $+10\ KV$ or $-10\ KV$, which is well beyond the capability of the most advanced TMS devices at the moment. Figure 5.1 and Figure 5.2 show this prototype.

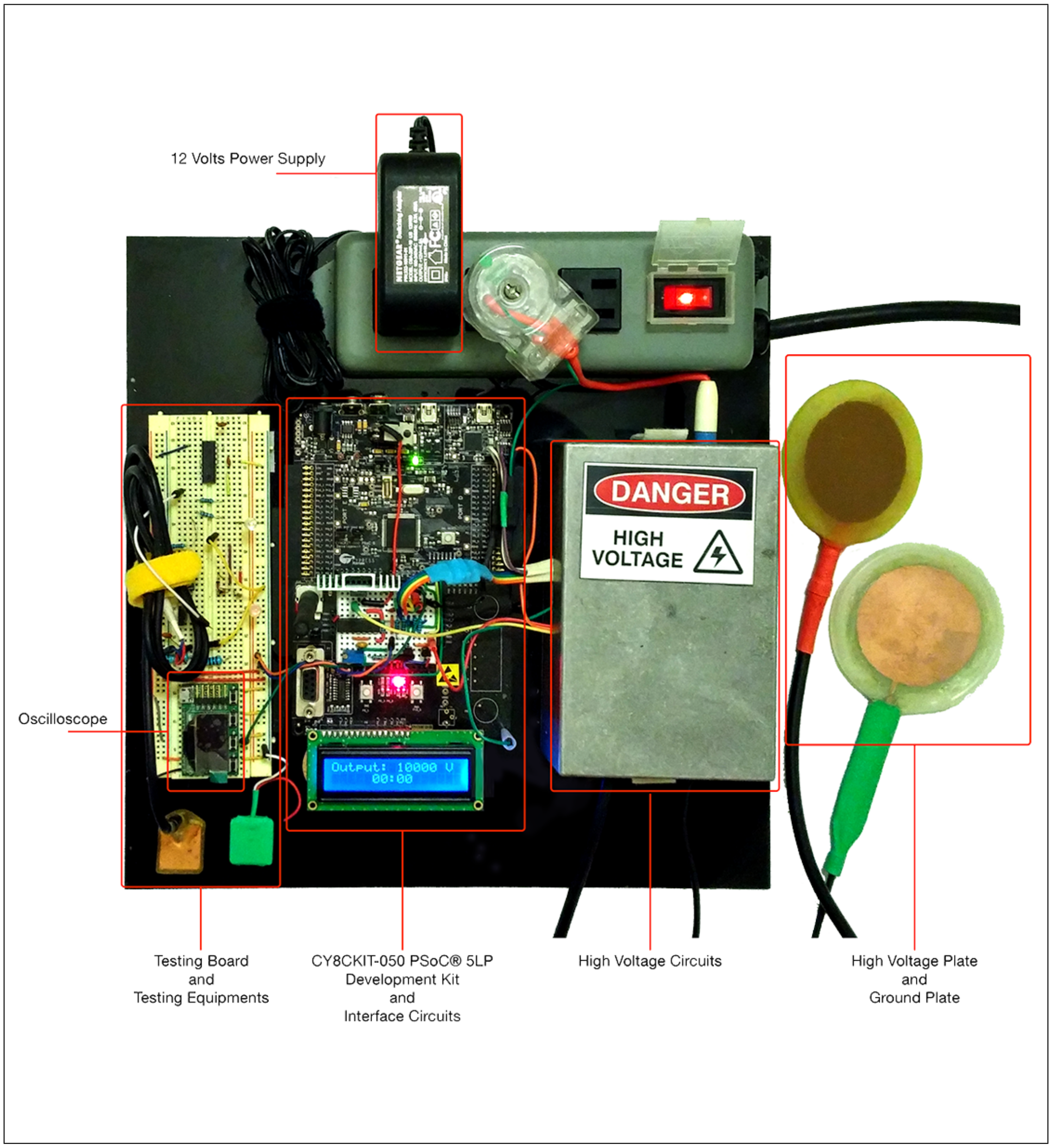


Figure 5.1. TEFS latest Prototype

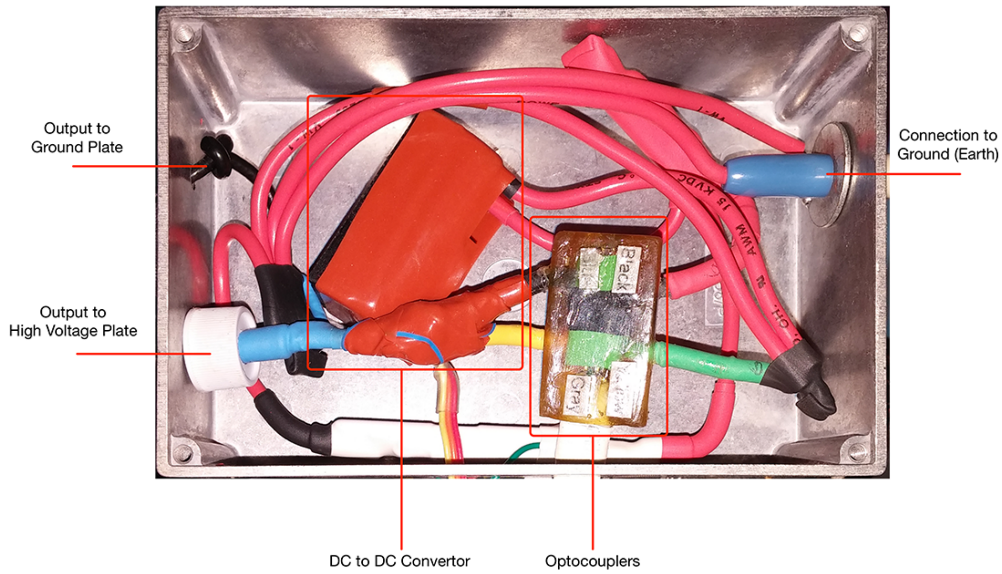


Figure 5.2. Inside the high voltage section of the TEFS latest Prototype

5.1 How to Use TEFS

To use TEFS, first the pate(s) should be secured on the subject's head at the desired targeted location(s). Figure 5.3 shows two typical possible placements of the TEFS output plates over a user's head.

Figure 5.3. TEFS prototype plate(s) placement. The right side shows the device typical use when one plate (high voltage plate) is placed over the the user's head. The left picture shows a typical use when two plates (high voltage plate and ground plate) are placed over the user's head. In these pictures no particular parts of the user's brain has been targeted and the pictures are taken solely for the demonstration purpose while the TEFS device is not turned on.

Then we turn the device on. A potentiometer allows us to adjust the output voltage magnitude. The value of the output voltage can be observed on an LCD monitor. At this point the voltage over the plate(s) is $0\ V$. Two LEDS represent the status of the voltage on the plate. One of the LEDs is on when we have the high voltage connected to the plate; the other one is on during the period that the output is connected to the ground. The output in this state is connected to the ground and the LED associate with it is on.

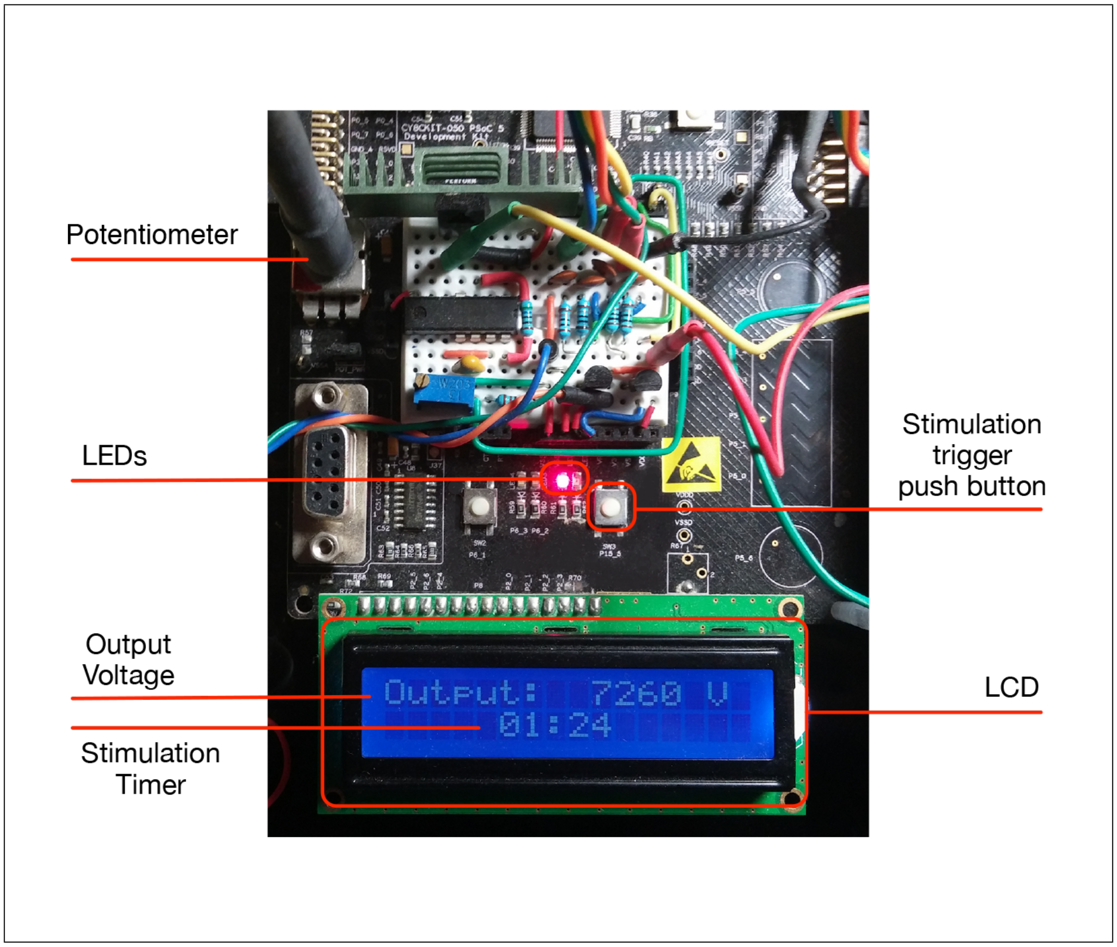


Figure 5.4. TEFS prototype User interface

A push button toggles the stimulation status. With the first push, the stimulation process starts. The user can observe the voltage pulse from the LEDs. during the stimulation period, whenever the output is connected to the high voltage or the ground, the LED associated with that state is on. Additionally, we can monitor the stimulation status and period on the LCD. During the stimulation period a timer keeps track of the stimulation period and shows that information on the LCD monitor (see Figure 5.4). At any time, including during the stimulation period, we can re-adjust the output voltage level and see the updated output level on the LCD monitor in real time.

With the second push of the push button, the stimulation stops. At this point, the

LCD shows the total stimulation time for the record, while the LEDs show that the plate is connected to the ground. If the user does not stop the stimulation manually, after 20 minutes the system automatically stops the stimulation.

We can restart the stimulation by pressing the push button again. This resets the time on the LCD, and we can again monitor the stimulation time on the LCD monitor and observe the voltage level by the LEDs.

The TEFS prototype is pre-programmed with a specific shape and set of frequencies of the output pulses. At this point, in order to change this programmed output, we need to connect the TEFS prototype to a computer and reprogram it.

During the stimulation time, the subject's skin should not have any connection to the ground. Furthermore, touching conductive objects in the surrounding which could be connected to the ground, should be prevented.

5.2 TEFS System Structural Description

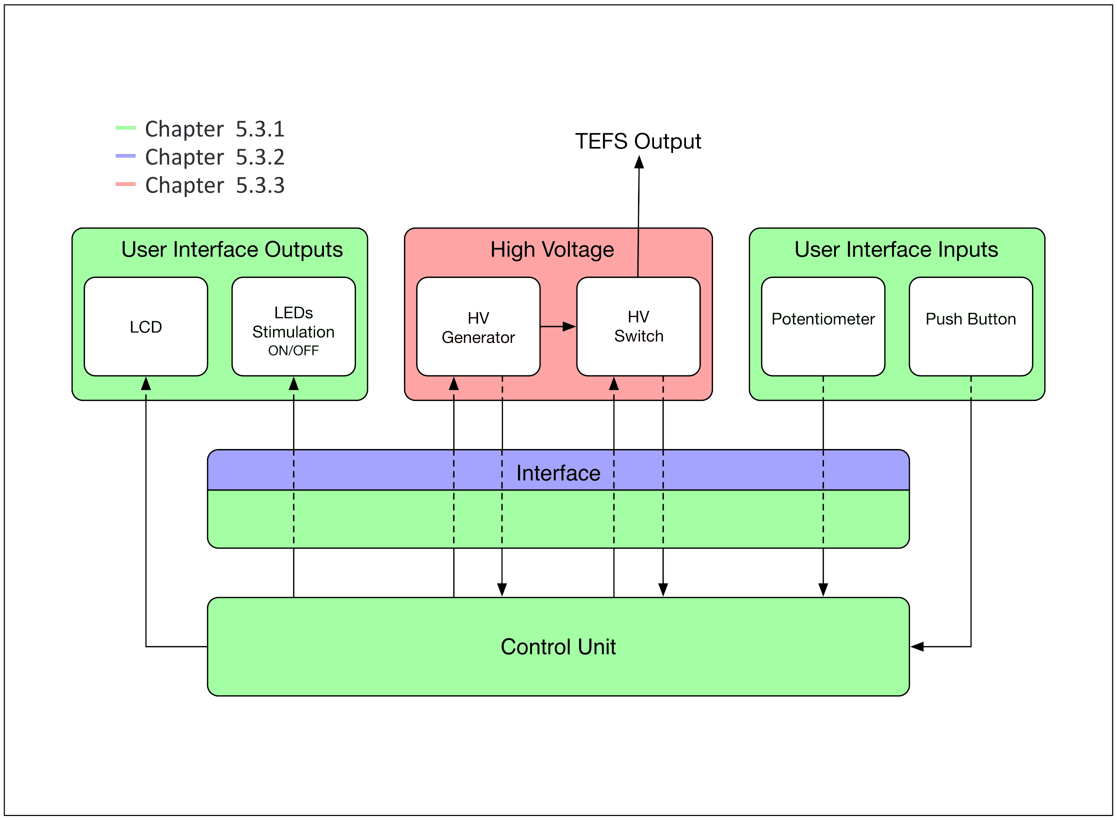


Figure 5.5. TEFS system block diagram showing structural design of a TEFS system and interactions between different parts of it in an abstract model.

Similar to many modern devices, TEFS is controlled with an embedded system. An embedded system is a simple computer system with a dedicated function within another machine that controls the machine's functions [54]. The embedded system in TEFS is made from a special type of microcontroller with some extended capabilities. A microcontroller is a small computer made on a single integrated circuit (IC) that holds all necessary parts of a computer within itself. One of the role's of the microcontroller in TEFS is acting as a control unit.

The control unit in TEFS controls user input and output, and sends appropriate control signals (commands) to the rest of the TEFS system to have them work in harmony.

Moreover, the control unit can monitor the status of the system and get feedback from different parts of the system to ensure that the system is in working order.

In order to communicate with the other parts of the system, any embedded system needs interface circuits to translate its signals to an understandable signal for other regions of the system (i.e. analog to digital and visa versa). This translation also happens in the opposite direction to receive feedback from the other parts of the system. Our special microcontroller is equipped with internal programmable digital and analog blocks that give us the capability to implement the majority of the interface circuits inside the microcontroller. A small portion of the interface that cannot be made by our microcontroller, is built outside of it. In section 5.3.1 we will discuss our microcontroller in detail, including the control unit and the portion of our interface that is implemented by the control unit. Additionally, in section 5.4 we will explain the program used in running our microcontroller.

From the functional perspective, the goal of a TEFS device is to switch a specific level of high voltage on and off, which generates a pulse. This is done in a pre-specified time interval. To do so, we need to have a source for high voltage with a controllable output voltage level and also a mechanism to connect or disconnect this high voltage to the TEFS system output in specified time interval.

To generate the high voltage, we used a DC to DC converter that amplifies its input voltage 2000 folds. For example for an input equal to 2.5 V the output of the DC to DC converter would be $2.5 \times 2000 = 5000\ V$ (which is 5 KV) and similarly for a 5 V input the output is 10 KV. Generating the specific input voltage for our DC to DC converter is discussed in detail in section 5.3.2 and the details of DC to DC converter itself are discussed in section 5.3.3.

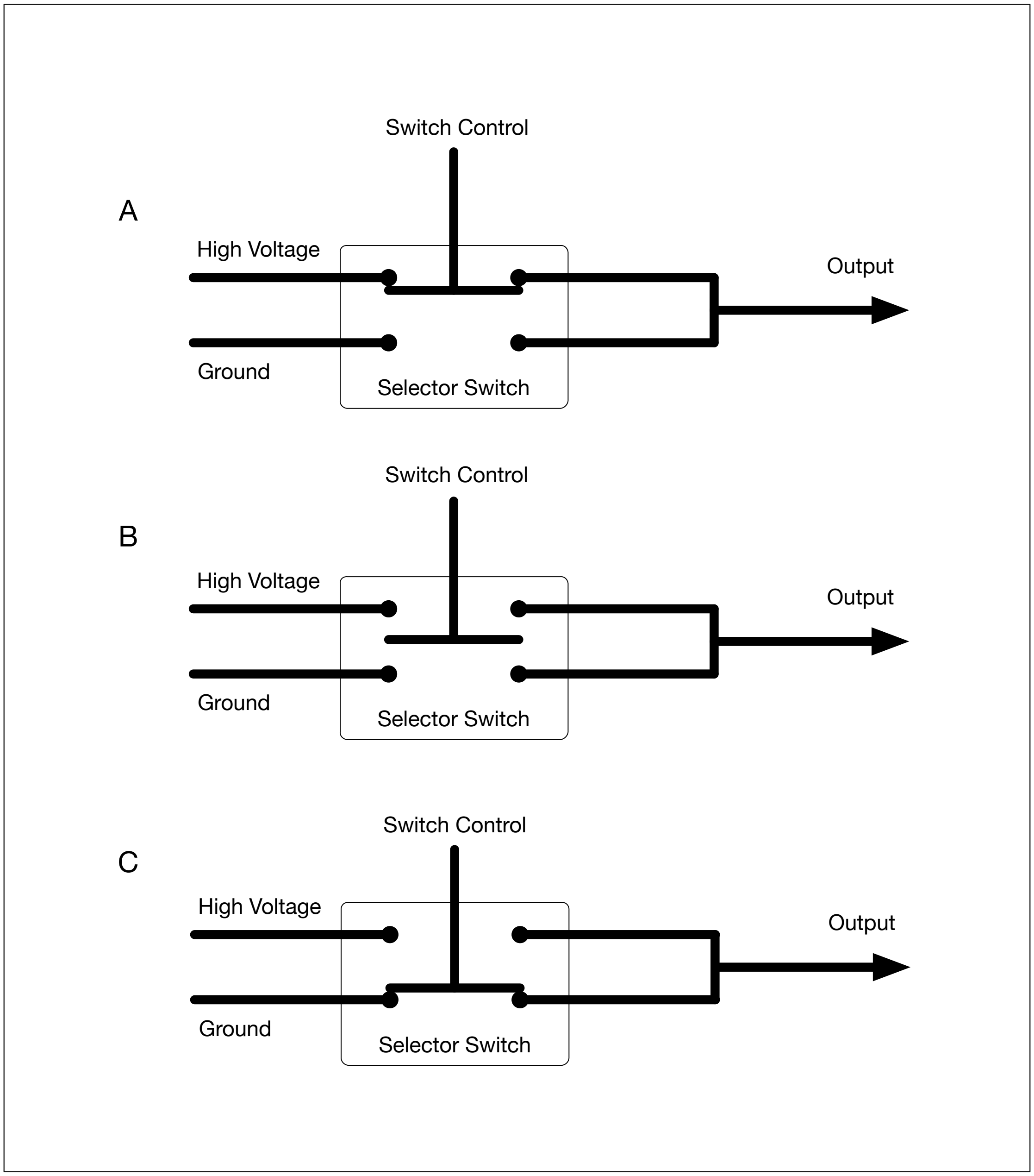


Figure 5.6. A simplified diagram of the high voltage switching mechanism modeled with a selector switch. A) The output is connected to the high voltage. B) Switch is in the deadband zone and the output is not connected to any inputs. C) The output is connected to the ground ($0\ V$).

Our high voltage switching mechanism acts like a selector switch. A selector switch is a switch that selects an input and connects it to an output and at any given time, only one input is connected to an output while the other ones are disconnected. Here, our switch has two inputs and two outputs (see Figure 5.6). In our switch, One of the inputs is connected to the high voltage and the other one is connected to the ground or 0 V. In our design both switches' outputs are connected to each other. Thus, at a single moment, either the high voltage is connected to the output, or the ground is connected to it. While toggle between these two options happens, there is a very short period that we call the deadband. During the deadband neither of these inputs is connected to the output. We cover the switching circuits and the deadband definition in section 5.3.2 and section 5.3.3 in more detail.

A TEFS system generates high voltage pulses by altering its output between a high voltage and 0 V. The high voltage pulse is connected to a plate over the head of the user. The plate is covered with a non-conductive material, so the user is not exposed to the high voltage. However, the user is exposed to electric fields emitted from the high voltage over the plate. The control unit through the interface circuitry controls the whole system by generating and sending appropriate control signals and receiving feedback signals from the system. It also provides a user interface to let the user control the device and observe its status over a screen. In the next section, we will go deeper into our design process and circuitry.

5.3 TEFS Design Detail

The current prototype from design and implementation point of view can be divided into three parts; The microcontroller and the development kit, the interface and the high voltage generator and switching.

5.3.1 Microcontroller and the Development Kit

To control the TEFS device operations, a control unit is necessary. In this section we introduce the hardware that is used for controlling the system. The central core of this section of the hardware is a special microcontroller that enables us to not only use it as a control unit, but also to implement some other parts of the hardware that are not generally implementable with typical microcontrollers.

All digital parts of the hardware and some of the analog parts of the circuits are implemented with the Cypress CY8CKIT-050 PSoC ® 5LP Development Kit [55]. This kit, shown in Figure 5.7, offers a low-power microcontroller embedded with mixed-signal arrays of configurable integrated analog and digital peripherals. In more plain English, the microcontroller is embedded with programmable blocks that can be configured, arranged and programmed to create a custom designed circuit.

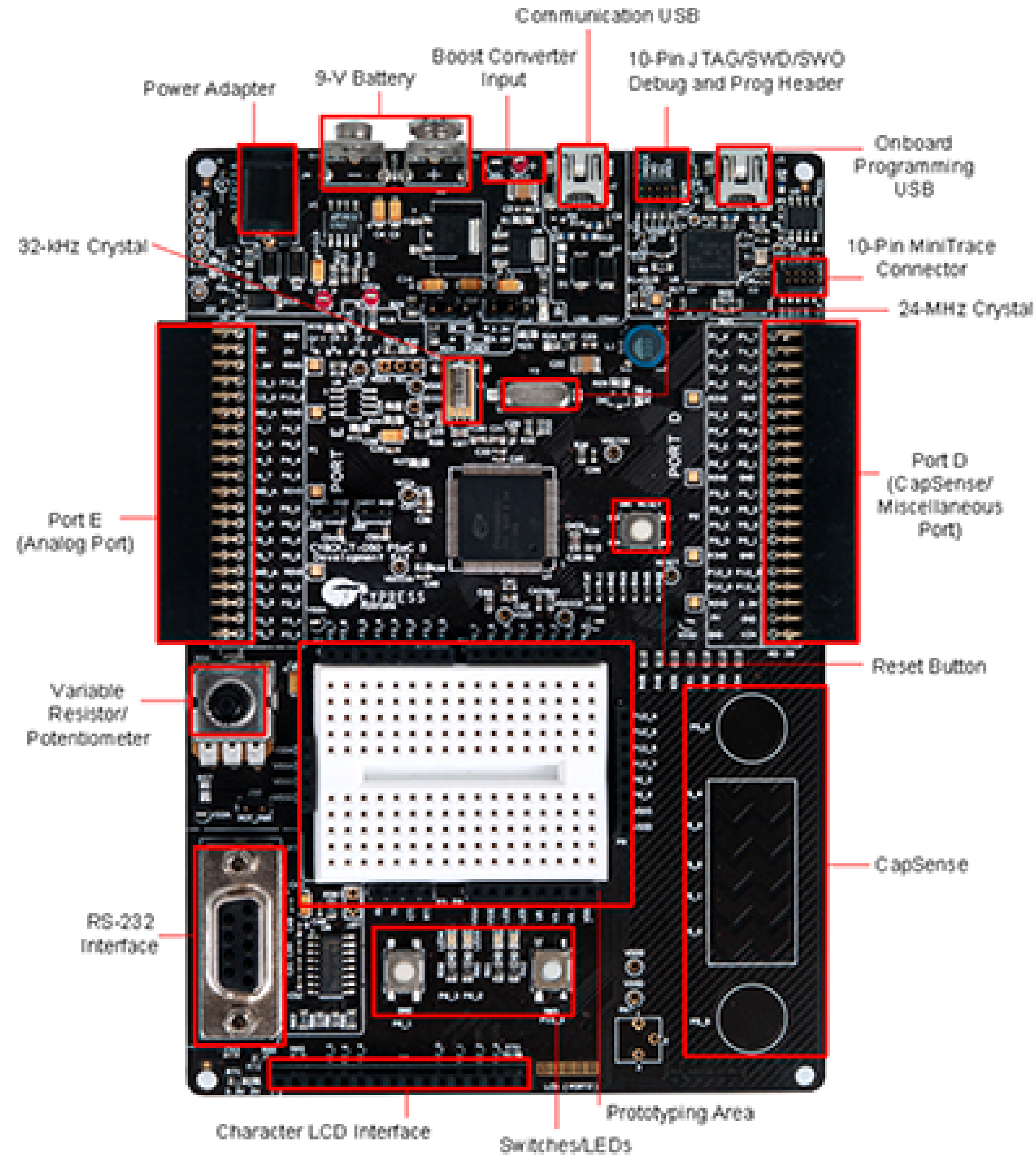


Figure 5.7. Cypress CY8CKIT-050 PSoC ® 5LP Development Kit [55].

The PSoC Creator that accompanies the Cypress kit is a strong development and debugging toolkit that is also easy to use. Along with the power of its Programmable System-on-Chip microcontroller, this kit is a suitable part to be used in an analog/digital project. In this project an external module for programming and debugging of the microcontroller, Cypress MiniProg3® (Figure 5.8) [56], has also been employed.

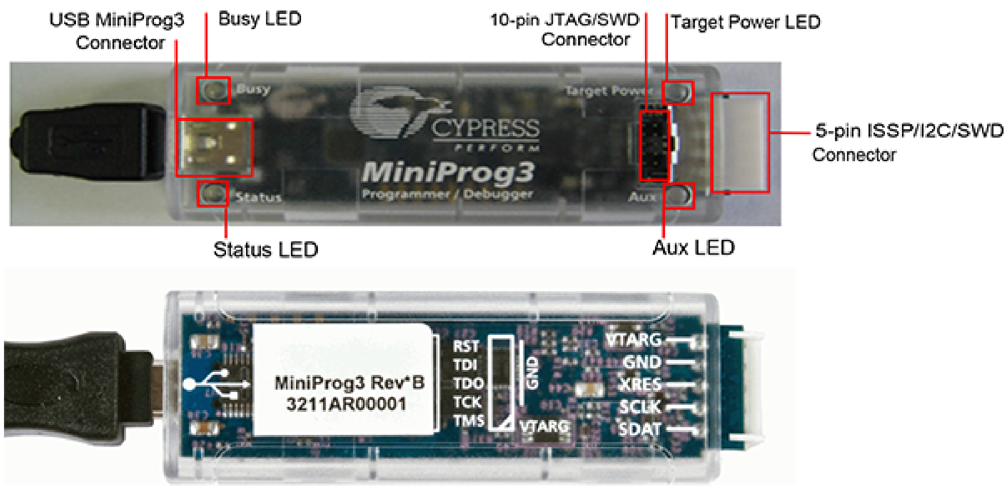


Figure 5.8. Cypress MiniProg3® facilitates programming and extra and in depth debugging for the development kit [56].

The development kit is modified in two places. The kit provides 5 v power supply, however we also need a 10 v power supply. An LM7810, voltage regulator is added to its power supply circuitry to provide VCC2=10 v for circuits in Figure 5.16 Part A. Furthermore, this kit's original circuitry does support an LCD with a backlight. A minor modification has been made on the kit to use an LCD screen with a backlight. We use this LCD to monitor the system status and output voltage magnitude.

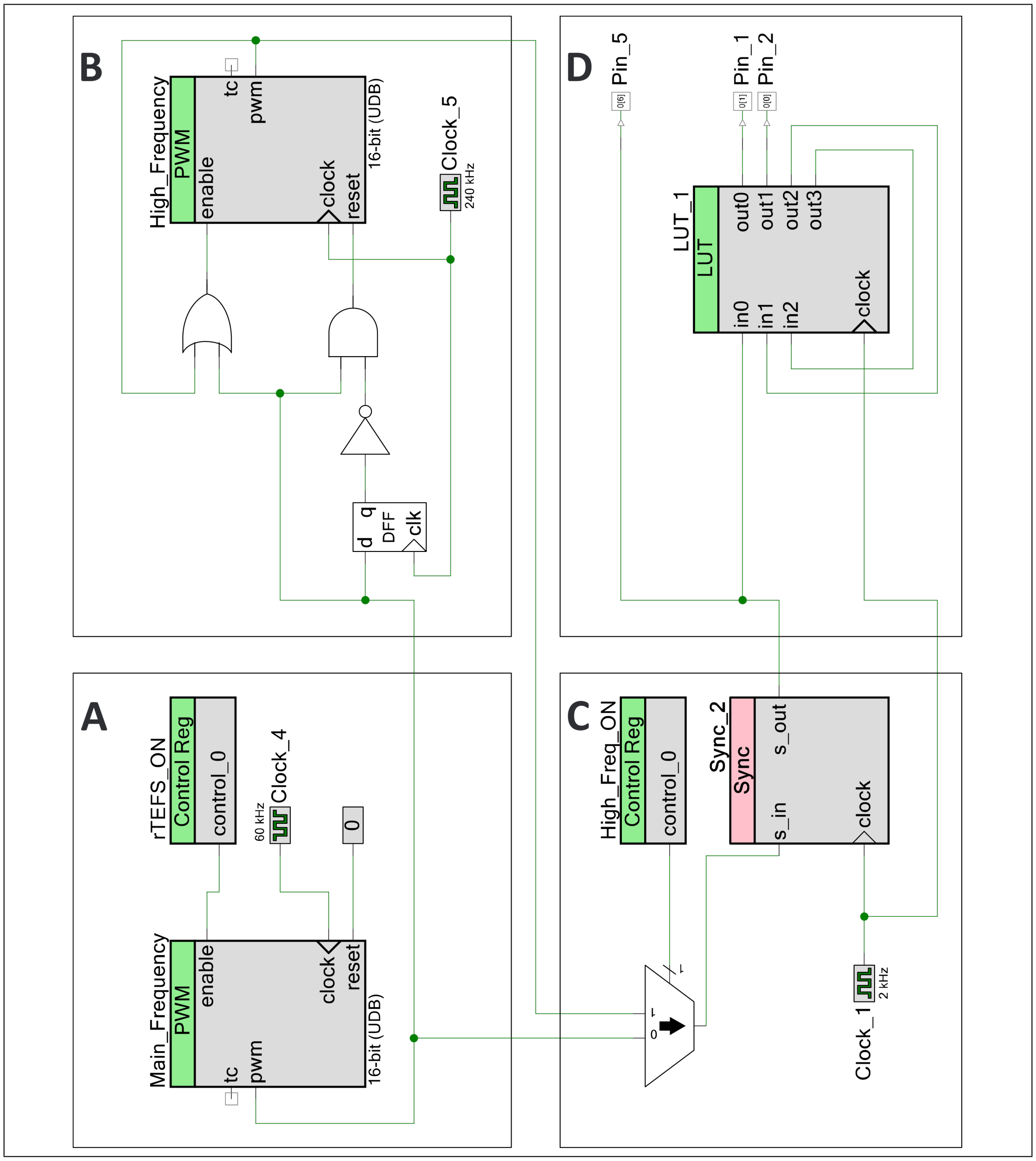


Figure 5.9. Digital blocks in PSOC used for pulse generation. Part A and B generate outputs in the formats represented in Figure 5.10 or a continuous series of pulses. In part C one of these two signals from Part A and Part B is selected and then synchronized with the clock of the state machine in Part D. Part D generates the necessary signals to control the high voltage optocouplers from the pulse generated in Part A, B and C. Table 5.1 shows the content of LUT1 lookup table that is also the state transition table. (more details in section 5.3.3). A 2 μs deadband is essential between any changes in their states. This minimum deadband timing is dictated by the T_{ON} and T_{OFF} of the high voltage relays (Appendix B). Currently the value is set to 500 μs, as a safety measure, and enforced by Clock_1 in Part C and state machine in Part D.

Circuits in Figure 5.9 and Figure 5.15 show the analog and digital part of the circuit that have been implemented using analog and digital programmable blocks in the PSoC microcontroller.

Our present prototype is capable of generating pulses with complexity similar to the general signal template in Figure 5.10 and Figure 5.11 shows an actual oscilloscope screen capture of Figure 5.10 from our prototype. The signal is formed from the combination of the Main_ frequency PWM output (lower frequency) and a higher frequency generated by High_ Frequency PWM. It can potentially stimulate the brain in two frequencies and/or generate a limited set of pulses in repeating cycles. This configuration can be considered an equivalent to rTMS (Figure (1.6 Part D), Trains (1.6 Part C) and Theta Burst (1.6 Part E) protocols.

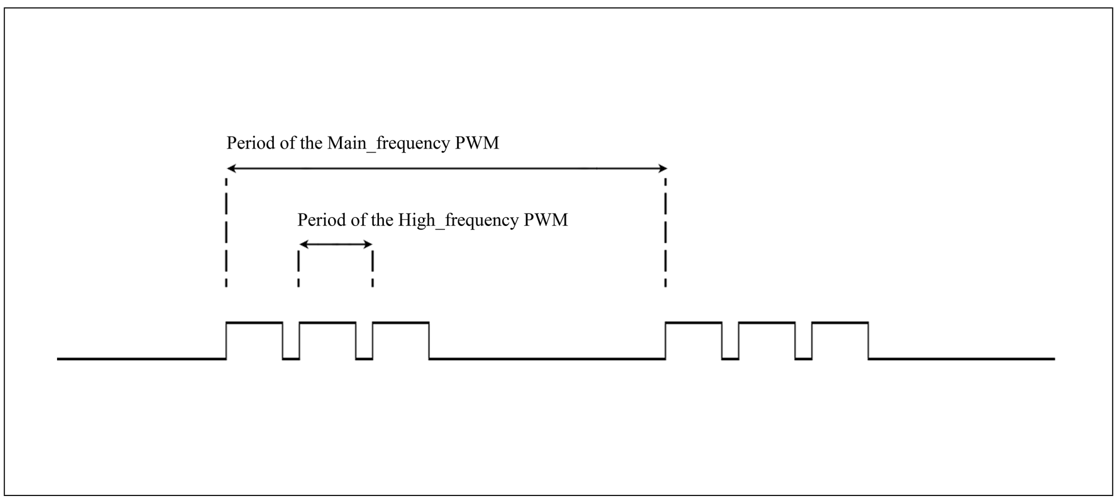


Figure 5.10. A typical pulse shape that can be generated by present version of TEFS prototype that can be set to emulate either rTMS or Trains protocols in TMS. (Actual output, screen capture from oscilloscope, of this typical signal can be seen on Figure 5.11)

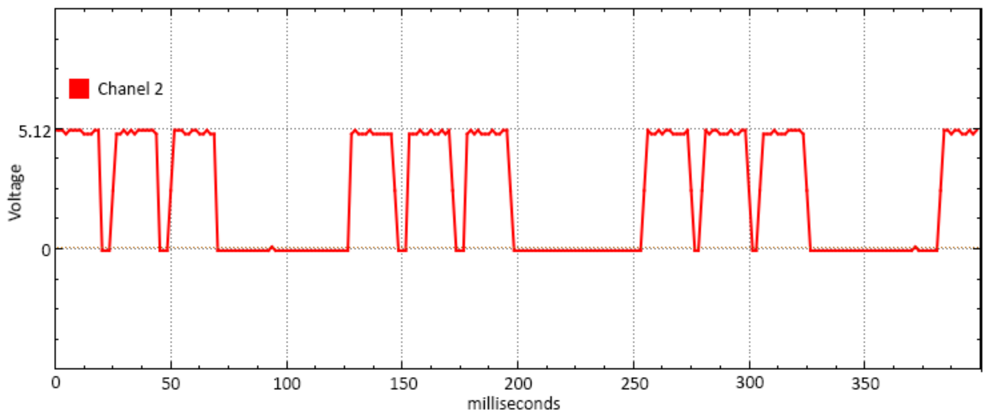


Figure 5.11. A typical pulse measured on Pin_5 (screen capture from oscilloscope) This signal is the output of Figure 5.9 Part C and demonstration of the typical pulse in Figure 5.10.

The PWM, in Figure 5.9 Part A controls timing and the main frequency pulse generation. PWM frequencies are adjustable both by hardware and software. The PWM in the Figure 5.9 Part B generates the higher frequency pulses. Logical gates and the D-flip-flop in this picture provide a synchronous enable and reset signals based on the status of the Main_ frequency and High_ frequency PWMs. In this configuration, the High_ frequency PWM is enabled in the rising edge of the Main_ frequency PWM pulse and it's synchronized with the Main_ frequency PWM. The rest signal gets activated after both the Main_ frequency PWM pulse and the High_ frequency PWM have ended, and it is synchronized with the falling edge of High_ frequency PWM output.

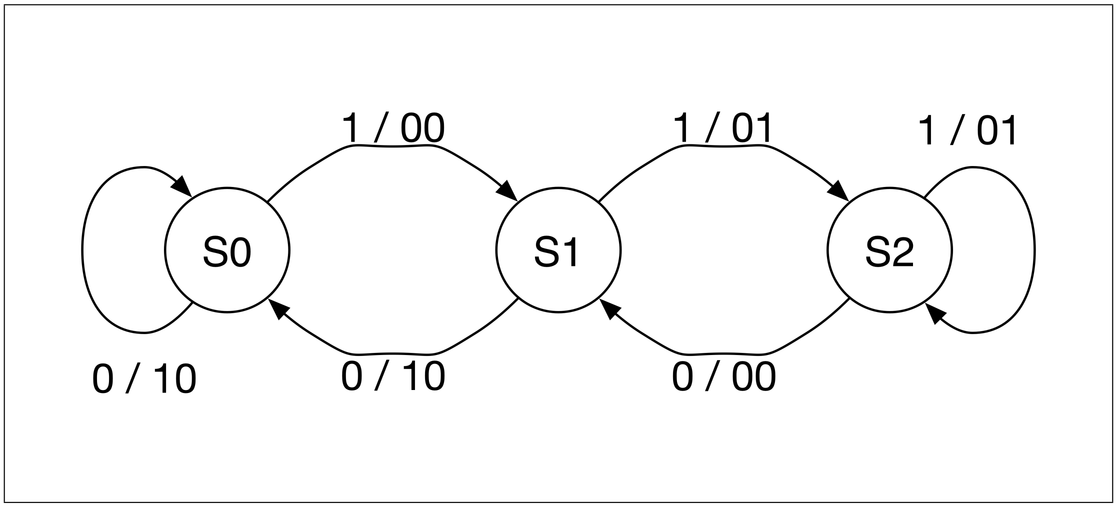


Figure 5.12. LUT1 is made based on this FSM Diagram that by adding an an extra state (S1) between transitions of the optocouplers for one cycle keeps both optocouplers OFF to add the deadband to their control signals.

Table 5.1. The content of this Lookup Table (LUT) is state transition table for the FSM diagram in Figure 5.12. It is also exactly the values that are stored in the LUT1 in Figure 5.15 Part D. This LUT takes present states and the FSM's input, and then generate the FSM's next state and outputs. These outputs are suitable for switching optocouplers in push-pull configuration with necessary deadband in our high voltage switching mechanism.

Present State		Input	Next State		Outputs	
In2	In1	In0	Out3	Out2	Out1	Out0
0	0	0	0	1	0	0
0	0	1	0	0	1	0
0	1	0	0	1	0	1
0	1	1	0	0	0	0
1	0	0	1	0	0	0
1	0	1	1	0	1	0
1	1	0	0	0	0	1
1	1	1	0	0	0	0

Figure 5.9 shows the pulse generation circuitry in detail. Figure 5.13 shows output signals, measured on Pin_1 and Pin_2 , generated from the input signal from part C that is measured on Pin_5 in the Figure 5.11. Circuits in this Figure create control signals for both optocouplers in Figure 5.16 Part B while adding necessary deadband to them. A deadband is an interval or 'band' where no action occurs or signals are 'dead'. Here this means that during a deadband both optocouplers are off. This Finite State machine is made based on the Figure 5.12 State diagram that is implemented with LUT1 (See Figure 5.9 Part D and Table 5.1 and Figure 5.14).

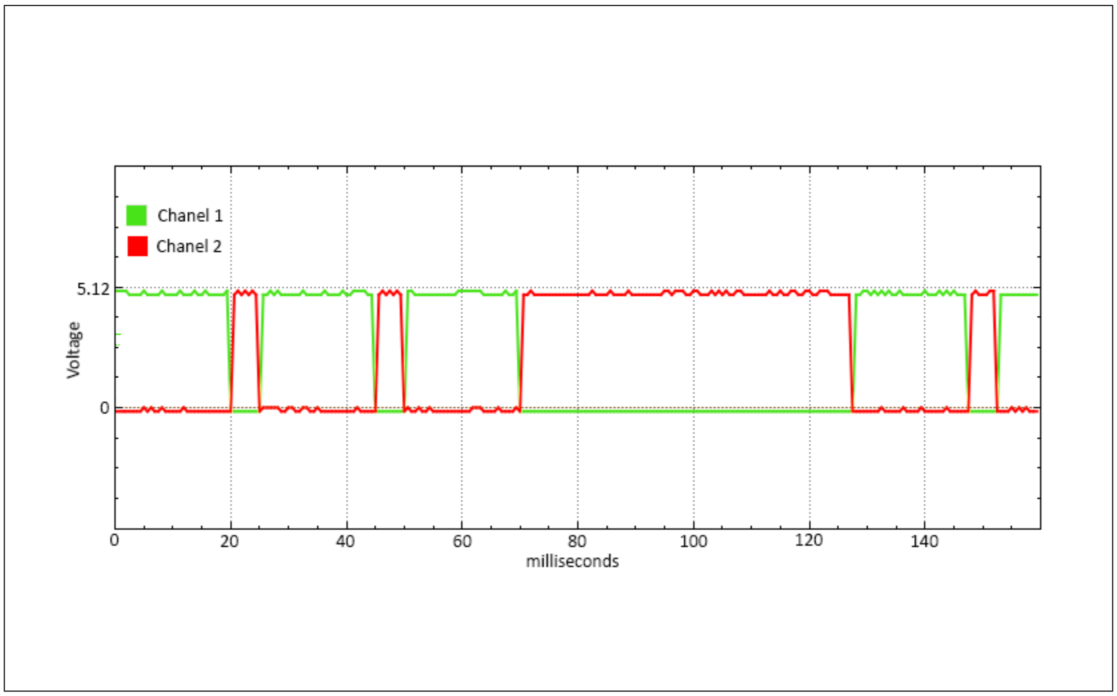


Figure 5.13. Optocopler control signals measured on Pin_1 and Pin_2 (screen capture from oscilloscope) A more detail picture of the toggle time is demonstrated on Figure 5.14.

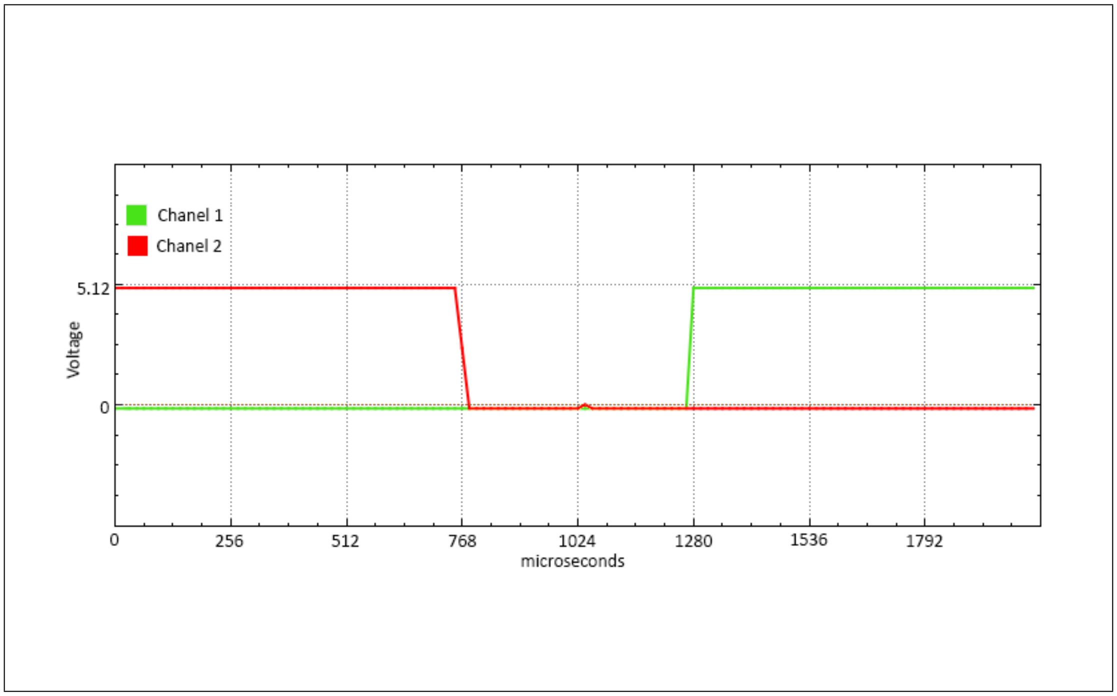


Figure 5.14. Optocopler control signal deadband measured on Pin_1 and Pin_2 (screen capture from oscilloscope). This Figure shows a signals toggle period in figure 5.13 in different timing scale.

Figure 5.15 shows the digital and analog blocks and parts responsible for I/O, Time tracking and generating programming voltage for the High voltage converter is in Figure 5.16 Part B.

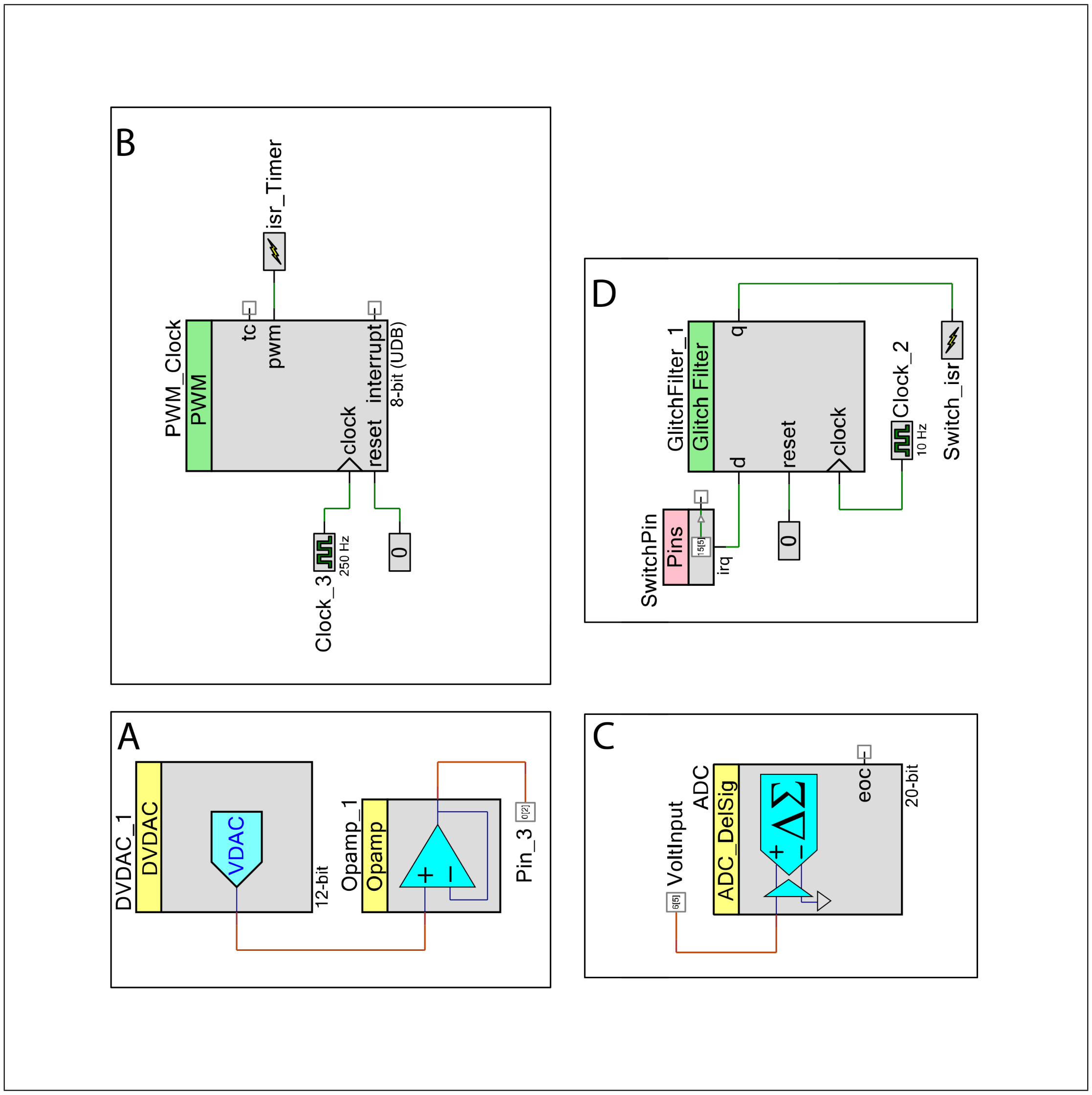


Figure 5.15. Digital and analog blocks used inside PSoC for I/O, time tracking and analog voltage for controlling the high voltage DC to DC converter. In Part A a Digital to Analog converter, DAC, is used to create an analog signal to be used for the high voltage DC to DC converter controlling pin (Input(-) pin of the EMCO Q101-5 in the Figure 5.16 Part B). Part B, shows a PWM that generates an interrupt every second that is used to track time. In the Part C an Analog-to-digital converter, ADC, has been used to measure a voltage generated by a potentiometer. The ADC is set to its highest resolution (20 bits) for more accuracy and a moving average of 128 samples is applied to the ADC readings to prevent it from sudden changes caused by noise. The output value of this ADC is used as an input to set the magnitude of the high voltage output. Circuits in Part D read a push button status and generates an interrupt with each keystroke that is used to control for turning ON and OFF the stimulation.

5.3.2 Interface

The digital parts of the system needs to be connected to the high voltage part of the system. This connection is provided by the interface circuits.

Since major part of the interface is implemented with programmable blocks inside the PSOC microcontroller, the remaining necessary interface circuitry is limited to minor voltage level correction at the digital to analog converter's output and simple current amplification to drive High voltage components which the 25 mA maximum current output of the microcontroller pins cannot handle.

The C5 capacitor in Figure 5.16 Part A is part of the microcontroller DAC circuit. This capacitor's value is varies depending on the microcontroller DAC's settings.

Since the microcontroller digital to analog converter maximum output voltage is 4.08 V, an op-amp, LM324N, is used to amplify this maximum voltage to maximum 5 V. The amplification magnitude can be adjusted by a 20 $K\Omega$ potentiometer, P, in Figure 5.16 part A. The gain (G) of the op-amp in this configuration can be calculated with G=$\frac{R_2+P}{P}$, that depending on the value of the P, is at least 1.2. This means that the op-amp output can be more than 5 V that is the maximum voltage needed to control the DC to DC converter. To ensure this voltage does not exceed 5 V, a zener diode (1N4733A) and R_3 are used before passing the voltage to the BD135 transistor that drives the current for the converter input voltage (Input (+) in the Figure 5.16 Part A). This transistor provides the necessary drive current for the DC to DC converter because the current is more than the microcontroller or op-amp outputs can handle. The microcontroller also cannot drive the LEDs in the optocouplers with its limited current output. For this reason, a 2SC945 transistor for each LED is used to amplify the microcontroller output pins' current. Since the voltage on Pin2 is 5 V, we not only have to amplify the microcontroller output current, we need to reduce this voltage to a safe level for the LEDs in the optocouplers. The

2SC945's emitter voltage to 4.3 V (0.7 less than the input voltage)(see Figure 5.16 Part A). To set the voltage over the LEDs to $1-1.5$ V, R_6 will limit the current on the optocoupler's LEDs to $180-150$ mA which makes both voltage and current on LEDs set to a safe level.

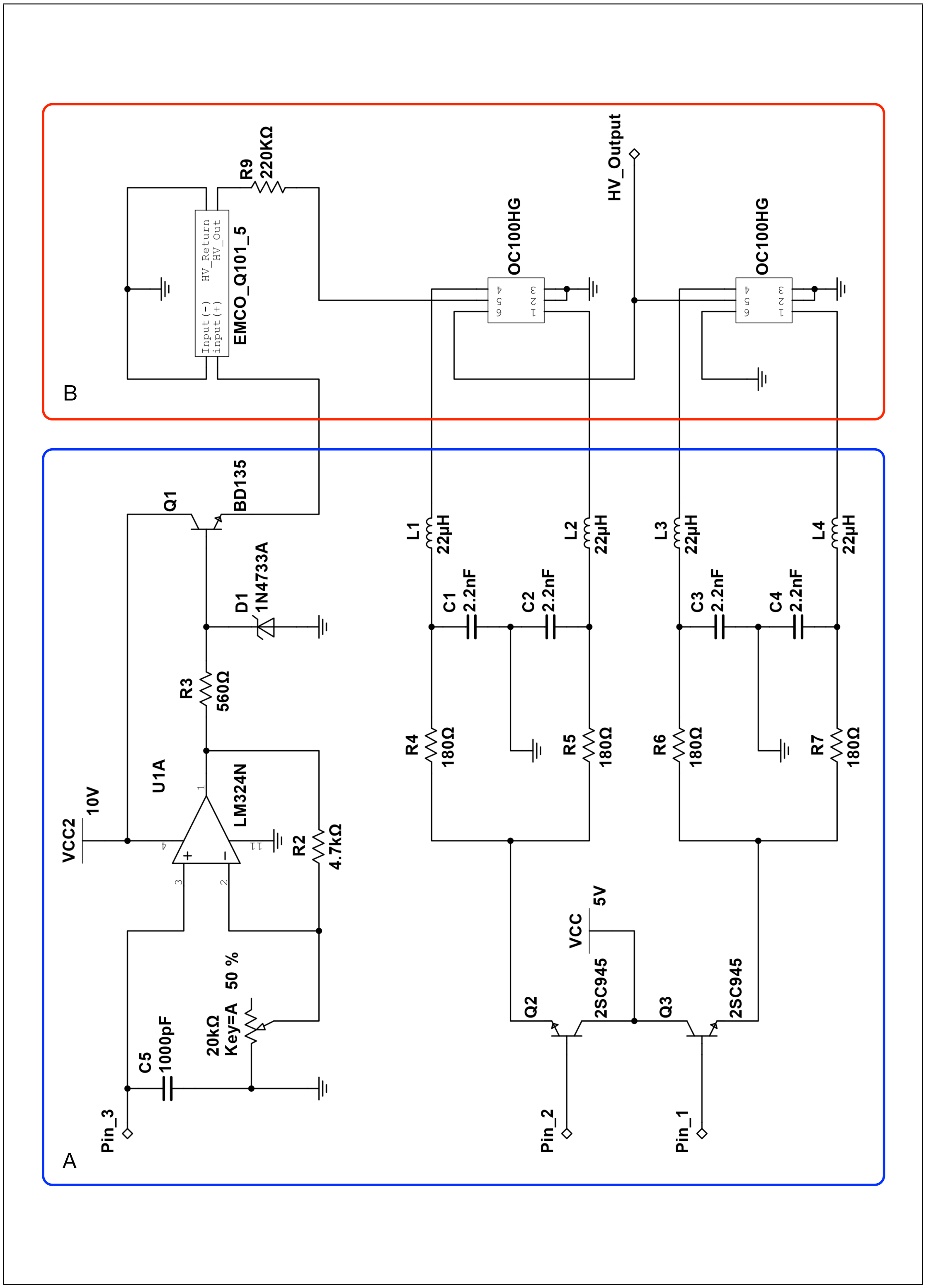


Figure 5.16. A) Interface Circuits B) High Voltage Circuits (see Figure 5.17 for more detailed high voltage circuitry.)

5.3.3 High Voltage

This section covers the design of the high voltage part of the hardware. It covers two major functions; the high voltage generator, and the high voltage switching.

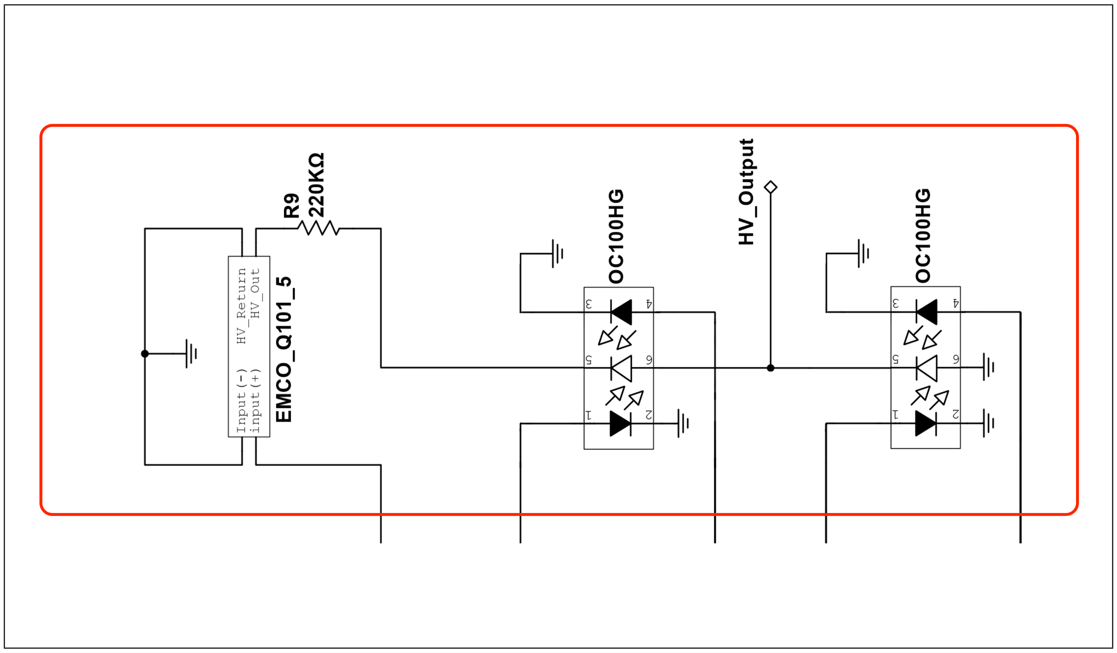


Figure 5.17. High Voltage Circuits. This is similar to Figure 5.16 Part B with the internal circuit of OC100HG optocouplers.

For creating high voltage pulses, we used optocouplers in the TEFS prototype as switching elements. Optocouplers connect current-isolated systems together through. The optocoupler used in our current prototype, OC100HG by Voltage Multipliers Inc. [57] (see Appendix B), is made from a high voltage optodiode in a reverse-biased topology at the output and a pair of the LEDs on the input side. The high voltage optodiode is covered with a thin layer of glass. When light emitted from LEDs shines on the light sensitive optodiode, some current leakage is caused in the optodiode. The magnitude of this current is proportional to the level of light emitted to the optodiode. Although this method limits the current in the output of the optocoupler, the current level is sufficient for our application. This rather new class of optocouplers are very helpful to replace very expensive commercial high voltage switches with a fraction of their cost and superior performance.

The optocouplers in our TEFS prototype are used in the push-pull configuration. In this configuration, one of the optocouplers supplies the current to the output and the other one sinks the current from the output. This configuration helps to set the output to high voltage and ground very fast, almost independent of the output capacitance. In the push-pull configuration, the optocouplers are turned on alternately, which means they cannot be turned on simultaneously. If they were turned on at the same time, there will be a high voltage shortcut in the circuit that is harmful to it and potentially is dangerous to the High voltage parts. However,if an error or noise cause both of them to be ON at the same time, R_9 limits the current in the optocouplers to a safe level and protects the optocouplers.

Four (4) DC to DC converters, SMHV05100 and ECHV05100 from HVM Technology Inc. and Q101-5 and Q101N-5 from EMCO High Voltage Co., have been tested as the high voltage generator for our device (See Appendix C). All of them convert voltages from the range of ($0\ V \leqslant Input\ Voltage \leqslant 5\ V$) into ($0\ V \leqslant Output\ Voltage \leqslant +10\ KV$), except Q101N-5 that converts voltage in rage of ($0\ V \leqslant Input\ Voltage \leqslant 5\ V$) into ($0\ V \leqslant Output\ Voltage \leqslant -10\ KV$). SMHV05100, ECHV05100 and Q101-5 can be used interchangeably (Figure 5.16 Part B), while to use Q101N-5, the polarity of the high voltage optodiode must be reversed. Therefore, connections to pin 5 must be switched to pin 6 and vice versa. SMHV05100 and ECHV05100 have separate 5 V power supplies from their programming pin (input (+) pin, Figure 5.16 Part B or Figure 5.17). SMHV05100 provides more control and monitoring options by having an input pin to control the maximum current at the output and an output voltage monitor pin, $0-1\ V$, based on the output.

Our design can be used for high voltage switching up to 50 KV by changing the DC to DC converters and optocouplers to the desired voltage. However, with this hypothetical design modification, much higher voltage magnitude could be switched using a series of optodiodes instead of the optocouplers. These optodiodes should be controlled by light sources where light is transferred from remote sources through optic light pipes [58]. In a typical optocoupler, the light source is very close to the light sensor which in our case is an optodiode. In very high voltages the presence of a very high voltage can cause two unwanted effects. First, it could affect the low voltage light source function, and second, the material between the light source and light sensor can have a voltage break down and become conductive and connect the output (very high voltage section) to the input (low voltage section). In the case that we want to use this design in higher than 50 KV, this issue needs to be addressed.

5.4 Software

All of the microcontroller codes are written in C. Since most of the control mechanism is implemented with programmable analog and digital blocks in the PSoC (Figure 5.9) and Figure 5.15, the software is relatively straightforward.

The program starts by initializing all the analog and digital blocks that are used for this design. It constantly monitors the voltage value of the potentiometer and produces the appropriate voltage for the programming pin of the DC to DC converter. Simultaneously, it shows the estimated High Voltage output on the LCD monitor. An interrupt routine reads a push button's activity which allows the software to initiate the toggle pulse generation process. As a safety precaution, another interrupt vector is used to measure standard time and the ON time. Through this interrupt vector also program stops the pulse generation at a pre-determined maximum time. At the OFF event, the software reprograms the programming pin of the DC to DC converter to its minimum for the duration of the idle time. Initial and idle states are designed to ensure that when the machine is just turned on, or in case of a microcontroller malfunction (mostly caused by high voltage circuits), it cuts the high voltage off from the output and does not expose the user to any unwanted fields. The high voltage part of the system creates a massive amount of noise. This triggered many disturbances for the digital part during the design and production process. During the initial design implementation, these noises generated many problems for the microcontroller and the low voltage part of the circuit. This issue was initially addressed by a series of LC filters that noticeably reduce the noise level. However, the issue has been completely resolved after encapsulating the high voltage parts in a Faraday cage and shielding the high voltage output.

The source code is attached in the Appendix A.

5.5 Conclusion

In this chapter we described the general design of our prototype. we discussed and presented different parts of the system and their design. Currently our device is completely stable for continuous long use. It can generate electric field pulses as small as 4 mus from a high voltage source with maximum magnitude of 10 KV in full intensity.

Also, the device is safe to be used *in vivo* and many safety precautions are engaged in the design, the implementation, and in real-time usage to ensure the safety of the user and the subject. We tested our device with its maximum output for a continuous 24 hours run and encountered no problem in either the digital or the analog parts of the system. Given the safety measures in place, the chance of high voltage shock to the user or the subject is minimal. However, just like any other medical device, inappropriate usage can cause harm to the user. Further studies are essential for the development of a safety guideline for TEFS.

Chapter 6

The Past, The Present, and the Future

6.1 Past

6.1.1 Motivation and the First TEFS Prototype

Meditation for many is an addictive habit. I, just like many others that can benefit from it the most, had difficulties stopping my wandering mind, and thus could not reliably repeat my occasional but unforgettable successful meditation sessions. Struggling with my general lack of success to repeat those successful sessions, I tried to shortcut my way into more successful meditation sessions, in the only way that as an engineer I could imagine: An electronic device.

I was at the University of California Santa Barbara, UCSB, in 2006. At the time, the University had just purchased an Egg Chair and the rumor was that they spent more than 20 thousand dollars setting it up. As it could be expected, there was a massive advertisement around the campus to encourage students to try it. After a stressful day in school, I gave it a try. To my surprise, although the experience was completely different from meditation, I found myself very relaxed after 20 minutes in that chair. Later I found out that the chair has multiple embedded speakers that stimulate the users brain with alpha waves [59].

A year later, Summer 2007, I was an intern at the Fujitsu company in northern

California. Except for me and my direct supervisor, everyone else in that lab was working on different aspects of cellular phone design and development. I had a chance to learn a lot about cellular phones from my lab-mates and had many interesting conversations with them. One particular conversation about a recently published paper remained in my mind: Cellphone usage increases our brain temperature.

My initial idea was to change the intensity of the outgoing cellphone signal in the range of brain wave frequencies, to create a positive effect alongside the negative impact of cell phones on our brain. Although I started to immediately play with one of my old cellphone's core, soon I abandoned the idea and moved to making a device that just creates my desired effect.

I think each of these three events and encounters, and the knowledge that I collected from them, played a significant role in forming the TEFS idea. However, I feel a major key factor was my lack of knowledge about TMS. In many ways, TMS was almost exactly the device that I was trying to make. And I was lucky to know nothing about it at that time.

From the electromagnetic waves that every cellphone generates, which causes the rise in brain temperature, I picked the electro part and decided to make a device that can simply stimulate the brain with electric fields. Seemingly it was a very simple engineering problem. All I needed was a source of high voltage and a mechanism to switch it ON and OFF at a certain frequency.

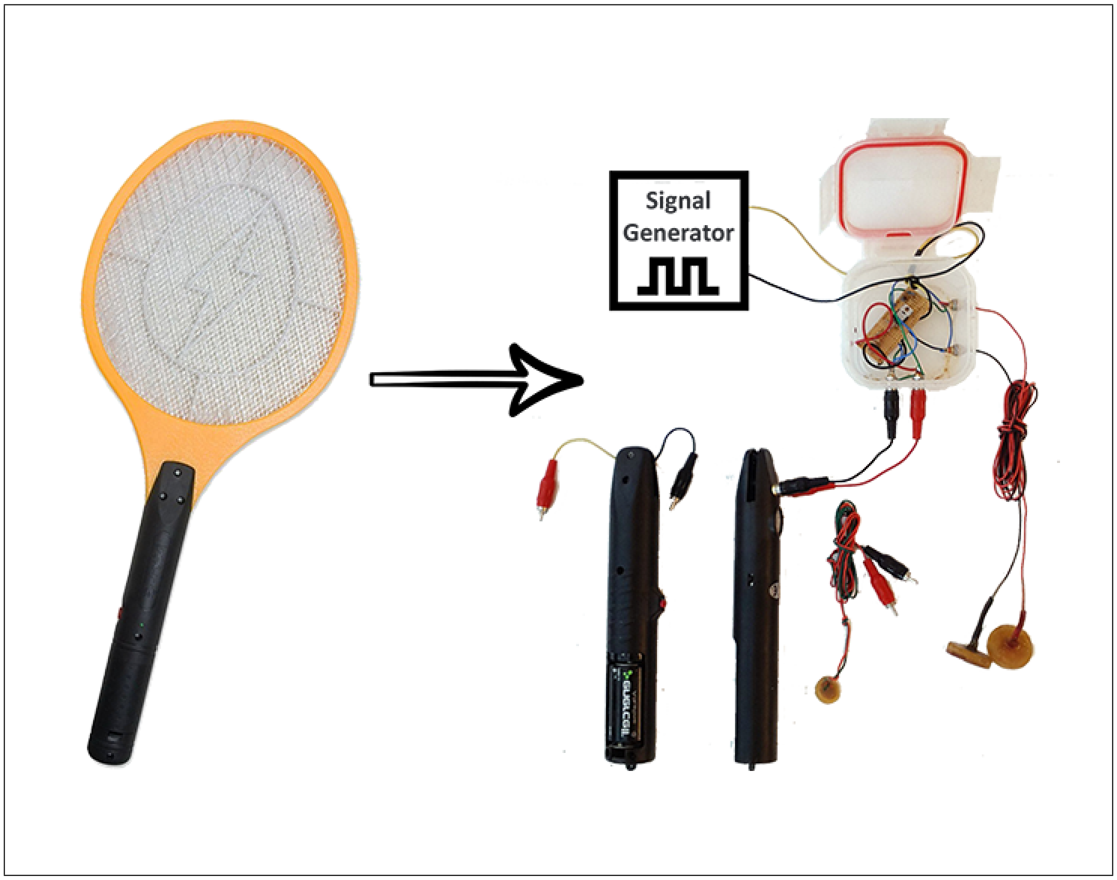


Figure 6.1. First working TEFS prototype mostly made from salvaged parts of a bug zapper racket in 2007

I found the high voltage source by salvaging a very cheap bug zapper (figure 6.1). However, the project became challenging when I could not find a way to readily switch such a high voltage on and off. After several attempts at trial and error and destroying many parts, I finally managed to make a switching mechanism using multiple optocouplers that could at least work for a short amount of time that it took to test the device. And there was light! (TEFS 6:1.1)

In the winter of 2008 I transferred from UCSB to UCSD, and soon after that my health and life complications stopped me for a couple of years from working on this project. Finally, a series of very unfortunates events landed me on one of the biggest opportunities in my life; a device (figure 6.1) that was made as a hobby from a bug zapper in a small and very limited home lab officially became my Ph.D. thesis project.

6.2 Present

6.2.1 Second Prototype

Before making the second prototype, an extended period of time had been spent on simulations; both to simulate effects of on external source of electric fields on the brain and to evaluate the impact of an internal source on the brain. Lack of budget stopped us from having access to an accurate human head model and purchasing a fully functional version of an electromagnetic simulator program. However, our simulation results, although not fully reliable, gave us some approximations for our design parameters and the maximum level of high voltage needed in our prototype.

For the second prototype, we used more accurate, controllable and regulated source of high voltage. The cost of making a second prototype was greater than the first given the improvement in the quality of the design and materials used. Fortunately, unlike the first prototype, new high voltage optocouplers in the market made our design and implementation of the switching mechanism much less challenging. Also, using a microcontroller which was made specifically for precision analog project development, we were given a very prodigious degree of control over the intensity and the timing of the device output.

Our hardware design is now capable of being programmed with the most advanced TMS protocols. It can also be programmed to function well beyond the capability of the most advanced TMS devices. The hardware can be programmed to generate a very complicated set of pulses where each pulse intensity and timing can be programmed separately.

Our maximum full intensity pulse-frequency is about one thousand times faster than the highest frequency that can be generated by the most advanced TMS devices. While the most advanced TMS machines can produce pulses in full intensity up to approximately 30 Hz, their pulses with frequencies higher than 30 Hz are not at their full intensity. The highest frequency on a TMS machine is approximately 120 HZ; however, the machine can generate pulses in full intensity at one-quarter of that maximum frequency.

A finalized/non-prototype version of our device can be a device carried in a pocket or hidden inside a hat. Furthermore, it can theoretically stimulate the brain for an unlimited period of time when neither size, nor generated heat, nor power consumption of TMS can uphold such an extended use.

6.3 Future

6.3.1 Future Prototype

The second prototype was made for testing different designs and is ready for adaptation to new ideas. It includes many redundancies that make its size much larger than an industrial version of TEFS.

For the next prototype, the plan is to remove most of these redundancies, reduce the size of the device and finally remove the programming parts and user inputs and outputs from the microcontroller. Those functions will be wirelessly passed to a computer or tablet with a more user-friendly interface which will include controlling and programming options. Moreover, separating and distancing the high voltage region from the digital segment will reduce the chance of high voltage interference and the effective damaging noises on the digital segment of the device. The idea is to connect the low voltage digital part to the high voltage part through some light pipes or cables in order to minimize the possibility of negative effects of high voltage on the digital parts.

Although in general most people with a novel idea or invention like to believe they are the first to come up with the idea, before TEFS comes to reality, in this project, many dreamt about such a device. One notable example, especially for a typical computer enthusiast of science fiction devices similar to TEFS, is the Cortical Stimulator device in the Star Trek series. Oddly, with above plans for the next prototype, it could end up looking similar to what was envisioned many decades ago as the cortical stimulator device.

6.3.2 Future Research

One essential step to prove that TEFS is at least as effective as TMS is still missing. While every evidence, simulation and *in/ex vivo* experiments support our claim, *in vivo* experiments are essential to prove beyond any doubt that TEFS is the next leap in brain stimulation devices.

Based on all of our results, I expect that *in vivo* experiments will further support our claim and support the validity of our results. However, it is important and necessary for the TEFS device to be examined *in vivo* and its effects should continue to be studied further. The device could evolve and be improved in many ways. Furthermore, its utility must be discussed and evaluated from an ethical and moral standpoint as it interferes with the brain.

Here is a short list of some of these concerns that come to this authors mind for further studies, developments and discussions:

Safety and ethical concerns :

- TEFS works by putting a very high voltage very close to the head. While, the voltage is isolated from the body, if the isolation fails it can be extremely dangerous. A commercial version of TEFS should include a mechanism that omits or minimizes such a danger in real time.

- TEFS is not as cheap and simple as TDCS but is simple and cheap enough that anyone with some basic computer and engineering skills and a limited budget can make one for themselves at home. It is not difficult to imagine that alongside many DIY versions, it can also be easily purchased at a very affordable price. While the author can imagine in some settings and for short time usage the device can be relatively safe and helpful for many, the device certainly can be set to configurations that could be hazardous, addictive, cause permanent brain damage, or cause undesirable temporary or permanent changes in the brain function. Small size, cheap price and portability of the device are advantages over TMS, but TEFS has potentially more of a chance of being used without a physicians supervision.

- Unlike TMS, TEFS can be portable and used for an extended period of time. Although it is an advantage, we never had the chance to evaluate such an extended use on the most similar device (TMS) before. So, we cannot even speculate the effects of such use.

- TEFS potentially opens a door to a degree of the functional brain manipulation by a machine that has never been experienced yet. One can just wonder about the possibilities and their consequences.

Plate design :

- Our current prototype plate is a flat conductive surface that emits electric fields perpendicular to its surface. The air gap between most of the plate and the scalp reduces its efficiency. A curved, or flexible plate can cause stronger and spatially more controlled stimulation. Also, the direction of the stimulation can be controlled with more complicated plates.

- Using multiple plates around the head could theoretically provide a very detailed and complex brain stimulation. Yet, we never had a chance to stimulate every part of our cortex in such detail. To jump from TMS-like stimulation to such a complicated stimulation, progress like our jump from X-ray machine to CT-Scan machine needs to be made through some prolonged and detailed research.

Signal shape :

- In both TEFS prototypes the output signal shape is rectangular and its magnitude is between $(0\ ,\ +High\,Voltage)$ or $(0\ ,\ -High\,Voltage)$. Expanding the device capability to produce more complicated signal shapes (i.e. sinusoids signals) and broaden range to $(-High\,Voltage\ ,\ +High\,Voltage)$, could be beneficial.

Plates placements :

- Unlike magnetic fields, electric fields can be disturbed and redirected with conductive material with different electrical potentials. Earth is an excellent example of such a thing. Although we can have a monopole electric field source, to minimize the effects of the environment on the device, a dipole electric field source can be helpful in generating a more accurate and controlled stimulation. Currently we can use our prototype in dipole mode, however the second source of the electric field is restricted to 0 volts. Potentially an adjustable electric field or in opposite polarity of the main pole could be more effective.

Appendix A

Source Code

main.c

```c
/***************************************************************************
* File Name: Main.c
*
* Version 0.001
*
* Description:
* This file contains the main function for TEFS project control unit.
* Copyright Arash Arfaee
* Note:
*
* Code tested with:
* PSoC Creator: 3.0
* Device Tested With: CY8C5868AXI-LP035
* Compiler    : ARMGCC 4.4.1, ARM RVDS Generic, ARM MDK Generic
*
****************************************************************************
* Copyright (2014, 2015), Arash Arfaee. All Rights Reserved.
****************************************************************************
* This software is owned and written by Arash Arfaee. Some codes partially are
* borrowed from CY8CKIT-050 examples.
*
***************************************************************************/

/***************************************************************************
*                            THEORY OF OPERATION
* This project demonstrates how ADC is used to read the input voltage at
* it's input and display it on the LCD while sends the voltage as the input to
* High Voltage DC to DC converter's input.
* The Potentiometer is connected to the input of the DelSig ADC. ADC is
* configured with 20 bit of resolution to measure the input voltage with
* higher accuracy. Moving average filter of 128 samples is applied to the ADC
* conversion result before displaying the estimated output result in  volts
* on the LCD.
* A DAC based on the ADC's result generate the DC to DC input voltage
* (through external interface).
* 2 PWMs and some complementary circuitry generate the high voltage switches.
* Lower edge of the SW3 starts and stops the stimulation process.
*
* Hardware connection on the Kit
* Potentiometer - PORT 6[5]
* LCD - PORT 2[0..6]
* DC to DC input - PIN VR
* Optocoupler LED input red - PORT 0[0]
* Optocoupler LED input green - PORT 0[1]
* DAC output - PORT 0[2]
* Optocouplers command signal (just for testing) - PORT 0[6]
* SW3 - PORT 15[5]
***************************************************************************/

#include <device.h>
#include "stdio.h"
#include "stdlib.h"
```

main.c

```
/* Number of samples to be taken before averaging the ADC value */
#define MAX_SAMPLE                  ((uint8)128)

/* Threshold value to reset the filter for sharp change in signal */
#define SIGNAL_SLOPE                1000

/* Number of shifts for calculating the sum and average of MAX_SAMPLE */
#define DIV                         7

/* defines for switch */
#define SWITCH_OPEN     (1)
#define SWITCH_CLOSE    (0)
#define ON              (1)
#define OFF             (0)
#define STARTUP         1
#define START_ZAP       2

/* defines pulse width in miliseconds 1000 for test, 100 for TMS like pulse.
#define PULSE_WIDTH    100 */

/* This flag is set inside Switch_isr.c file whenever there is
 * interrupt on the falling edge of the switch */
volatile uint8  switchIsrFlag = 0;
int Time_s_Counter=0;

struct Timings
{
    int Start_S;
    int End_s;
    int mfreq;
    int hfreq;
    int Vpercentage;
    char ID[];
} Timimg[10];

char Timings_name[5][10];

/*********************************************/

int main(void)
{
    uint8 i,s;
    int min=0;
    int sec=0;

    /* Array to store ADC count for moving average filter */
    int32 adcCounts[MAX_SAMPLE] = {0};

    /* Variable to hold ADC conversion result */
    int32 result = 0;

```

main.c

```
/* Variable to store accumulated sample for filter array */
int32 sum = 0;

/* Variable for testing sharp change in signal slope */
int16 diff = 0;

/* Variable to hold the result in micro/mili volts converted from filtered
 * ADC counts */
int32 microVolts = 0;
int16 miliVolts = 0;
int16 KVolts_Display =0;

/* Variable to hold the moving average filtered value */
int32 averageCounts = 0;

/* Index variable to work on the filter array */
uint8 index = 0;

/* Character array to hold the micro volts*/
char displayStr[15] = {'\0'};

/*uint8 debounceState = 0;*/

/* Default pin state */
/*uint8 switchState = SWITCH_OPEN;*/
uint8 state;

/*Clock_1_Stop();*/

/*initialize the input/program state*/
state = STARTUP;

/*initialize the input interrupt*/
Switch_isr_Start();
isr_Timer_StartEx(isr_Timer_Interrupt);
isr_Timer_Start();
CYGlobalIntEnable;

/*initialize PWMs and their settigs*/
Main_Frequency_Start();
High_Frequency_Start();

High_Freq_ON_Write(1);

/* Start ADC and start conversion */
ADC_Start();
ADC_StartConvert();

DVDAC_1_Init();
DVDAC_1_SetValue(0xFF0);
DVDAC_1_Start();
Opamp_1_Start();
```

main.c

```
/* Start LCD and set position */
LCD_Start();
LCD_Position(0,0);
LCD_PrintString("Output: ");

/* Print μV unit on the LCD */
LCD_Position(0,14);
/*LCD_WriteData(0xE4);*/
LCD_PrintString("V");

/* Read one sample from the ADC and initialize the filter */
ADC_IsEndConversion(ADC_WAIT_FOR_RESULT);
result = ADC_GetResult32();

for(i = 0; i < MAX_SAMPLE; i++)
{
    adcCounts[i] = result;
}

/* Store sum of 128 samples*/
sum = result << DIV;

/* Average count is equal to one single sample for first ADC reading */
averageCounts = result;
s=0;

while(1)
{
    ADC_IsEndConversion(ADC_WAIT_FOR_RESULT);
    result = ADC_GetResult32();

    diff = abs(averageCounts - result);

    /* If sharp change in the signal then reset the filter with the new
     * signal value */
    if(diff > SIGNAL_SLOPE)
    {
        for(i = 0; i < MAX_SAMPLE; i++)
        {
            adcCounts[i] = result;
        }

        /* Store sum of 128 samples*/
        sum = result << DIV;

        /* Average count is equal to new sample */
        averageCounts = result;
        index = 0;
    }

    /* Get moving average */
```

main.c

```
else
{
    /* Remove the oldest element and add new sample to sum and get
     * the average */
    sum = sum - adcCounts[index];
    sum = sum + result;
    averageCounts = sum >> DIV;

    /* Remove the oldest sample and store new sample */
    adcCounts[index] = result;
    index++;
    if (index == MAX_SAMPLE)
    {
        index = 0;
    }
}
microVolts = ADC_CountsTo_uVolts(averageCounts);

/*miliVolts = ADC_CountsTo_mVolts(averageCounts);*/

miliVolts = (microVolts/1000);
if( miliVolts <1 )
{
    miliVolts = 0;
}
if ( miliVolts> 0xFF0 )
{
    miliVolts = 0xFF0;
}
DVDAC_1_SetValue(miliVolts);
KVolts_Display =  (miliVolts*1.22549019608*0.2);
KVolts_Display *= 10;

/* Convert mili volts to string and display on the LCD */
sprintf(displayStr,"%5d",KVolts_Display);

LCD_Position(0,8);
LCD_PrintString(displayStr);

if(Time_s_Counter>=1200)
{
    rTEFS_ON_Write(0);
    PWM_Clock_Stop();
    s=0;
}

/*sec to min to display*/

min=Time_s_Counter/60;
sec=Time_s_Counter%60;

sprintf(displayStr,"%02d:%02d",min,sec);
```

main.c

```
        LCD_Position(1,5);
        LCD_PrintString(displayStr);

        /* In startup state, discard the first switch interrupt. This is
invalid */
        if ((state==STARTUP) && (switchIsrFlag == 1))
        {
                switchIsrFlag = 0;
                state = START_ZAP;

        }

        /* if key pressed initiates one 250ms paulse*/
        if ((state==START_ZAP) && (switchIsrFlag == 1))
        {
            /*resets SW interrupt flag for the next key press*/
            switchIsrFlag = 0;

            if(s==0)
            {
                rTEFS_ON_Write(1);
                Time_s_Counter=0;
                PWM_Clock_Start();
                s=1;
            }
            else
            {
                rTEFS_ON_Write(0);
                PWM_Clock_Stop();
                s=0;
            }

        }
    }
}

 /**********************************************/

/* [] END OF FILE */
```

Appendix B

High Voltage Relay Data Sheet

OC100 OC100G OC100HG

Optocoupler · Axial Leaded · Epoxy Molded

ABSOLUTE MAXIMUM RATINGS

	OC100	OC100G	OC100HG
LED			
Forward DC Current	100mA		
Surge Current	(tp = 10 µs) 2.5A	(tp = 100 µs) 1.5A	(tp = 10 µs) 1.5A
Reverse Voltage	5 V		
Power Dissipation	(25°C) 200 mW	(25°C) 160 mW	(25°C) 180 mW
Photodiode			
Reverse Voltage	15,000 V		
Power Dissipation	1.0 W		

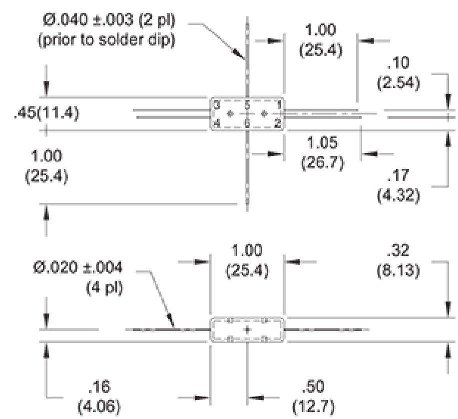
- Storage Temperature: -40°C to +100°C
- Operating Temperature: -40°C to +70°C
- Isolation Test Voltage: 25 kV (From Pins 1, 2, 3 & 4 to Pins 5 & 6)

ELECTRICAL CHARACTERISTICS

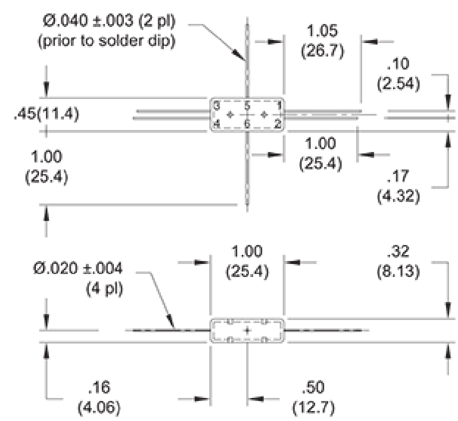
	OC100	OC100G	OC100HG
LED			
Forward Voltage	(If = 100 mA) 1.5 V		
Reverse Leakage Current VR = 5 V	10 nA	10 µA	
Photodiode			
Forward Voltage	(If = 0.6 A) 12.0 V MAX		
Reverse Leakage Current			
VR = 10 kV, I_{LED} = 0 mA	250 nA Typical		
VR = 10 kV, I_{LED} = 50 mA	50 µA Typical	200 µA Typical	250 µA Typical
Coupled			
DC Current Transfer Ratio			
I_{LED} = 50 mA, VR = 10 kV,	0.064% MIN	0.32% MIN	0.38% MIN
t_{ON} = (Typical)	2 µs		
t_{OFF} = (Typical)	2 µs		

(25°C UNLESS OTHERWISE NOTED)

OC100 OC100HG

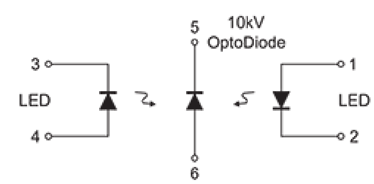


OC100G



Tolerance:
.XX ±.020

Simplified Circuit Schematic



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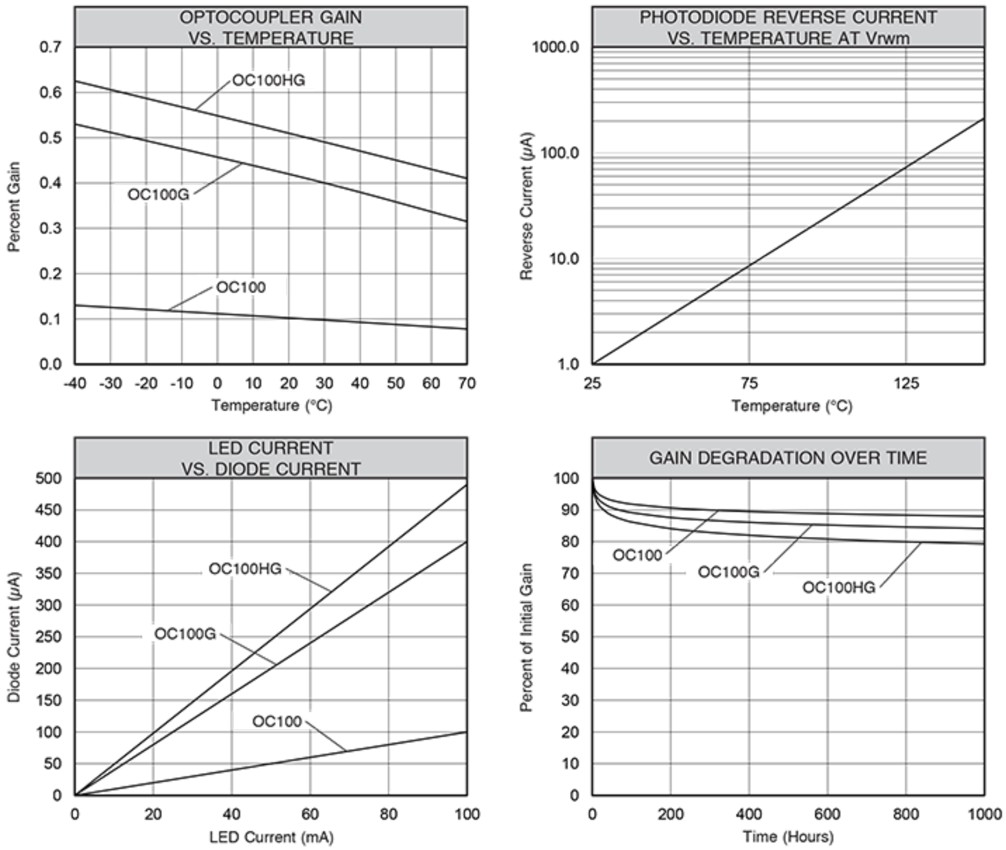
www.highvoltagepowersupplies.com

OC100 OC100G OC100HG



Appendix C

High Voltage Generators' Data Sheets

Proven Reliability

Q SERIES

ISOLATED, PROPORTIONAL DC TO HV DC CONVERTERS

100V to 10,000V @ 0.5 and 1.25 Watts

NOW UL RECOGNIZED

PRODUCT DESCRIPTION

The Q Series is a broad line of ultra-miniature, high reliability DC to HV DC converters supplying up to 5,000 volts in only 0.125 cubic inches and up to 10,000 volts in only 0.614 cubic inches. These component-sized converters are ideal for applications requiring minimal size and weight. The output is directly proportional to the input voltage and is linear from <0.7V input to maximum input voltage, allowing for an adjustable output voltage.

OPTIONS

0.5 Watt and 1.25 Watt versions available (1.25W up to 5KV)
Center Tap Option available (up to Q09 / QH09)
External Copper Shield (S suffix))
Control Pin Option available (up to Q50 / QH20) (C suffix)
Extended operating temperature (0.5W - Q models) (T suffix)
RoHS Version Available (R suffix)
Ordering Information (see Page 13)
Low Outgassing Epoxy (NASA approved per ASTM E-595-93) (consult factory)
Alternate Input / Output Voltages (consult factory)
Alternate Pin Pattern, see VA units (Page 10)
Reduced Input Power (consult factory)

APPLICATIONS

Avalanche Photodiodes
Photomultiplier Tubes
Light Sources
Piezo Devices
Sustaining Ion Pumps
Electrophoresis
Printers
Igniters
Capacitor Charging

FEATURES

Ultra-Miniature Case Size
Proven Reliability
No External Components Required
Low Ripple and EMI/RFI
Proportional Input/Output
Input/Output Isolation
Low Leakage Current <250nA
Low input/output coupling capacitance, <50 pF typical
Designed to meet UL 94 V0
MTBF: >3 million hrs. per Bellcore TR 332
Short circuit protection, 1 minute minimum
Control Pin can be used for ON/OFF control

PRODUCT OVERVIEW

OUTPUT VOLTAGE*2	Q MODELS 0.50 Watt	QH MODELS 1.25 Watt
100 VDC	Q01	QH01
150 VDC	Q015	QH015
200 VDC	Q02	QH02
250 VDC	Q025	QH025
300 VDC	Q03	QH03
350 VDC	Q035	QH035
400 VDC	Q04	QH04
450 VDC	Q045	QH045
500 VDC	Q05	QH05
600 VDC	Q06	QH06
700 VDC	Q07	QH07
800 VDC	Q08	QH08
900 VDC	Q09	QH09
1,000 VDC	Q10	QH10
1,200 VDC	Q12	QH12
1,500 VDC	Q15	QH15
2,000 VDC	Q20	QH20
2,500 VDC	Q25	
3,000 VDC	Q30	
4,000 VDC	Q40	
5,000 VDC	Q50	
6,000 VDC	Q60	
8,000 VDC	Q80	
10,000 VDC	Q101	

Complete List of Models on pages 2-5

ISO 9001:2008 CERTIFIED ISO 14001:2004 CERTIFIED RoHS COMPLIANT c UL us E344664 CE IPC Certified J-STD-001 Application Specialist

ELECTRICAL SPECIFICATIONS[3] (100V - 900V)

	Q MODELS - 0.50 Watt			QH MODELS - 1.25 Watt		
OUTPUT VOLTAGE*2	MODEL[6]	MAXIMUM OUTPUT CURRENT[1]	RIPPLE P-P	MODEL[6]	MAXIMUM OUTPUT CURRENT[1]	RIPPLE P-P
REVERSIBLE: 0 TO (+) OR (-) Vout						
0 to 100VDC	Q01	5.000 mA	<1.000 %	QH01	12.500 mA	<2.500 %
0 to 150VDC	Q015	3.333 mA	<0.500 %	QH015	8.333 mA	<1.125 %
0 to 200VDC	Q02	2.500 mA	<0.250 %	QH02	6.250 mA	<1.125 %
0 to 250VDC	Q025	2.000 mA	<0.250 %	QH025	5.000 mA	<1.125 %
0 to 300VDC	Q03	1.667 mA	<0.250 %	QH03	4.167 mA	<1.125 %
0 to 350VDC	Q035	1.429 mA	<0.250 %	QH035	3.571 mA	<1.125 %
0 to 400VDC	Q04	1.250 mA	<0.100 %	QH04	3.125 mA	<0.500 %
0 to 450VDC	Q045	1.111 mA	<0.150 %	QH045	2.778 mA	<0.625 %
0 to 500VDC	Q05	1.000 mA	<0.150 %	QH05	2.500 mA	<0.625 %
0 to 600VDC	Q06	0.833 mA	<0.100 %	QH06	2.083 mA	<0.500 %
0 to 700VDC	Q07	0.714 mA	<0.250 %	QH07	1.786 mA	<0.625 %
0 to 800VDC	Q08	0.625 mA	<0.300 %	QH08	1.563 mA	<1.0 %
0 to 900VDC	Q09	0.556 mA	<0.250 %	QH09	1.389 mA	<1.0 %

PARAMETER	VALUE
INPUT VOLTAGE	0 to 5, 12, 15 or 24 VOLTS
TYPICAL TURN-ON VOLTAGE	<0.7 VOLTS
ISOLATION	< +/- 500 VDC BIAS ON OUTPUT RETURN (PIN4)
OUTPUT VOLTAGE TOLERANCE	+10%, -10% (AT 100% OUTPUT, FULL LOAD)
FREQUENCY	75-350KHZ (TYPICAL)
CONTROL PIN	0 to VIN (SEE PAGE 12 FOR DETAILS)
STORAGE TEMPERATURE	-55 to +105°C
STANDARD OPERATING TEMPERATURE	-25 to +70°C[4] (CASE)
EXTENDED OPERATING TEMPERATURE	-55 to +75°C[4] (CASE) [Q models / 0.5W]

	INPUT CURRENT			
	Q MODELS - 0.50 Watt		QH MODELS - 1.250 Watt	
VIN	NO-LOAD	FULL-LOAD	NO-LOAD	FULL-LOAD
5 VDC	<100 mA	<250 mA	<250 mA	<550 mA
12 VDC	<40 mA	<100 mA	<100 mA	<250 mA
15 VDC	<32 mA	<80 mA	<80 mA	<200 mA
24 VDC	<20 mA	<50 mA	<50 mA	<125 mA

ELECTRICAL SPECIFICATIONS*3 (100V - 900V)

	Q MODELS - 0.50 Watt			QH MODELS - 1.25 Watt		
OUTPUT VOLTAGE*2	MODEL	MAXIMUM OUTPUT CURRENT*1	RIPPLE P-P	MODEL	MAXIMUM OUTPUT CURRENT*1	RIPPLE P-P*5
CENTER TAP: 0 TO (+) AND (-) Vout						
0 to +/- 50 VDC	Q01CT	5.000 mA	<1.000 %	QH01CT	12.500 mA	<2.500 %
0 to +/- 75 VDC	Q015CT	3.333 mA	<0.500 %	QH015CT	8.333 mA	<1.125 %
0 to +/-100 VDC	Q02CT	2.500 mA	<0.250 %	QH02CT	6.250 mA	<1.125 %
0 to +/-125 VDC	Q025CT	2.000 mA	<0.250 %	QH025CT	5.000 mA	<1.125 %
0 to +/-150 VDC	Q03CT	1.667 mA	<0.250 %	QH03CT	4.167 mA	<1.125 %
0 to +/-175 VDC	Q035CT	1.429 mA	<0.250 %	QH035CT	3.571 mA	<1.125 %
0 to +/-200 VDC	Q04CT	1.250 mA	<0.100 %	QH04CT	3.125 mA	<0.500 %
0 to +/-225 VDC	Q045CT	1.111 mA	<0.150 %	QH045CT	2.778 mA	<0.625 %
0 to +/-250 VDC	Q05CT	1.000 mA	<0.150 %	QH05CT	2.500 mA	<0.625 %
0 to +/-300 VDC	Q06CT	0.833 mA	<0.100 %	QH06CT	2.083 mA	<0.500 %
0 to +/-350 VDC	Q07CT	0.714 mA	<0.250 %	QH07CT	1.786 mA	<0.625 %
0 to +/-400 VDC	Q08CT	0.625 mA	<0.300 %	QH08CT	1.563 mA	<1.0 %
0 to +/-450 VDC	Q09CT	0.556 mA	<0.250 %	QH09CT	1.389 mA	<1.0 %

PARAMETER	VALUE
INPUT VOLTAGE	0 to 5, 12, 15 or 24 VOLTS
TYPICAL TURN-ON VOLTAGE	<0.7 VOLTS
ISOLATION	< +/- 500 VDC BIAS ON OUTPUT RETURN (PIN4)
OUTPUT VOLTAGE TOLERANCE	+10%, -10% (AT 100% OUTPUT, FULL LOAD)
FREQUENCY	75-350KHZ (TYPICAL)
CONTROL PIN	0 to VIN (SEE PAGE 12 FOR DETAILS)
STORAGE TEMPERATURE	-55 to +105°C
STANDARD OPERATING TEMPERATURE	-25 to +70°C*4 (CASE)
EXTENDED OPERATING TEMPERATURE	-55 to +75°C*4 (CASE) [Q models / 0.5W]

	INPUT CURRENT			
	Q MODELS - 0.50 Watt		QH MODELS - 1.250 Watt	
VIN	NO-LOAD	FULL-LOAD	NO-LOAD	FULL-LOAD
5 VDC	<100 mA	<250 mA	<250 mA	<550 mA
12 VDC	<40 mA	<100 mA	<100 mA	<250 mA
15 VDC	<32 mA	<80 mA	<80 mA	<200 mA
24 VDC	<20 mA	<50 mA	<50 mA	<125 mA

ELECTRICAL SPECIFICATIONS[*3] (1,000V - 2,000V)

	Q MODELS - 0.50 Watt			QH MODELS - 1.25 Watt		
OUTPUT VOLTAGE[*2]	MODEL	MAXIMUM OUTPUT CURRENT[*1]	RIPPLE P-P	MODEL	MAXIMUM OUTPUT CURRENT[*1]	RIPPLE P-P
POSITIVE						
0 to +1000 VDC	Q10	0.500 mA	<0.250 %	QH10	1.250 mA	<1.0%
0 to +1200 VDC	Q12	0.417 mA	<0.250 %	QH12	1.042 mA	<1.0%
0 to +1500 VDC	Q15	0.333 mA	<0.250 %	QH15	0.833 mA	<1.0%
0 to +2000 VDC	Q20	0.250 mA	<0.250 %	QH20	0.625 mA	<1.0%
NEGATIVE						
0 to -1000 VDC	Q10N	0.500 mA	<0.250 %	QH10N	1.250 mA	<1.0%
0 to -1200 VDC	Q12N	0.417 mA	<0.250 %	QH12N	1.042 mA	<1.0%
0 to -1500 VDC	Q15N	0.333 mA	<0.250 %	QH15N	0.833 mA	<1.0%
0 to -2000 VDC	Q20N	0.250 mA	<0.250 %	QH20N	0.625 mA	<1.0%

PARAMETER	VALUE
INPUT VOLTAGE	0 to 5, 12, 15 or 24 VOLTS
TYPICAL TURN-ON VOLTAGE	<0.7 VOLTS
ISOLATION	< +/- 500 VDC BIAS ON OUTPUT RETURN (PIN4)
OUTPUT VOLTAGE TOLERANCE	+10%, -10% (AT 100% OUTPUT, FULL LOAD)
FREQUENCY	75-350KHZ (TYPICAL)
CONTROL PIN	0 to VIN (SEE PAGE 12 FOR DETAILS)
STORAGE TEMPERATURE	-55 to +105°C
STANDARD OPERATING TEMPERATURE	-25 to +70°C[*4] (CASE)
EXTENDED OPERATING TEMPERATURE	-55 to +75°C[*4] (CASE) [Q models / 0.5W]

	INPUT CURRENT			
	Q MODELS - 0.50 Watt		QH MODELS - 1.250 Watt	
VIN	NO-LOAD	FULL-LOAD	NO-LOAD	FULL-LOAD
5 VDC	<100 mA	<250 mA	<250 mA	<550 mA
12 VDC	<40 mA	<100 mA	<100 mA	<250 mA
15 VDC	<32 mA	<80 mA	<80 mA	<200 mA
24 VDC	<20 mA	<50 mA	<50 mA	<125 mA

ELECTRICAL SPECIFICATIONS[3] (2,500V - 5,000V)

	Q MODELS - 0.50 Watt		
OUTPUT VOLTAGE*[2]	MODEL	MAXIMUM OUTPUT CURRENT[1]	RIPPLE P-P
POSITIVE			
0 to +2,500 VDC	Q25	0.200 mA	<0.500 %
0 to +3,000 VDC	Q30	0.167mA	<0.500 %
0 to +4,000 VDC	Q40	0.125 mA	<0.500 %
0 to +5,000 VDC	Q50	0.100 mA	<0.500 %
NEGATIVE			
0 to -2,500 VDC	Q25N	0.200 mA	<0.500 %
0 to -3,000 VDC	Q30N	0.167 mA	<0.500 %
0 to -4,000 VDC	Q40N	0.125 mA	<0.500 %
0 to -5,000 VDC	Q50N	0.100 mA	<0.500 %

PARAMETER	VALUE
INPUT VOLTAGE	0 to 5, 12, 15 or 24 VOLTS
	0 TO 5V (FOR MODELS OVER 3KV)
TYPICAL TURN-ON VOLTAGE	<0.7 VOLTS
ISOLATION	< +/- 500 VDC BIAS ON OUTPUT RETURN (PIN4)
OUTPUT VOLTAGE TOLERANCE	+10%, -10% (AT 100% OUTPUT, FULL LOAD)
FREQUENCY	75-350KHZ (TYPICAL)
CONTROL PIN	0 to VIN (SEE PAGE 12 FOR DETAILS)
STORAGE TEMPERATURE	-55 to +105°C
STANDARD OPERATING TEMPERATURE	-25 to +60°C[4] (CASE)
EXTENDED OPERATING TEMPERATURE	-55 to +70°C[4] (CASE) [Q models / 0.5W]

	INPUT CURRENT	
	Q MODELS - 0.50 Watt	
VIN	NO-LOAD	FULL-LOAD
5 VDC	<250 mA	<400 mA
12 VDC	<100 mA	<250 mA
15 VDC	<75 mA	<125 mA
24 VDC	<35 mA	<75 mA

0 TO 5V ONLY (FOR MODELS OVER 3kV)

ELECTRICAL SPECIFICATIONS[3] (6,000V - 10,000V)

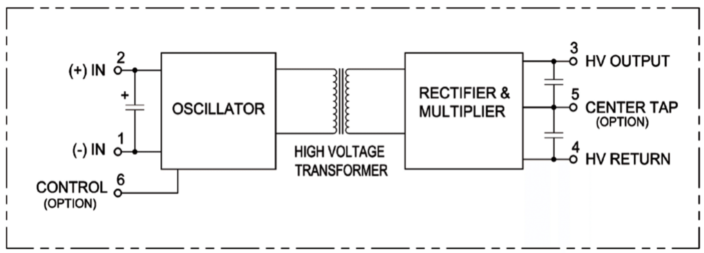
	Q MODELS - 0.50 Watt		
OUTPUT VOLTAGE*2	MODEL	MAXIMUM OUTPUT CURRENT*1	RIPPLE P-P
POSITIVE			
0 to +6,000 VDC	Q60	83 µA	<1.000 %
0 to +8,000 VDC	Q80	62.5 µA	<1.000 %
0 to +10,000 VDC	Q101	50 µA	<1.000 %
NEGATIVE			
0 to -6,000 VDC	Q60N	83 uA	<1.000 %
0 to -8,000 VDC	Q80N	62.5 uA	<1.000 %
0 to -10,000 VDC	Q101N	50 uA	<1.000 %

PARAMETER	VALUE
INPUT VOLTAGE	0 to 5 VOLTS
TYPICAL TURN-ON VOLTAGE	<0.7 VOLTS
ISOLATION	< +/- 500 VDC BIAS ON OUTPUT RETURN (W4)
OUTPUT VOLTAGE TOLERANCE	+10%, -10% (AT 100% OUTPUT, FULL LOAD)
FREQUENCY	75-350KHZ (TYPICAL)
STANDARD TEMPERATURE RANGES	OPERATING: -10 TO +60°C*4 (CASE)
	STORAGE: -20° TO +105°C

	INPUT CURRENT	
	Q MODELS - 0.50 Watt	
VIN	NO-LOAD	FULL-LOAD
5 VDC	<175 mA	<250 mA

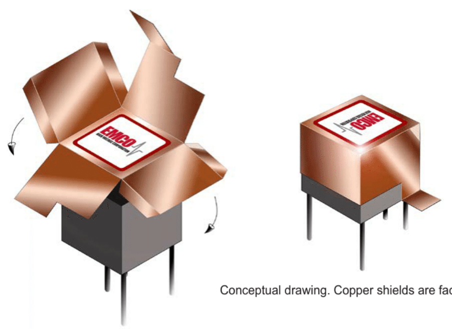
Q SERIES

BLOCK DIAGRAM



NOTE: Pin designators for pin out models up to 5KV.

COPPER SHIELD PLACEMENT



Conceptual drawing. Copper shields are factory installed.

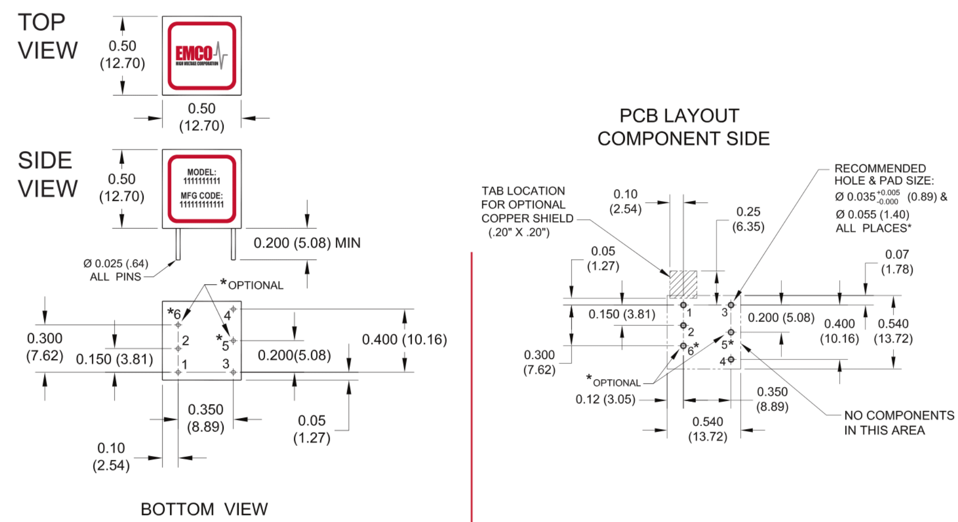
DETAILED PRODUCT DESCRIPTION

The Q Series is a broad line of ultra-miniature, high reliability DC to HV DC converters supplying up to 5,000 volts in only 0.125 cubic inches and up to 10,000 volts in only 0.614 cubic inches. These component-sized converters are ideal for applications requiring minimal size and weight. The output is directly proportional to the input voltage and is linear from <0.7V input to maximum input voltage, allowing for an adjustable output voltage. Output is load dependent. A control pin option allows full control of the output via a high impedance input, ideal for error-amplifier control in closed-loop systems. Isolation is <+/- 500V bias on output return and output power is either 0.5 watt or 1.25 watts. No external components or minimum load are required. The output ripple is extremely low for this package size, as low as .1%. Light weight and wide temperature range make these units ideal for portable, battery-powered equipment. Many models feature a center-tap option, which creates both a positive and a negative output from miniature, one low cost unit. An alternate pin pattern is available for users wishing to upgrade without modifying their board design. Output is load dependent.

Application notes are available on this series, and technical assistance is readily available.

Small quantities available from stock from our factory or our stocking distributor in Switzerland, Condatas AG. If stock should be depleted standard lead time is one to two weeks. For large quantity requests please consult our factory or our stocking distributor in Switzerland, Condatas AG.

MECHANICAL SPECIFICATIONS (100V - 2,000V)



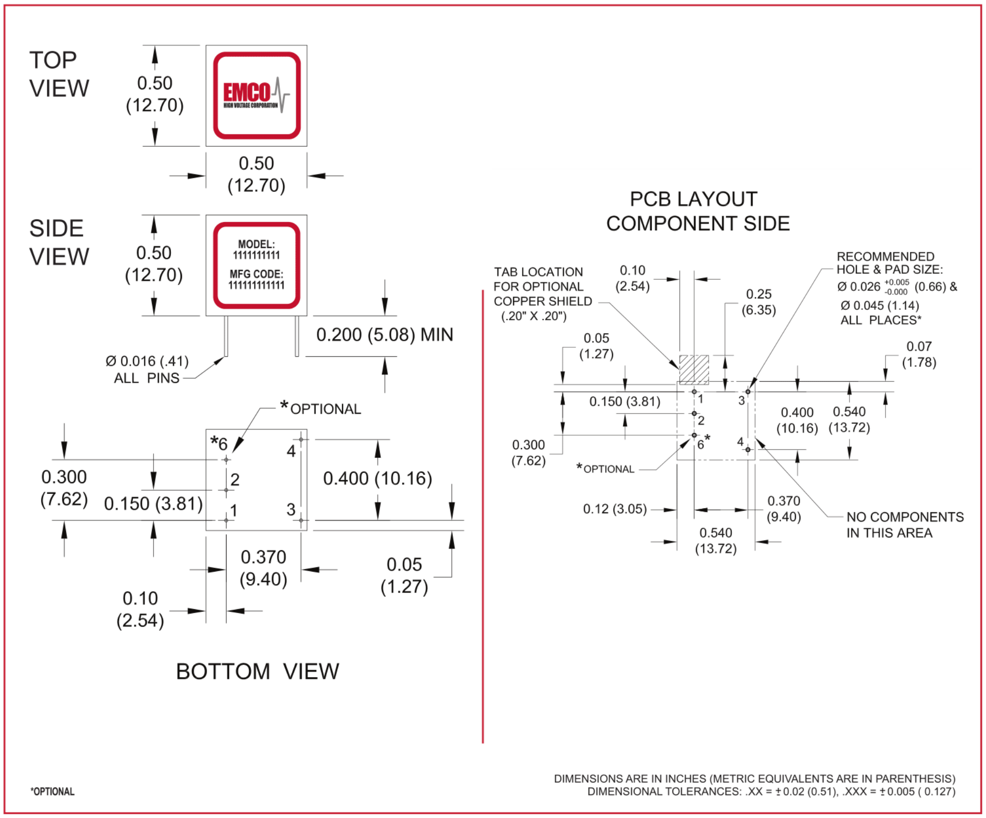
*OPTIONAL

DIMENSIONS ARE IN INCHES (METRIC EQUIVALENTS ARE IN PARENTHESIS)
DIMENSIONAL TOLERANCES: .XX = ±0.02 (0.51), .XXX = ±0.005 (0.127)

PARAMETER	VALUE
WEIGHT	0.15 OUNCES APPROX. (4.25 GRAMS)
VOLUME	0.125 CUBIC INCHES (2.05CM^3)
DIMENSIONS	0.50L (12.7) X 0.50W (12.7) 0.50H (12.7)

PIN #	100V TO 900V	1,000V TO 2,000V
1	INPUT (-)	INPUT (-)
2	INPUT (+)	INPUT (+)
3	OUTPUT (+)	HV OUTPUT
4	OUTPUT (-)	OUTPUT RETURN
5*	CENTER TAP	
6*	CONTROL PIN	

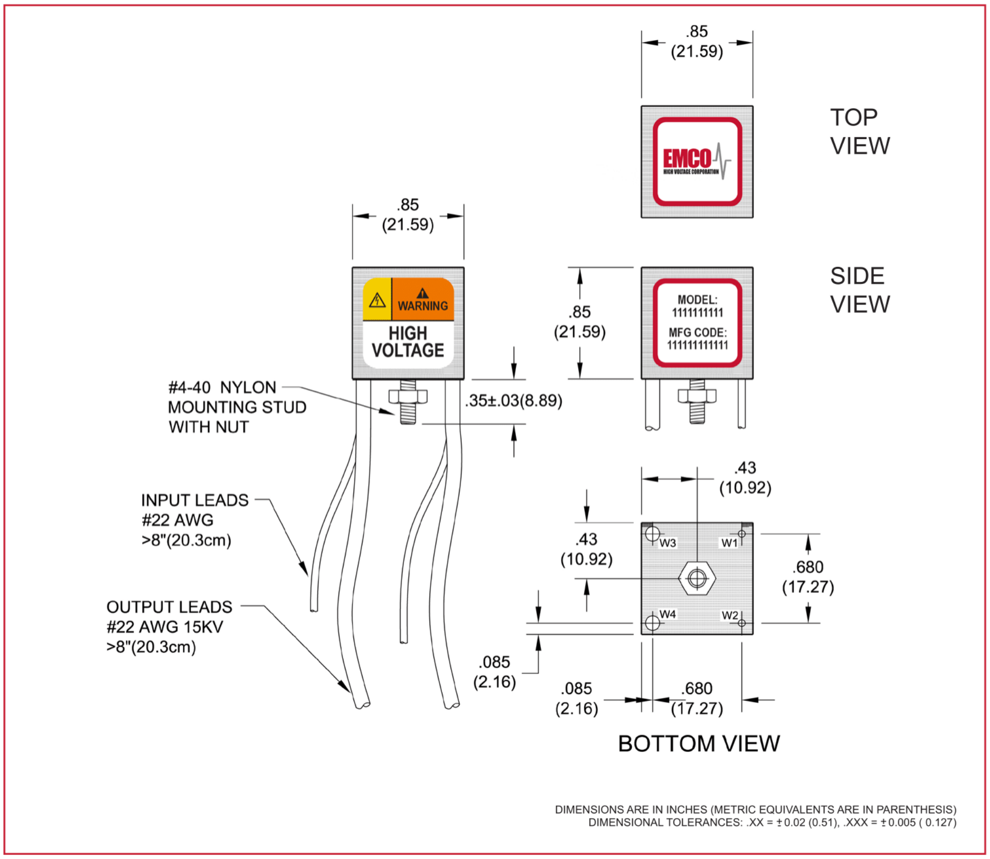
MECHANICAL SPECIFICATIONS (2,500V - 5,000V)



PARAMETER	VALUE
WEIGHT	0.15 OUNCES APPROX. (4.25 GRAMS)
VOLUME	0.125 CUBIC INCHES (2.05CM^3)
DIMENSIONS	0.50L (12.7) X 0.50W (12.7) 0.50H (12.7)

PIN #	FUNCTION
1	INPUT (-)
2	INPUT (+)
3	HV OUTPUT
4	HV RETURN
5*	
6*	CONTROL PIN

MECHANICAL SPECIFICATIONS (6,000V - 10,000V)

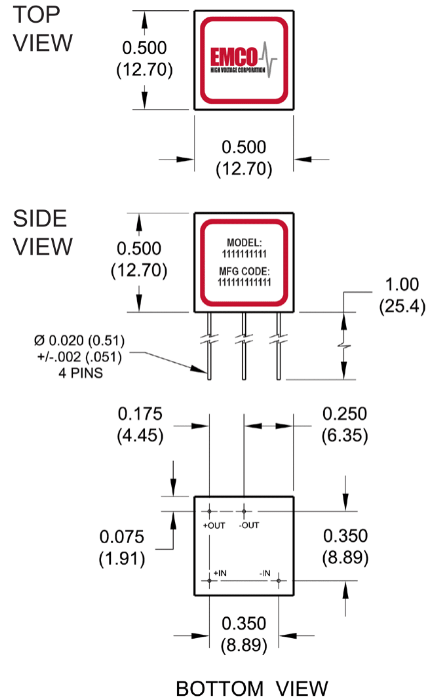


PARAMETER	VALUE
WEIGHT	1 OUNCE (28.3 GRAMS)
VOLUME	0.614 CU INCHES (10.06 CU CM)
DIMENSIONS	0.85L (21.59) X 0.85W (21.59) X 0.85H (21.59)

WIRE	COLOR	FUNCTION
1	RED	INPUT (+)
2	BLACK	INPUT (-)
3	BROWN	HV OUTPUT
4	VIOLET	HV RETURN

MECHANICAL SPECIFICATIONS, ALTERNATE PIN PATTERN (100V - 1,000V)

Not Recommended for New Designs

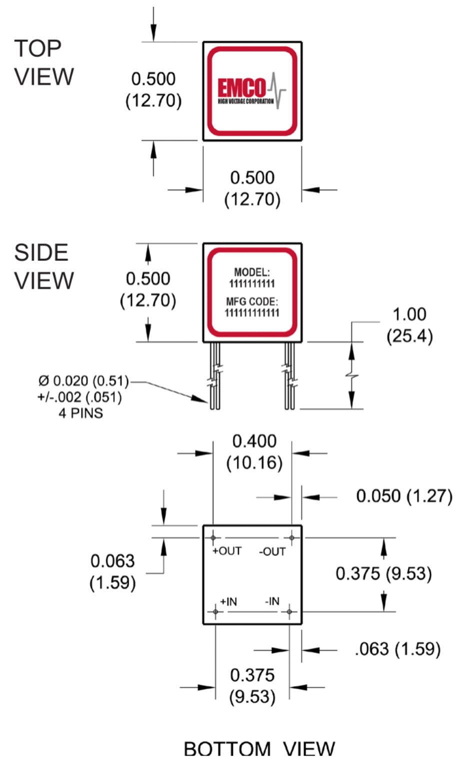


DIMENSIONS ARE IN INCHES (METRIC EQUIVALENTS ARE IN PARENTHESIS)
DIMENSIONAL TOLERANCES: .XX = ± 0.02 (0.51), .XXX = ± 0.005 (0.127)

PARAMETER	VALUE
WEIGHT	0.15 OUNCE (4.25 GRAMS)
VOLUME	0.125 CUBIC INCHES (2.05CM^3)
DIMENSIONS	0.50L (12.7) X 0.50W (12.7) 0.50H (12.7)

PIN #	FUNCTION
1	INPUT (-)
2	INPUT (+)
3	HV OUTPUT
4	HV RETURN

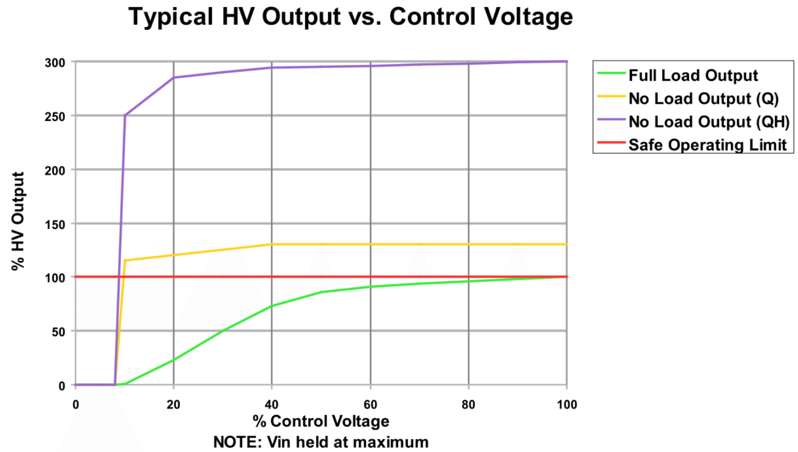
MECHANICAL SPECIFICATIONS, ALTERNATE PIN PATTERN (1,500V - 5,000V)

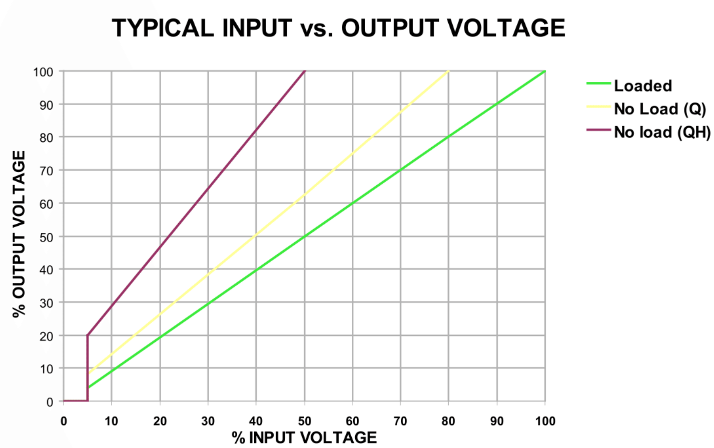


DIMENSIONS ARE IN INCHES (METRIC EQUIVALENTS ARE IN PARENTHESIS)
DIMENSIONAL TOLERANCES: .XX = ± 0.02 (0.51), .XXX = ± 0.005 (0.127)

PARAMETER	VALUE
WEIGHT	0.15 OUNCE (4.25 GRAMS)
VOLUME	0.125 CUBIC INCHES (2.05CM^3)
DIMENSIONS	0.5L (12.7) X 0.5W (12.7) 0.5H (12.7)

PIN #	FUNCTION
1	INPUT (-)
2	INPUT (+)
3	HV OUTPUT
4	HV RETURN


Typical HV Output vs. Control Voltage
% HV Output
300
250
200
150
100
50
0
0
20
40
60
80
100
% Control Voltage
NOTE: Vin held at maximum
Full Load Output
No Load Output (Q)
No Load Output (QH)
Safe Operating Limit


TYPICAL INPUT vs. OUTPUT VOLTAGE
% OUTPUT VOLTAGE
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
100
% INPUT VOLTAGE
Loaded
No Load (Q)
No load (QH)

OPTION CODES

ORDERING INFORMATION		ORDER CODE	AVAILABILITY
TYPE	0.5 WATT	Q	ALL MODELS
	1.25 WATT	QH	UP TO 5KV
	1.25 WATT (Alternate Pin Pattern)[4]	VA	UP TO 5KV
OUTPUT VOLTAGE	SEE TABLES		
POLARITY DESIGNATOR	POSITIVE OUTPUT	BLANK	
	NEGATIVE OUTPUT	N	
	BIPOLAR, CENTER TAP OPTION	CT	UP TO 900V
INPUT VOLTAGE	5 VDC	5	ALL MODELS
	12 VDC	12	UP TO 3kv
	15 VDC	15	UP TO 3kv
	24 VDC	24	UP TO 3kv
OPTIONS	CONTROL PIN	C	UP TO 5KV
	EXTENDED TEMP	T	UP TO 5KV, 0.5W
	ROHS	R	ALL MODELS
	External Copper Shield	S	ALL MODELS

HOW TO ORDER

PART NUMBER SELECTOR:

Model Number:

Q 10 N - 5 C T R S

Q, QH, VA Series
10 Output Voltage (See table...)
N Polarity Designator
S for Shield (optional)
R for RoHS (optional)
T for Extended Temperature
C for Control Pin (optional)
5 Input Voltage

EXAMPLE - **Q10N-5CTRS: Q** Series 0.5W, **1000** VDC, **N** negative, **5** VDC input, **C** for Control Pin, **T** for Extended Temperature, **R** with RoHS, **S** for Shield.

*Note:
1. At maximum rated output voltage
2. Output Voltage is load dependent. Under light or no-load conditions, reduce the Input Voltage so maximum rated Output Voltage is not exceeded.
3. Specifications are after 30 minute warm-up, full-load at 25ºC, unless otherwise noted.
4. Proper thermal management techniques are required to maintain safe case temperature at maximum power output.
5. Ripple specification for center-tapped units applies to the voltage between the positive and negative output terminals.
6. For Center tap output units [CT option], the negative output voltage with be 10% larger than the positive output voltage with respect to the center tap pin.

Updated: 01/26/15

HVM TECHNOLOGY
Innovative High Voltage Products

ECHV Series

Miniature Case Size (1.8"L x 1.0"W x 0.40"H) in a Low Profile
PCB Mount Configuration
High Impedance Programming Input
Low Quiescent Input Current
5V or 12V Input, Models up to 10kV @ 1W
Adjustable from 3% to Full Output
Low Ripple and EMI/RFI
Wide Operating Temperature Range
±1kV Input/Output Isolation

RoHS

Mechanical Characteristics

- **Size:** 1.8" x 1.0" x 0.40"
- **Weight:** 15 grams typical
- **Packaging:** Encapsulated in high performance epoxy

Environmental Characteristics

- **Operating Temp Range:** -55°C to +70°C
- **Storage Temp Range:** -55°C to +85°C

Description

The ECHV Series is an economical and versatile high voltage DC to DC converter perfectly suited for small, portable, high performance equipment requiring high voltage biasing. Designed for affordability and reliability, the ECHV Series is manufactured using all surface mount construction and tested using state-of-the-art automatic test equipment.

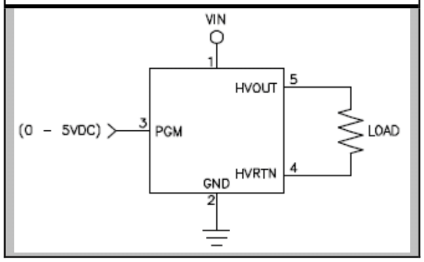
The ECHV Series includes a range of models with output voltages up to 10kV and input/output isolation of ± 1kV. Fully encapsulated in a compact (1.8"L x 1.0"W 0.40"H) package, the ECHV Series has easy-to-use features that enable the designer to quickly integrate high voltage into any design. A high impedance programming input makes the ECHV Series very easy to use.

HVM's proprietary resonant converter design minimizes quiescent current and operating noise while delivering maximum performance and reliability. A special feature of this power supply is its extremely low input current, making it ideal for battery powered applications.

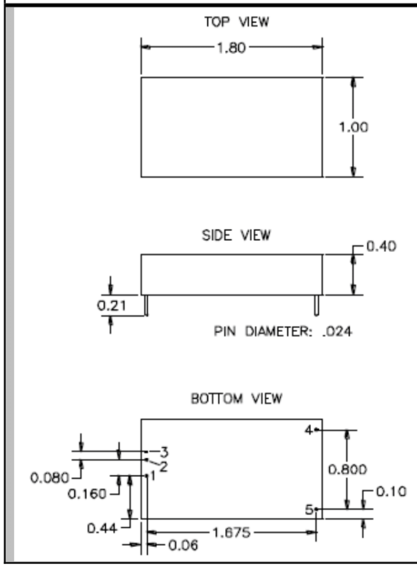
The device operates directly from 5V or 12V input and the output power rating is 1W. Output voltage is independent of input power voltage and is proportional to the programming voltage (0 to 5V produces 0 to full scale output) and features excellent linearity. The ECHV Series is designed for stable operation over a wide temperature range of -55°C to +70°C.

www.hvmtech.com

APPLICATION



MECHANICAL



PIN#	FUNCTION
1	Vin
2	GND
3	Program
4	HVRTN
5	HVOUT

Electrical Characteristics

Input Power Voltage (VIN): 5V or 12V ± 0.5V

Programming Voltage: 0 to 5VDC results in 0 to rated output; Note: regulation not guaranteed below 3% of full scale

Programming Input Impedance: >50kΩ

Output Tolerance at No Load: ± 2%

Input/Output Isolation: ± 1kV

Load Regulation: 20% (over entire load range)

Output Ripple: <0.1%

Oscillator Frequency: 45 kHz – 100 kHz

Efficiency: 60% typical at full load

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Model Selection Guide

Model	Input Voltage	Output Voltage	Maximum Output Load
ECHV0505	5V	0 to +500V	250kΩ
ECHV0505N	5V	0 to -500V	250kΩ
ECHV1205	12V	0 to +500V	250kΩ
ECHV1205N	12V	0 to -500V	250kΩ
ECHV0510	5V	0 to +1kV	1MΩ
ECHV0510N	5V	0 to -1kV	1MΩ
ECHV1210	12V	0 to +1kV	1MΩ
ECHV1210N	12V	0 to -1kV	1MΩ
ECHV0520	5V	0 to +2kV	4MΩ
ECHV0520N	5V	0 to -2kV	4MΩ
ECHV1220	12V	0 to +2kV	4MΩ
ECHV1220N	12V	0 to -2kV	4MΩ
ECHV0530	5V	0 to +3kV	9MΩ
ECHV0530N	5V	0 to -3kV	9MΩ
ECHV1230	12V	0 to +3kV	9MΩ
ECHV1230N	12V	0 to -3kV	9MΩ
ECHV0540	5V	0 to +4kV	16MΩ
ECHV0540N	5V	0 to -4kV	16MΩ
ECHV1240	12V	0 to +4kV	16MΩ
ECHV1240N	12V	0 to -4kV	16MΩ
ECHV0550	5V	0 to +5kV	25MΩ
ECHV0550N	5V	0 to -5kV	25MΩ
ECHV1250	12V	0 to +5kV	25MΩ
ECHV1250N	12V	0 to -5kV	25MΩ
ECHV0560	5V	0 to +6kV	36MΩ
ECHV0560N	5V	0 to -6kV	36MΩ
ECHV1260	12V	0 to +6kV	36MΩ
ECHV1260N	12V	0 to -6kV	36MΩ
ECHV0580	5V	0 to +8kV	64MΩ
ECHV0580N	5V	0 to -8kV	64MΩ
ECHV1280	12V	0 to +8kV	64MΩ
ECHV1280N	12V	0 to -8kV	64MΩ
ECHV05100	5V	0 to +10kV	100MΩ
ECHV05100N	5V	0 to -10kV	100MΩ
ECHV12100	12V	0 to +10kV	100MΩ
ECHV12100N	12V	0 to -10kV	100MΩ

Updated: 1/26/15

HVM TECHNOLOGY
Innovative High Voltage Products

SMHV Series

Models up to 10kV@1W
Sub-Miniature Case Size (.85”x.85”x.6”)
Adjustable, 0 to full output
Low Ripple, High Impedance,
Operating Temp (-55°C to +70°C)
DC/DC Converters

RoHS

Mechanical Characteristics

- **Weight:** 15 grams typical
- **Packaging:** Encapsulated in high performance epoxy
- **Case Materials:** Thermoset Plastic (Diallyl Phthalate) –Optional Metal shield Case Available

Environmental Characteristics

- **Operating Temp Range:** -55°C to +70°C
- **Storage Temp Range:** -55°C to +85°C

Description

The SMHV Series is a family of sub-miniature single-output, fully regulated DC to DC converters supplying up to 10kV @1W in 0.434 cubic inches (0.85” x 0.85” x 0.6”). These ultra-compact converters are ideal for applications requiring small size, high performance, and ease of use. HVM’s proprietary, ultra-compact resonant converter design minimizes quiescent current and operating noise while delivering maximum performance and reliability.

The devices operate directly from 5VDC ± 0.5VDC input. Output voltage is independent of input power voltage and is proportional to the programming voltage (0 to 5V produces 0 to full scale output) and features excellent linearity.

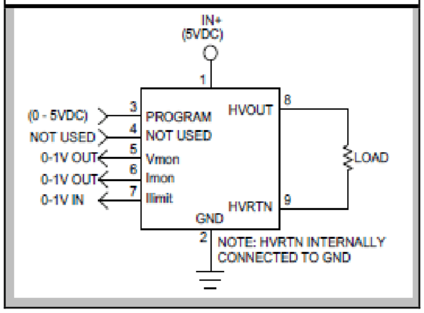
Voltage and current monitor outputs provide the user with operational information for maximum control.

The SMHV Series has additional features such as voltage and current monitor outputs, and current limit control input. The SMHV Series is very stable over a wide operating temperature range.

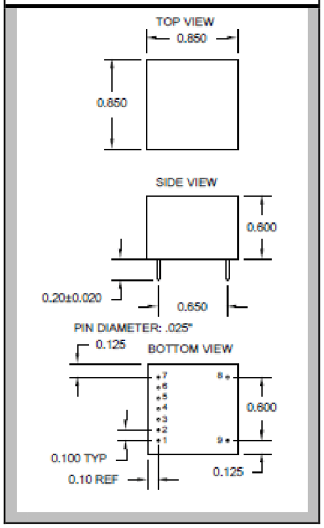
Available with alternate output voltages, consult sales for additional information.

www.hvmtech.com

APPLICATION



MECHANICAL



PIN#	FUNCTION	PIN#	FUNCTION
1	V in	6	Imonitor
2	GND	7	Ilimit
3	Program	8	HVOUT
4	Not Used	9	HVRTN
5	Vmonitor		

Electrical Characteristics

Input Power Voltage (V+):	**5V ± 10%**
Programming Voltage:	0 to 5VDC results in 0 to rated output
Programming Input Impedance:	10kΩ
Input Current Limit:	0 to 1VDC input results in a current load limit to 0 to 100% of rated current **Note: To disable current limit, connect Ilimit pin to 5V.**
Output Tolerance at No Load:	± 5%
Output Voltage Monitor:	0 to 1VDC output, corresponding to 0 to 100% of rated output
Output Current Monitor:	0 to 1VDC output, corresponding to 0 to 100% of rated current
Input-Output Isolation:	Not isolated, HVRTN internally connected to GND
Load Regulation:	0.2% (over entire load range)
Line Regulation:	0.01%
Output Ripple:	<.01%
Oscillator Frequency:	45 kHz – 80 kHz
Efficiency:	60% typical at full load

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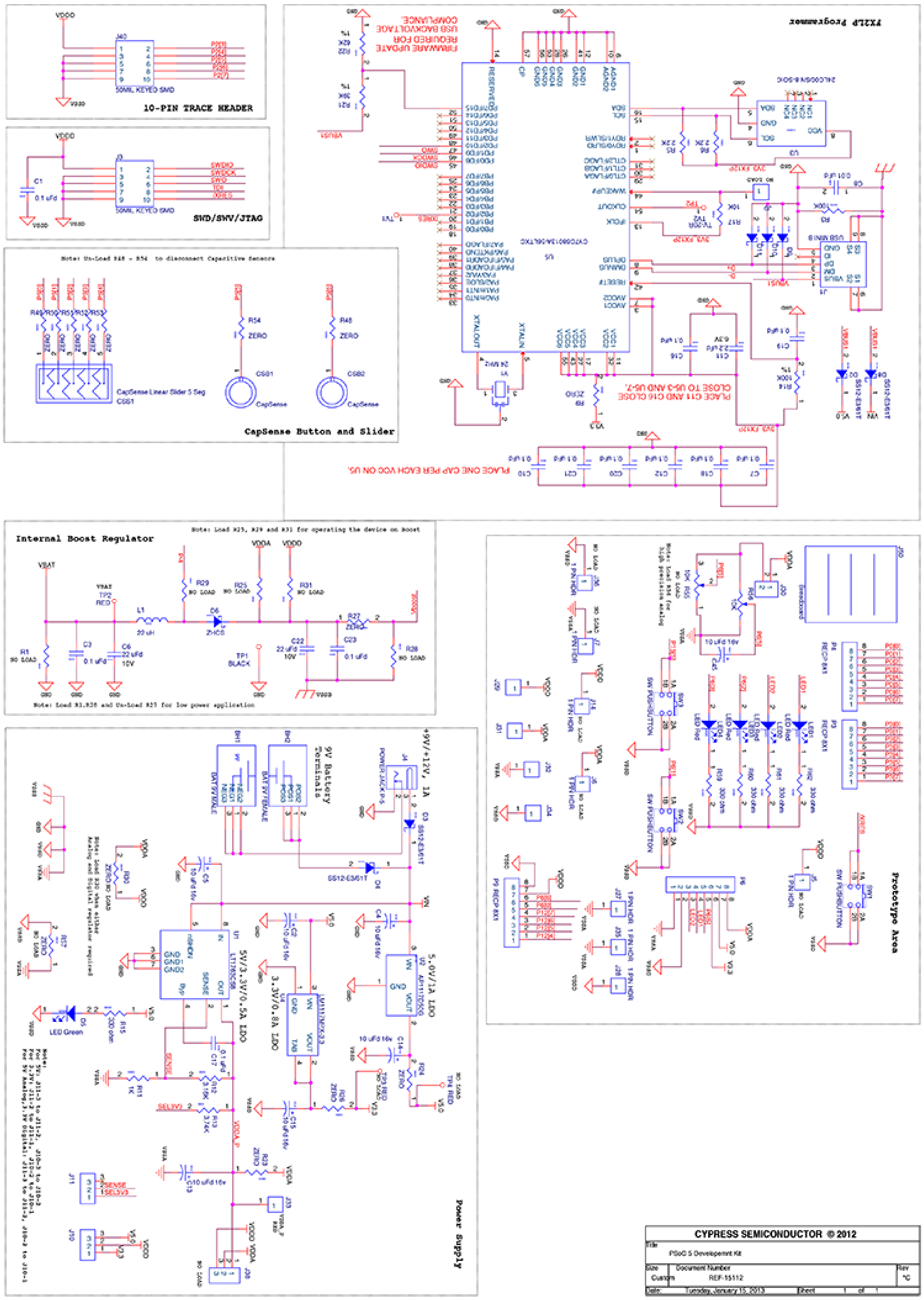
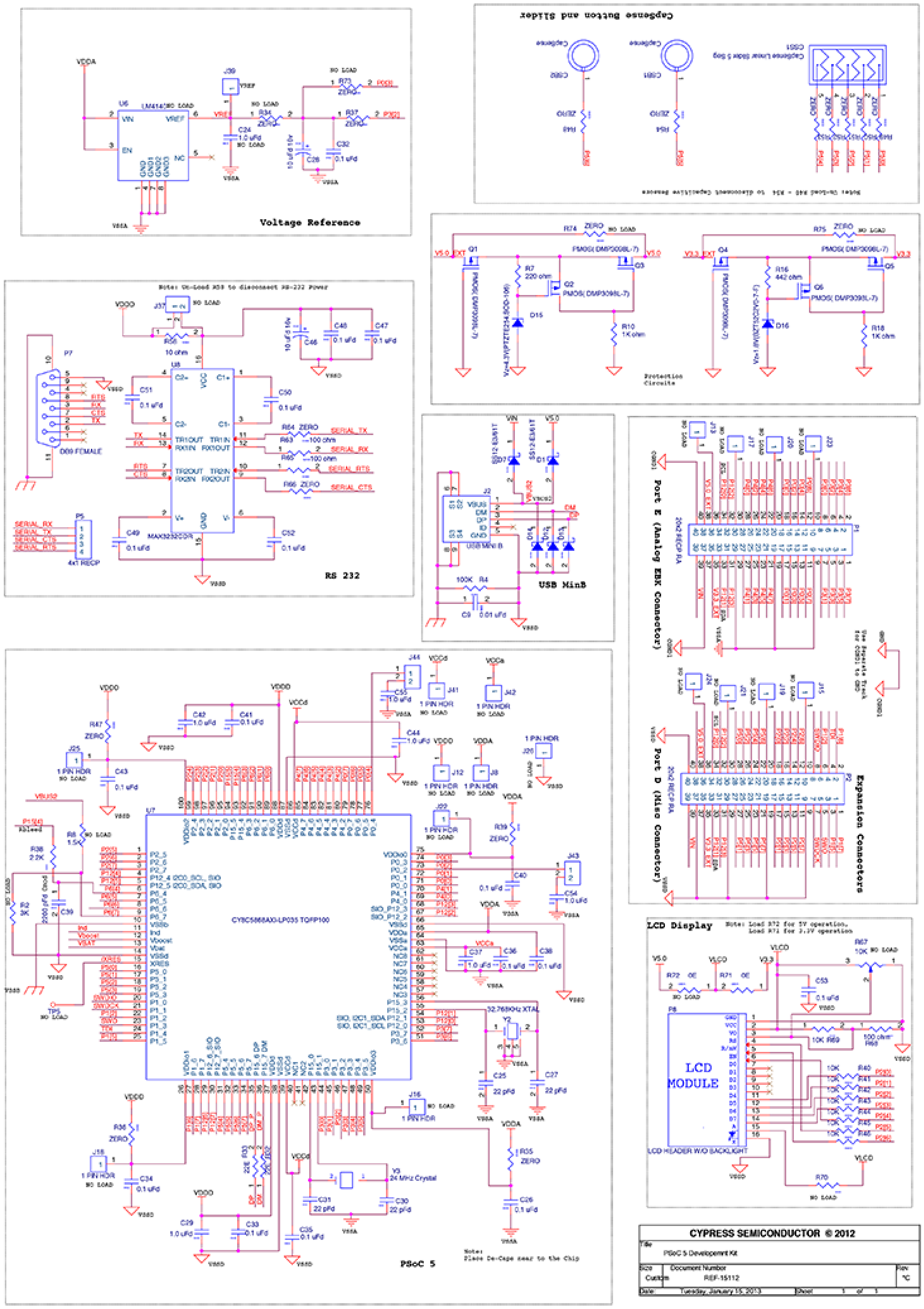
Model Selection Guide

MODEL	Input Voltage	Output Voltage	MAX Output Current	Input Current No Load	Input Current Max Load
SMHV0505	5V	0 to +500V	2mA	<35mA	<350mA
SMHV0505N	5V	0 to -500V	2mA	<35mA	<350mA
SMHV0510	5V	0 to +1kV	1mA	<35mA	<350mA
SMHV0510N	5V	0 to -1kV	1mA	<35mA	<350mA
SMHV0520	5V	0 to +2kV	500µA	<35mA	<350mA
SMHV0520N	5V	0 to -2kV	500µA	<35mA	<350mA
SMHV0530	5V	0 to +3kV	333µA	<35mA	<350mA
SMHV0530N	5V	0 to -3kV	333µA	<35mA	<350mA
SMHV0540	5V	0 to +4kV	250µA	<35mA	<350mA
SMHV0540N	5V	0 to -4kV	250µA	<35mA	<350mA
SMHV0550	5V	0 to +5kV	200µA	<35mA	<350mA
SMHV0550N	5v	0 to -5kV	200µA	<35mA	<350mA
SMHV0560	5V	0 to +6kV	167µA	<35mA	<350mA
SMHV0560N	5V	0 to -6kV	167µA	<35mA	<350mA
SMHV0580	5V	0 to +8kV	125µA	<35mA	<350mA
SMHV0580N	5V	0 to -8kV	125µA	<35mA	<350mA
SMHV05100	5V	0 to +10kV	100µA	<35mA	<350mA
SMHV05100N	5V	0 to -10kV	100µA	<35mA	<350mA

Appendix D

Development Kit Schematic


10-PIN TRACE HEADER
SWD/SWV/JTAG
CapSense Button and Slider
Internal Boost Regulator
CYPRESS SEMICONDUCTOR © 2012
PSoC 5 Development Kit
REF-15112


Voltage Reference
Capsense Button and Slider
Protection Circuits
RS 232
USB MinB
Port E (Analog EBK Connector)
Port D (Misc Connector)
Expansion Connectors
PSoC 5
LCD Display
LCD MODULE
CY8C5868AXI-LP035 TQFP100
CYPRESS SEMICONDUCTOR © 2012
PSoC 5 Development Kit
REF-15112
Tuesday, January 15, 2013

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