16 Channel Brain Tissue Stimulator

BME 301
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I. Abstract

The pathways of brain circuitry can be studied by delivering current impulses to brain tissue and observing the tissue response. The goal of this project is to develop a current source to be used for *in vitro* stimulation of rat brain tissue. The current source must deliver independently controlled currents to 16 separate electrodes on a 16 microelectrode array. In addition, the currents must be controllable via TTL computer logic and have a short response time to the initial signal. The design described in this report uses DC/DC converters to supply a constant isolated voltage to 16 voltage-to-current converters (VIC) which will each contain a potentiometer to adjust the amplitude of current flow. In addition, voltage to each channel will be turned on and off using TTL impulses from a computer program which will result in a square wave current impulse output from the VIC. This design will successfully deliver independently controlled currents to each of the 16 electrodes in the microelectrode array.

II. Problem Statement

In order to more realistically stimulate brain tissue, a current source is needed which is capable of delivering 0 to 1 mA of current to 16 electrodes in a microelectrode array. The amplitude and impulse timing of each current must be independently controlled. The impulse timing must be controllable through parallel computer logic and the device must be isolated from 60 Hz noise.

III. Background Information

i. Brain Tissue Stimulation

The mammalian brain is a very complex organ whose mechanism of operation is still largely unknown. It is responsible for innumerable functions varying from regulation of body temperature to food foraging to complex emotions and thought patterns. Further investigation of the brain is necessary in order to understand how and why living beings behave as they do and what happens when this organ malfunctions. One important aspect of brain physiology that is being investigated is the brain's ability to relay information via electrical circuits. Electrical stimulation of brain tissue is the predominant method of studying these circuits.

The component of brain tissue that relays information is composed of cells called neurons. Neurons are long cells which pass electrical current from one end to the other. Neurons are connected end-to-end by synapses. When current (called an action potential in a neuron) travels down a neuron and reaches the synapse where the cell releases chemicals called neurotransmitters (depicted in Figure 1). These neurotransmitters either stimulate or inhibit the beginning of another action potential in the next neuron [15]. Such interconnections of millions of neurons within the brain comprise a complex electrical circuit which gives rise to the many functions of the nervous system.

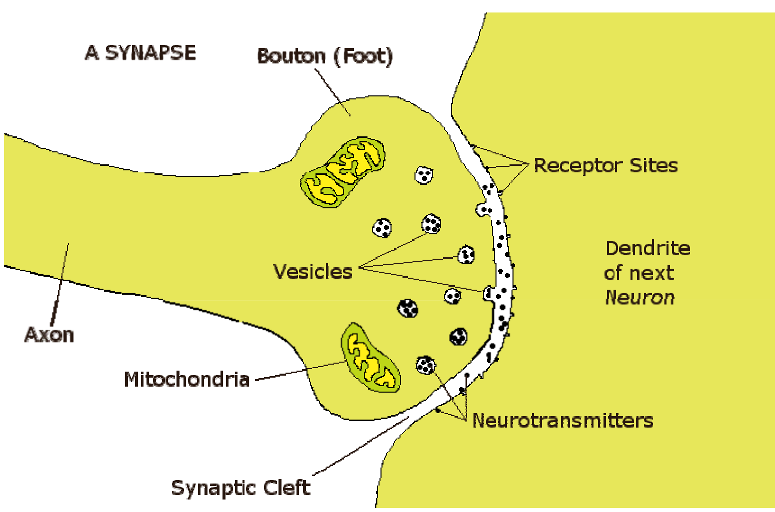

Figure 1: An chemical synapse in the brain [2].

This circuitry can be artificially stimulated in laboratory experiments in order to study the workings of the neurons and synapses. An electrode is placed on the brain tissue and delivers a current to the neurons. The current depolarizes the neurons and begins action potentials which may then spread to other neurons via synaptic connections. This basic principle is currently used to help treat tremors in patients suffering from Parkinson's disease. An electrode is placed in the thalamus of the brain tissue and delivers a current impulse which inhibits the portion of the brain causing the tremors [6]. In addition to clinical treatments, brain tissue stimulation is being used in many lab experiments to study *in vivo* and *in vitro* brain function.

ii. Client Information

Our client is Dr. Mathew Jones of the Department of Physiology. Dr. Jones studies the effect of *in vitro* stimulation of rat brain tissue. His research focuses primarily on the role that the inhibitory chemical messenger GABA plays on the timing and pathway of electrical impulses through the neural circuitry of brain tissue. In order to study these effects, he must apply a current impulse to a slice of rat brain tissue and observe the tissue's response [7].

Presently, he is using a single electrode to deliver a large impulse to the entire tissue. This does not realistically model how the brain tissue really functions because, in live brain tissue, many neurons may be functioning at one time and the signal transmission intensity may vary at each synapse. For this reason, he wishes to place multiple electrodes at several different locations within the tissue and then independently control the amplitude and timing of the current through each electrode. This requires a current source that can supply current to each of the 16 electrodes so that the electrodes can be activated independently of one another. This will allow for non-synchronous stimulation of individual or small groups of neurons.

Products that meet Dr. Jones' needs are commercially available; however, these are all much more sophisticated than the client desires. These devices are generally intended for *in vivo* studies and therefore, contain complex functions to prevent tissue damage. In addition, they often can produce various waveform impulses and can record the tissue response [14]. Dr. Jones only wishes to stimulate the tissue with positive square wave currents and does not need all of the excess expensive functions that accompany the available systems.

iii. Client Design Requirements

Our task is to develop a device to drive a current stimulus of up to 1 mA across each of 16 channels of a microelectrode array that Dr. Jones will be using in his experiments. The microelectrode array has a very high impedance—somewhere on the order of 1 to 3 MOhms—and our device must be able to successfully drive the current waveform regardless of such high load resistance. Secondly, each of the channels must have an independent gain adjustment so the amplitude of the current waveform can be adjusted on each channel between 0 and 1 mA in increments of 0.01 mA. The current waveform square pulse needs to be able to be adjusted between 25 and 200 microseconds, meaning that our device must have a very high bandwidth. The device must be completely isolated from 60 Hz noise that comes from using an alternating current power source. This is because the current stimuli being supplied on each electrode are very small, and any noise could disrupt the experiments. Finally, the final design should be enclosed in a rack-mount chassis that can easily be integrated in the existing laboratory setup. The enclosure should have a chassis ground built in that is isolated from in the internal circuitry.

IV. Components of the Design

We found it beneficial to split the design of the device into three components: Power supply and isolation, control of the amplitude of the current waveform, and the method of current waveform generation. Once the components were split, we came up with several alternative designs for each component.

i. Power Supply and Isolation

Alternative 1: Rechargeable Battery

The first, and definitely simpler, method that we considered to supply and isolate the power for the device is to use a large rechargeable battery. This is very similar to the system that Dr. Jones presently has in place. When a stimulus is going to be supplied, the device is simply disconnected from wall (AC) power, and left to run solely on battery (DC) power, free of any significant noise.

While using a battery would be simpler, it has several significant drawbacks. First of all, rechargeable batteries can be expensive, and non-rechargeable batteries would have to be replaced often. Secondly, the battery supply unit would be fairly bulky, as many batteries (or several very large batteries) would be needed to supply the current across such large load impedances.

Alternative 2: DC/DC Converters

The other method that we considered to both supply the device with power and to isolate the power from AC noise is to use a bank of DC/DC converters. DC/DC converters work by taking a DC voltage in, and then outputting a DC voltage, typically at a different voltage level than the input. They can be configured to isolate power by including opposing transformers in them (Figure 2). This type of DC/DC converter configuration is called a “Flyback Converter.” The converter takes a DC input, and transforms it first to AC power, and then back to DC power to be output. This double conversion effectively removes any noise in the original DC signal [11].

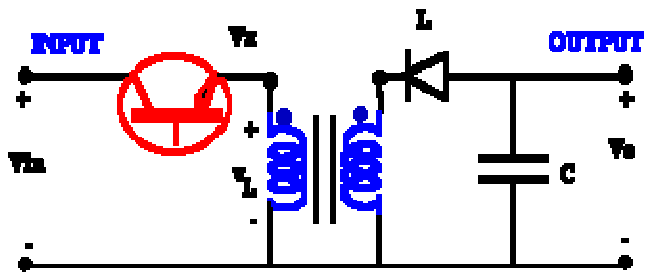

Figure 2: A schematic of a DC/DC converter that will isolate the signal [11]

In addition to power isolation, using DC/DC converters carries with it an added benefit. DC/DC converters can be configured using inductors to step up the voltage. Thus, using a bank of the converters as shown in Figure 3 will allow us to increase our supply voltage from an initial 12 volts, to somewhere in the area of 200 volts [3]. The high voltage is necessary to ensure that we can successfully supply up to 1 mA of current regardless of the load impedance.

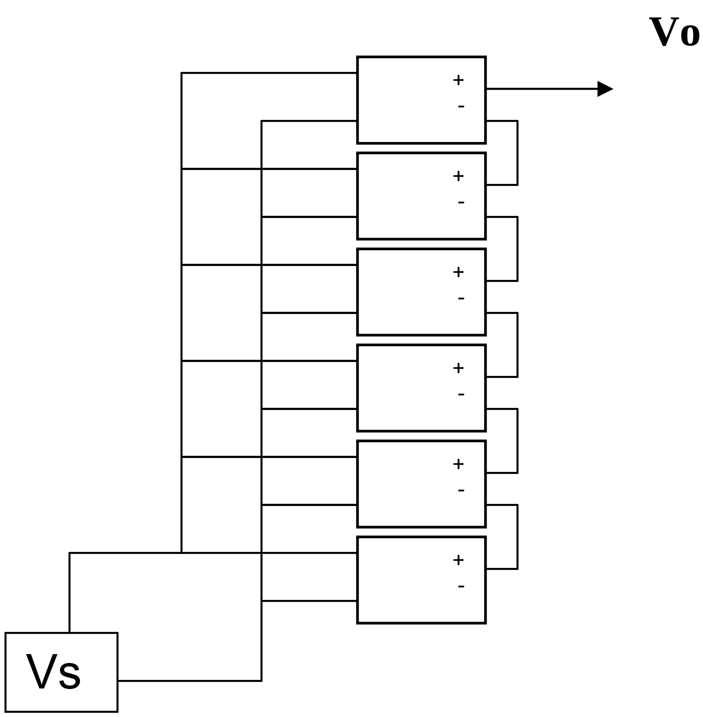

Figure 3: A bank of DC/DC converters in series to amplify the voltage supplied

After evaluating both alternatives for supplying and isolating power to the device, we decided to move forward using DC/DC converters. DC/DC converters will not only provide a more elegant solution in that they allow us to isolate the power and amplify the voltage at once, but they avoid bulky and expensive batteries that would have to be replaced often.

ii. Current Control:

There are two aspects of current control that we need to deal with. According to our client's specifications we need to have a square pulse that is simply either "on" or "off." Therefore one aspect of controlling the current requires controlling when the pulse is "on" and for how long it should remain "on." The second aspect of current control involves controlling the amplitude of the current waveform, or the magnitude of the stimulus supplied. As stated earlier our client would like to be able to adjust the current amplitude on each channel independently.

a. Pulse Duration and Amplitude Control:

Using Potentiometers & Transistors

Dr. Jones will be using a 25DIN parallel port from an Apple computer to send the control signal for all 16 channels. The signal will pass through an analog-digital converter and then output through another 25DIN digital port. The client currently uses a Digidata 1322A converter. The output levels for this device are CMOS level TTL logic. CMOS level output logic is slightly different in that range of 0-0.05V is '0' or off, and the range from 4.95-5.0 v is '1' or on [1]. The digital outputs specify an output at 4mA at these voltages. The client would like to control these outputs to '1' when the pulse is on and '0' when the pulse is off. We have two circuit designs that will use this pulse and modulate a V_{out}. The modulated V_{out} will be converted to a corresponding current via a voltage-to-current converter (VIC).

Alternative 1:

The first circuit uses a MOSFET to gate the circuit on/off, Figure 4. When the TTL pulse is 5V the transistor will turn on. This effectively allows current flow and a voltage to be produced at Vo. This voltage can be modulated and

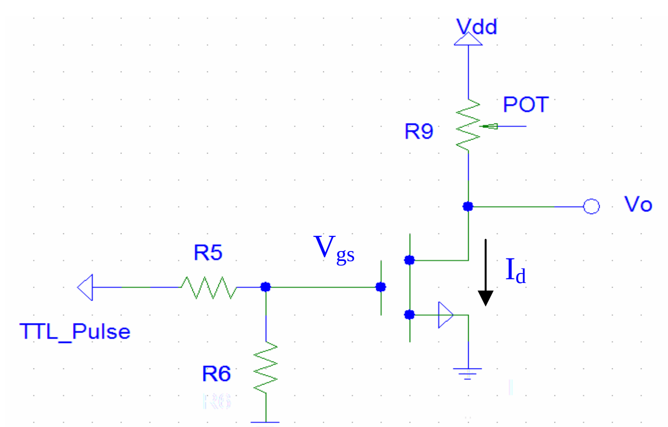

Figure 4: The transistor will be gated on when the TTL level exceeds the threshold voltage Vt of the transistor. Vo can be modulated by the potentiometer R9.

seen by the VIC. The circuit is governed by the following equations:

Eq1: $$Id = \frac{1}{2}\frac{Kn\,W(Vgs - Vt)^2}{L}$$

Eq2: $$Vo = Vdd - IdR9$$

Where Kn, W, L and Vt are all properties of the transistor. As one can see, Vgs will remain constant and therefore a constant current will pass through the transistor. Modulating the resistance at R9 will change Vo accordingly for the VIC.

This solution is relatively simple and has several important advantages. This alternative presents the largest advantage in terms of signal resolution. As noted above the 'on' voltage for CMOS varies between 4.95 and 5.00v. This means Vgs could vary by +/- .025v if designed to be at 4.975v. The change in current with this variation is much less because Vgs exists in the squared term for Id, which results in +/- 0.625mV. In addition, the voltage change at Vo with respect to changing R9 has a linear response which is not the case with alternative 2. Also, Vgs can be controlled by adjusting the values of R5 and R6. This allows control of the current passing through the circuit. As Vdd does not appear anywhere in the equation governing the current flow through the transistor, having multiple channels operating simultaneously will not change Vo.

Alternative 2:

The second alternative would be to use the CMOS TTL pulse as the voltage source and vary a Vo by potentiometer directly, Figure 5. When 'on' the TTL pulse will be between 4.95-5.00 V. Vo can be varied by the potentiometer R11. Vo is governed by the Following equations:

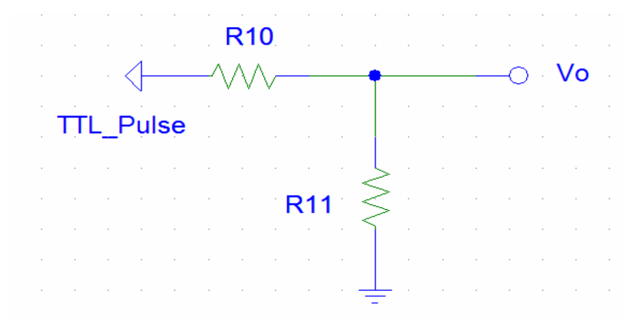

Figure 5: Alternative circuit design 2. Vo can be varied by varying the potentiometer R11.

Eq3: $$Vo = \frac{Vttl\ R11}{R11 + R10}$$

This solution is much simpler then the first alternative however, there are many disadvantages. First, the Vo response to a changing R11 will not be linear. Second, the +/- 0.025 V that is possible from the TTL pulse will not be reduced at all in Vo.

b. Pulse Amplitude VIC*:*

Based on Vo from one of the alternative design circuits above the VIC will output a corresponding current. This is based on the Transconductance, g_m, of the VIC. The equations governing the VIC seen in figure 6 are below:

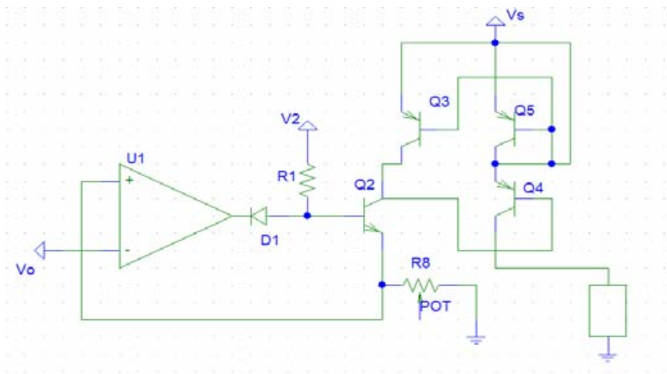

Figure 6: Example of a simplified VIC. The voltage Vo will appear across R5 and this modulates gm. [8]

Eq4: $$\frac{Il}{Vo} = \frac{0.99}{R8}$$

From Eq. 4 it can be seen that an additional method of varying current can be to simply vary R8 and provide a constant Vo [8]. However, this is not advisable due to the large variation required for R8 to achieve an output current range of 0-1mA. Transconductance is defined as Io/Vin so the value in equation 4 is essentially the transconductance. The value 0.99 is derived from the transistors properties and can be selected.

Digital Pulse and Amplitude Control:

It may be possible to control the operations above entirely with the PC. This is advantageous for increased output resolution and versatility in programming. The client has one available analog output that has a 16 bit resolution over the range of +/- 10v. This is sufficient to control one channel at a time but not all 16 simultaneously. It may be possible to use a microcontroller to record and set current amplitudes for the various channels. However, the code for this operation may be somewhat complex. In addition the design will still require much of the circuitry described above to convert voltage values to current values. We have decided to pursue the earlier described method at this time, and leave digital pulse and amplitude control as a potential later addition.

V. Proceeding from Midsemester:

i. Final Design:

Due to the fact that the problem statement for this project was very specific, there were limited options for design alternatives of the entire system. Despite this limitation, it was possible to break the project into its components and choose the best alternative for each. The first of these alternatives is regarding the form and amount of isolation needed in the device, either battery power or DC/DC converters. DC/DC converters will be implemented in the final design rather than batteries because they are much easier to work with and offer some distinct advantages. Converters isolate the device from 60 Hz noise and can be used to amplify the voltage. An amplified voltage will be needed to guarantee the current amplitude over the high impedance micro-electrode array. Initially, optical isolation of the TTL pulse from the computer was a concern, but further analysis deemed it unnecessary.

Current control and pulse control were the other two aspects of the design that allowed for variation. The current will be produced by a transconductance amplifier (also known as a voltage to current converter or VIC). Since commercially available voltage to current converters do not meet the criteria of this project, the VIC will be constructed by hand. Constructing our own VIC allows us to use transistor and resistor combinations which meet the specifications of the design. Altering the combination of transistors and resistors will allow us to change the bandwidth and transconductance range. The voltage input to the VIC will be varied using a standard potentiometer, and it will be gated on and off by a transistor using the TTL pulse. The pulse will ultimately be controlled by a computer program. In summary, the VIC will be powered by a bank of DC/DC converters and turned on and off via TTL pulses from a computer, thus converting the voltage to a current.

ii. Future Work:

The remainder of the semester will be focused on the completion of a fully functional prototype. However, before creating an entire device ourselves, we are going to continue searching for commercially sold components such as the Analog Devices 1B22 that will do the voltage to current conversion and isolation simultaneously. We will also look for commercial voltage to current converters that meet the design requirements for input and output ranges as well as with bandwidth specifications. Also, we will do experimental testing on the sample voltage to current converters received from Texas Instruments to test our design for the proposed current gating component.

Initially, the most important task is to complete a working diagram of the final design concept. Once this is constructed the team can begin to work as individuals or part of smaller teams to construct each component of a single channel stimulator. We will test the channel at multiple resistances to ensure accurate readings and a high resolution. If the single channel is non-functional or not completely in accordance with our design specifications, modifications will be made until a design is working for a single channel.

Once a channel is constructed and deemed functional we can begin to construct the rest of the channels. Testing will again be important once all the channels are correctly connected. Again, we will use a computer program (likely LabView) to simulate the settings with which the device will actually be used. After the device has passed this inspection, we can begin to concentrate on the aesthetics of the device. The device will be enclosed in a rack-mount chassis to fit into Dr. Jones' laboratory setting.

iii. Potential Problems:

Constructing our own voltage to current converter and pulse control system, and doing testing could potentially pose a problem regarding time limitations. However, if everything continues smoothly and the initial channel works as planned the construction of subsequent channels would be much faster. Thus, time could be an issue based on the functionality of the initial channel design. The only other problem that could be a potential difficulty is finding all the correct parts for the design while keeping the cost as economical as possible.

VI. Conclusion:

This project's goal is to design a multichannel brain tissue stimulator device. We are currently at the midpoint of the semester, and have a viable solution to move forward with. The remainder of the semester will be devoted to prototype construction and testing, and we are on track to deliver a working prototype. If the project continues smoothly and we do not encounter unexpected obstacles, the proposed design should result in a device that meets the specifications set forth by the client.

Appendix A: Product Design Specification (PDS)

Multichannel Brain Tissue Stimulator Project – March 2, 2006
Team Members - Roles

- Marty Grasse - Team Leader
- Erik Yusko – Communications
- Danielle Ebben – BSAC
- Tony Wampole – BWIG

Function
In order to stimulate neurons in a more realistic manner, a controller device is needed to independently control current on 16 electrodes in a multiple-electrode array. The device must use parallel logic from a computer to control the current. The device must be isolated from electrical noise so the measurements are accurate.

Client Requirements

- The device should take a signal from a 16-bit analog to digital converter using a 25-pin parallel connection.
- As the parallel logic data bits are turned on and off, current on the corresponding electrode should be turned on and off. There should be very small lag time.
- The device must be isolated; electrical noise (60 Hz) must be minimized.
- There should be an independent gain adjustment for each channel; the current available on each channel should be adjustable between 0.1 to 10 mA.
- When the data bit is turned on, the corresponding electrode should get a square pulse of current with a very fast rise time. When the data bit is turned off, the current should stop almost immediately.
- The square pulse should have a time length of 25 to 200 microseconds, controlled with the computer.
- The impedance of the electrodes is between 0.2 and 3 MOhms on each channel.

Design Requirements

1. **Physical and Operational Characteristics**
    - **a.** *Performance requirements:* See client requirements.
    - **b.** *Safety*: As with any device using electricity, the risk of electrical shock is always present. However, in our case this risk is especially great because we will be working with very high voltages and supplying direct current to electrodes. The finished device needs to be fully enclosed to prevent accidental shock, and the connection to the electrodes should be secure. The device should use several fuses to ensure that electrocution does not occur.

c. *Accuracy and Reliability*: Each of the 16 channels must be capable of consistently producing the current desired by the operator. The operator may choose from a series of current options which vary by 0.1 mA increments from 0.1 mA to 10 mA. Therefore, the device should supply a current that is accurate to within 0.01mA of the set current.

d. *Life in Service:* Although the device is unlikely to be used in such a manner, each channel must be able to produce a steady current for several hours at a time. In addition, the device must be able to withstand daily use for a minimum of 10 years.

e. *Shelf Life:* If stored in a dry, clean area of a moderate temperature, the device may be stored for many years without causing damage. If batteries are used as a power source, they should be removed before storage for long periods of time and replaced when the device is returned to operation.

f. *Operating Environment:* The device will not be subjected to very strenuous conditions. It will be kept in a dry, room temperature, laboratory setting and will not often be moved from one place to another. It should be kept clean and as dust free as possible to avoid interference with the circuitry. Only the electrode will be subjected to fluids and organic material and therefore may need to be replaced periodically.

g. *Ergonomics:* The device should be designed such that it is as easy as possible to operate. Any dials and buttons should be clearly labeled in a font that is easy to read and should require minimal force to adjust.

h. *Size:* The prototype should be easily contained in a laboratory setting. Thus, the approximate size for the prototype should be under the dimensions of 2 ft by 2 ft by 1 ft.

i. *Weight:* Prototype weight should be under 40 pounds allowing for relatively easy movement throughout the lab, and general transportation.

j. *Materials:* The materials used in the device will mostly be electrical components. The outer portion of the device that houses the circuitry will likely be made of a low quality plastic that will provide the inner workings with some resistance to normal lab accidents such as spills and slight impact forces.

k. *Aesthetics, Appearance, and Finish:* While the appearance of the device is relatively unimportant, it would be preferable to have the finish of the prototype match similar finishes on other devices used in the lab for aesthetics.

2. Production Characteristics

a. *Quantity:* A single prototype is expected. If this prototype is effective, more devices may be constructed.

b. *Target Product Cost:* The target price for the product has not been determined. The value will likely depend upon availability of circuitry items and the overall design.

3. Miscellaneous

a. *Standards and Specifications:* As the research is preformed in vitro minimal guidelines and restrictions apply. However, because samples are obtained using sacrificed rodents animal research ethics and restrictions apply. Federal Restrictions:

Very general guides:
- USDA-Animal Welfare Act
- U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training

More specific guidelines:
- National Research Council publishes the Guide for the Care and Use of Laboratory Animals
- AAALAC (American Association for Accreditation of Laboratory Animal Care) accredits institutional compliance with the Guide

b. *Customer:* The customer had some specific requests that are also common similar commercially available stimulus generators:

i. The device should take standard TTL signals from a 25DIN connection as the signal input.
ii. Current should be in an “On” or “Off” position with a very small rise time (~10 μs).
iii. Stimulus must have all 60Hz noise removed. It was suggested to do this by separating the supply voltage from a land line voltage via batteries or DC-DC converters.
iv. Independent current amplitude control (exact current range has yet to be determined)
v. The length of the square pulse should be able to hold 25-200 μs

c. *Patient-related Concerns:* This stimulus generator will be used specifically on mice brain tissue segments *in vitro*. As a result typical safety and comfort concerns are most likely negligible. However, the generator should be designed with the user in mind in that, their will likely be researchers and expensive equipment (microscopes, computers, etc.) in proximity of the generator and electrodes. Care should be taken to prevent shock to these researchers and equipment.

d. *Competition:* There are various commercial variations capable of creating the stimulus our client requires. However, all commercial variations are capable of much more then a simple “on”, “off’ pulse and this increases their cost significantly. In addition many commercial products are designed to operate *invivo* which requires additional circuit control to prevent electro-metal plating. Commercial stimulus generators also are usually capable of recording in addition to stimulating. The excessive amount of hardware and capabilities leads to a cost that places most stimulus generators out of reach for the common research laboratories. Two stimulus generators can be found:

http://www.a-msystems.com/physiology/Instruments/Model3600/default.aspx

http://www.alascience.com/products/mcs_stg2000.html

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