The Development of Electroconvulsive Device for Anti-Convulsion Drug Trials

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Abstract. A Low cost electroconvulsive device is developed to evoke artificial convulsions in mice for anti-convulsion drug trials. The device is expected to consume not more than 70 Watts of electric power supply and to produce single burst of pulses of electric voltage or current through its corneal electrodes when its foot pedal is pressed. The output specifications are 0.1 to 1 second of burst duration, 10 to 100 Hertz of pulse frequency, 0.5 to 20 milliseconds of pulse width and 0 to 200 Volts or milliamperes of amplitude of electric voltage or current. The electroconvulsive device is built from several blocks of electronic circuits which exploit the features of popular and low cost 555 timer and low offset OP07 op-amp Integrated circuits. The experiments show that the device has met the specifications and been able to evoke artificial convulsions in 20 to 22 grams of mice at 0.2 seconds of burst duration, 100 Hertz of pulse frequency, 0.5 milliseconds of pulse-width and 25 to 35 milliamperes of amplitude of electric current of output signal's parameters.

Keywords: *Anti-convulsion, artificial convulsion, electroconvulsive, evoking artificial convulsion.*

1 Introduction

Epilepsy is a chronic disorder of the brain that affects people in every country of the world. It is characterized by recurrent seizures - which are physical reactions to sudden, usually brief, excessive electrical discharges in a group of brain cells [1]. Epilepsy increases a person's risk of premature death by about two to three times compared to the general population. Around 50 million people in the world have epilepsy [1]. Close to 90% of epilepsy cases worldwide are found in developing regions [1].

Many drugs are used to treat epilepsy, generally referred to as anticonvulsants [2]. The older and well tested anticonvulsants include phenobarbital and primidone, neither of which are in common use today because of side effects. Newer anticonvulsants, such as felbamate, gabapentin, lamotrigine, tiagabine and topiramate, are technically marketed in the United States as "adjunctive anticonvulsants" because they are used in combination with older anticonvulsants [2]. Such newer anticonvulsants may prove more useful in treating epilepsy than older drugs, but more testing and research will be necessary [2].

Research into the effectiveness of new anticonvulsant drugs typically involves screening candidate drugs in small mammals such as mice or rats prior to clinical evaluation on humans [2]. In order to gauge the efficacy of a candidate drug, its anticonvulsive effect is observed in a test animal that may have been electrically induced to have a grand mal seizure [2]. An electrical stimulator is used to generate a sufficient stimulus to induce a grand mal seizure in a test animal [2].

A qualified and commercial stimulator such as Ugo Basile Model and its accesories cost more than $3000 [4]. Such cost is too high for nost resarch laboratories in developing regions.

An alternative design of low cost and qualified electroconvulsive device is proposed in this paper. The electroconvulsive device is expected to consume not more than 70 Watts (W) of electric power supply, to cost not more than $100 and to produce an electrical stimulus through its corneal electrodes when its foot pedal is pressed. The stimulus is performed as a single burst of pulses of electric voltage or current. The stimulus specifications are 0.1 to 1 second (s) of burst duration, 10 to 100 Hertz (Hz) of pulse frequency, 0.5 to 20 milliseconds (ms) of pulse width and 0 to 200 Volts (V) or milliamperes (mA) of amplitude of electric voltage or current.

2 The Design

The electroconvulsive device is built from 8 main circuit modules, 2 interface modules and 2 safety circuit modules. The main circuit modules are: low voltage power supply circuit (LVPS), high voltage power supply circuit (HPVS), trigger circuit, stimulus duration controller circuit (SDC), pulse frequency controller circuit (PFC), pulse width controller circuit (PWC), amplitude modulator circuit (AM) and converter circuit. The interface modules are: control panel, buzzer and LED indicators. The safety circuit modules are: under load detector circuit (ULD) and over current protector circuit (OCP). Figure 1 shows the positions of the modules and the connections between the modules.

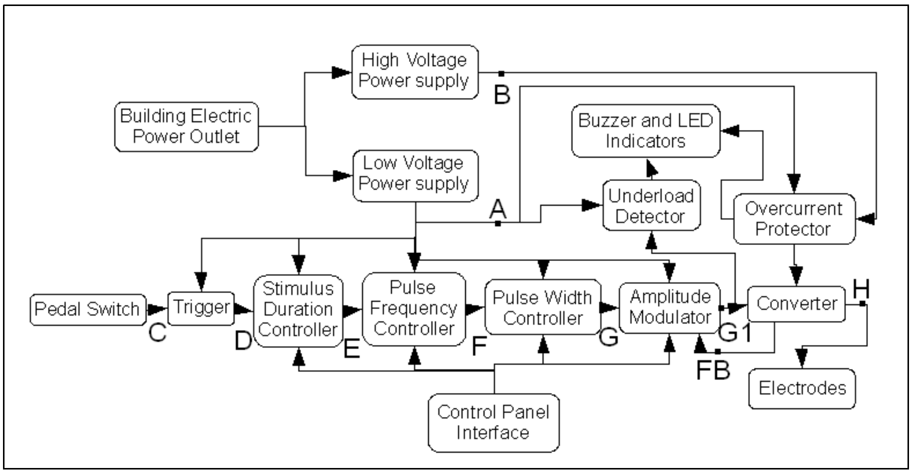


Figure 1 Positions and connections of circuit modules of the electroconvulsive device.

The LVPS convert 220 V, 50 Hz of AC voltage from building electric power outlet into lower, constant, electric DC voltage and supplies plus 12 V for trigger circuit module, SDC, PFC, PWC, AM, OCP and LED indicator. The LVPS also supplies minus 12 V for AM and ULD. The HVPS convert 220 V, 50 Hz of alternating current (AC) voltage from building electric power outlet into high, constant, electric direct current (DC) voltage and supplies about plus 300 V for converter circuit module. The trigger circuit modules converts short interval of short circuit connection from pedal switch into trigger signal for SDC. The SDC will produce 0.1 - 1 s of high logic signal (H) before return to low logic signal (L), if it reads trigger signal from the trigger circuit modules. The PFC produces 10 - 100 Hz of frequency of repeated L pulses as long as it read H from SDC. The PWC will produce 0.5 - 20 ms of H before return to L, if it reads L pulse from the PFC. The AM modulate PWC output signal amplitude as high as 0 - 10 V. The converter circuit module multiplies AM output signal by 20 V for voltage type stimulus or 20 mA for current type stimulus and passes the electrical stimulus to test animal through the corneal electrodes or other type electrodes. The OCP will break electric supply from the HVPS to the converter circuit module and light the LED indicator, if the stimulus current reaches over 200 mA. The ULD will sound and light the buzzer and light indicators, if the electrodes and the test animals are not connected properly, while the current type stimulus are conducted. The control panel module interfaces between users and the device. Users reads and manipulates electrical stimulus parameter via the control panel module.

2.1 The Low Voltage Power Supply Circuit Module

The LVPS uses low cost, reliable and 'easy to find' 78XX series and 79XX series of regulator intergrated circuit to minimize size, additional external components and cost. Figure 2 shows positions and connection between electronic components of the LVPS. In the LVPS, switch SW1 is used by users to turn on and turn off the electroconvulsive device. The fuse will disconect external AC power supply from the device if enexpected short circuit ocurrs.

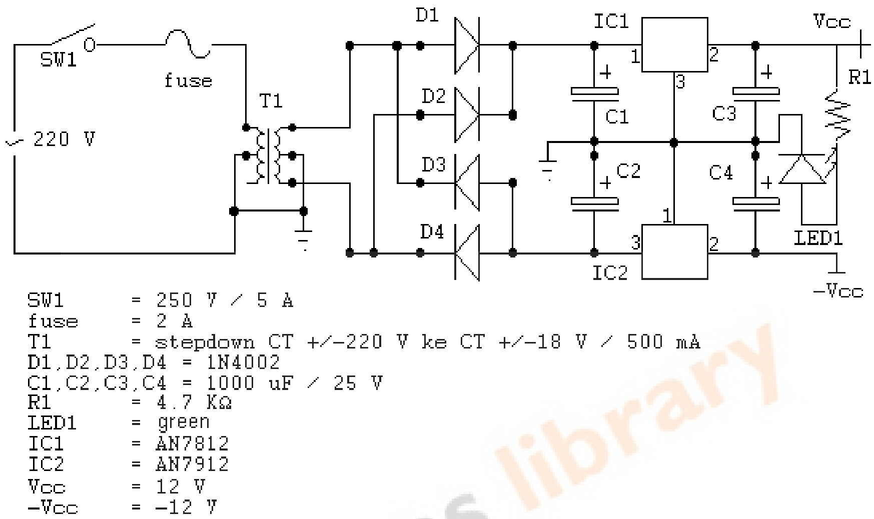


Figure 2 Electronic schematic of the LVPS.

The transformer T1 converts 220 V, 50 Hz from the external AC power supply into 18 V of AC voltage. The brigde diodes D1, D2, D3 and D4 rectify the 18 V of AC voltage into +18 V and -18 V of DC voltage. The capacitors C1 and C2 hold charges from the DC voltage, make them more stable and rise them up to above +19 V and below -19 V of DC voltage at maximum 0.5 A of load current consumtion. Those voltages are more than enough for regulator intergrated circuit IC1 and IC2 to convert them into +12 V and -12 V of constant DC volttage. The capacitors C3 and C4 clean additional noise from intergrated circuit IC1, IC2 and from loads. The resistor R1 and light emitting diode LED1 tells user that the LVPS working properly.

2.2 The High Voltage Power Supply Circuit Module

Figure 3 shows positions and connection between electronic components of the HVPS. In the HVPS, resistor R2 and neon light bulb tells users the right polarity of external AC power supply. The neon light bulb will light orange when the test screw is by grounded users and reversed polarity of external AC power supply is conducted.

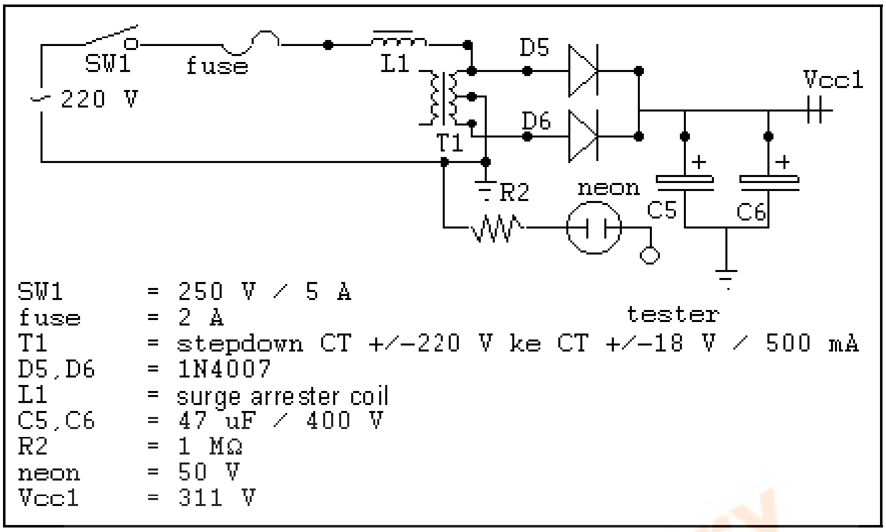


Figure 3 Electronic schematic of the HVPS.

The transformer T1 creates counter polarity of active pole of external AC power supply, so that the diodes D5 and D6 do full wave rectifying as bridge diode do and creates 220 V of DC voltage. The capacitors C5 and C6 stabilize the DC voltage and rise them up to above 289 V of DC voltage at maximum 200 mA of load current consumtion. This 289 V of DC voltage is more than enough to supply the converter circuit module.

2.3 The Trigger Circuit Module

The trigger circuit module is used to mantain single short interval trigger signal for the SDC. Figure 4 shows positions and connection between electronic components of the trigger circuit module. When the pedal switch is pressed and realease to start the stimulation, the interval of short circuit connection is undetermine and bounce signal is ocurr at signal transition.

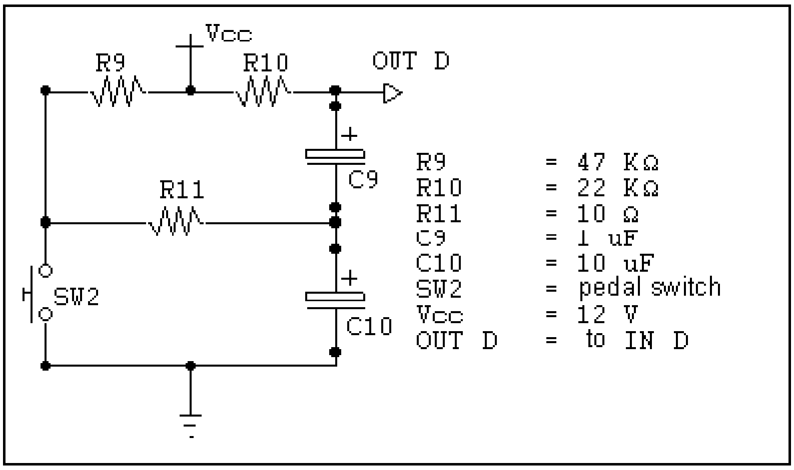


Figure 4 Electronic schematic of the trigger circuit.

When the pedal switch SW2 is close, current will dischage capacitor C10 fastly through resistor R11 and capacitor C9 will be charged through resistors R10 and R11. Because capacitor C10 is much bigger than capacitor C9, the output D creates short interval of L and then return to H. Bounces signal from pedal switch SW2 is supressed by capacitor C10. When the pedal switch returns to open, current will slowly charge capacitor C10 and capacitor C9 will be dischaged through resistors R9, R10 and R11. Because capacitor C10 is much bigger than capacitor C9, the output D will rise higher from H for a moment and then return to H. Figure 5 is respose signal at pedal switch SW2 which produced by simulation of the trigger circuit when it is pressed and release.

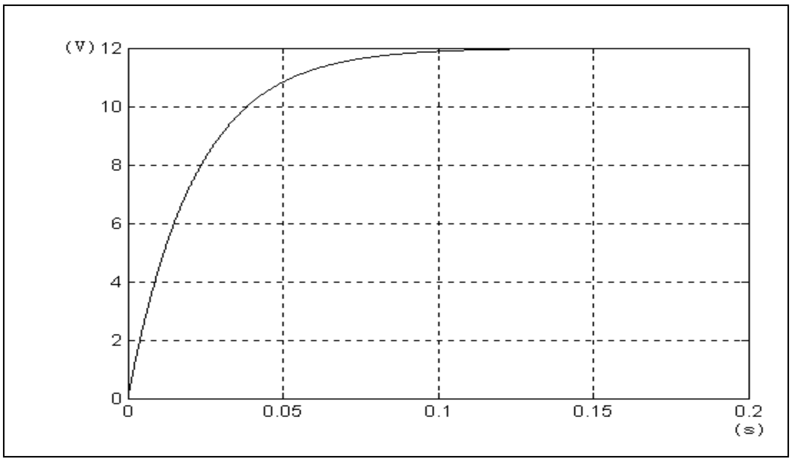


Figure 5 Ideal input signal from the pedal switch SW2 when it is pressed and release.

Figure 6 is respose signal at output D which produced by simulation of the trigger circuit when the pedal switch SW2 is pressed.

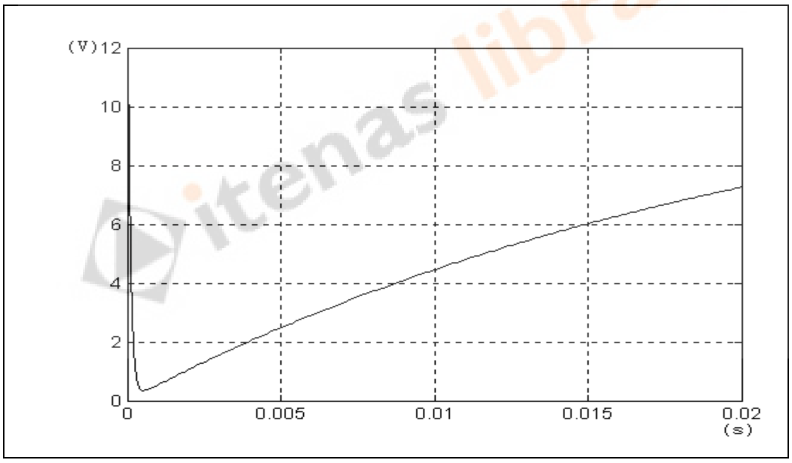


Figure 6 Ideal signal of output D when the pedal switch SW2 is pressed.

2.4 The Stimulus Duration Controller Circuit Module

The SDC uses low cost, reliable and 'easy to find' 555 series of timer intergrated circuit in monostable configuration to minimize size, additional external components and cost. The monostable operations of 555 series of timer intergrated circuit is explained in fairchild semiconductor corporation document [3]. Figure 7 shows positions and connection between electronic components of the SDC.

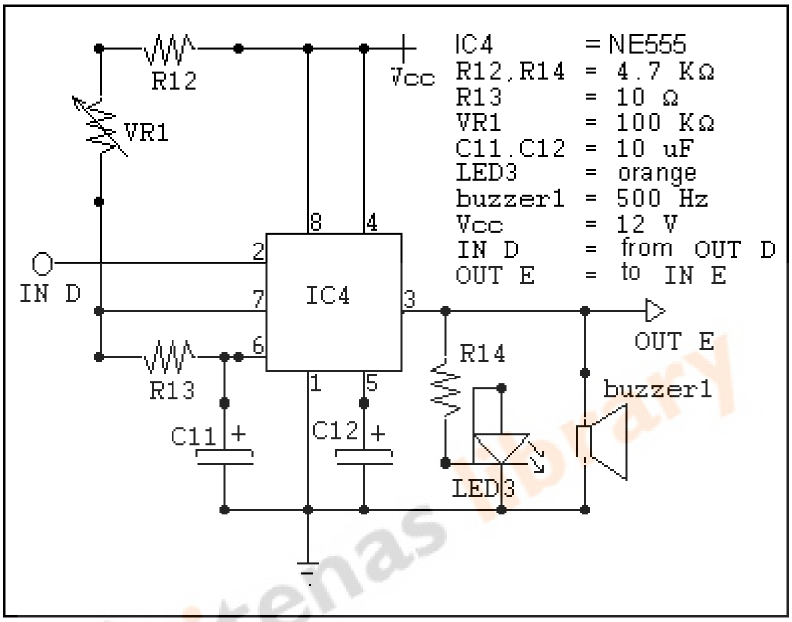


Figure 7 Electronic schematic of SDC.

When the timer intergrated circuit IC4 reads trigger signal from the trigger circuit module through input D, it will produce H signal through output E, light LED3 and sound buzzer1 as long as capacitor C11 is charged from 0 - 8 V through resistors R12, VR1 and R13. After that output E returns to L signal and capacitor C11 is discharged to empty through resistor R13. The SDC is expected to produce 0.1 - 1 s of H pulse when it reads trigger signal. The values of resistors R12, R13, VR1 and capacitor C11 are determined by using the 555 monostable operation equation in fairchild semiconductor corporation document [3]. Figure 8 shows theoritical signal from output E. The resistor VR1 is put at control panel and tuned by users to manipulate stimulus' duration. The 0.1 s of interval duration determine by the resolution of the control panel.

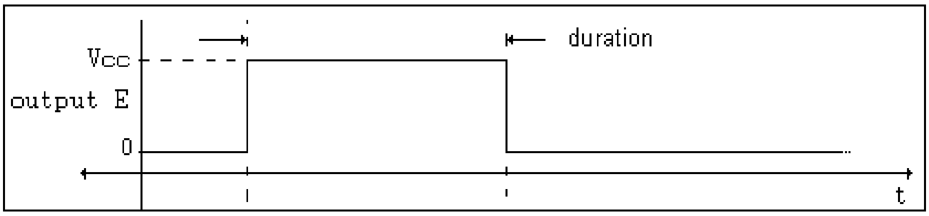


Figure 8 Ideal signal of output E when SDC reads trigger signal from the trigger circuit module.

2.5 The Pulse Frequency Controller Circuit Module

The PFC uses low cost, reliable, 'easy to find' 555 series of timer intergrated circuit in astable configuration and 741 opamp intergrated circuit in buffer operation to minimize size, additional external components and cost. The astable operations of 555 series of timer intergrated circuit is explained in fairchild semiconductor corporation document [3]. Figure 9 shows positions and connection between electronic components of the PFC.

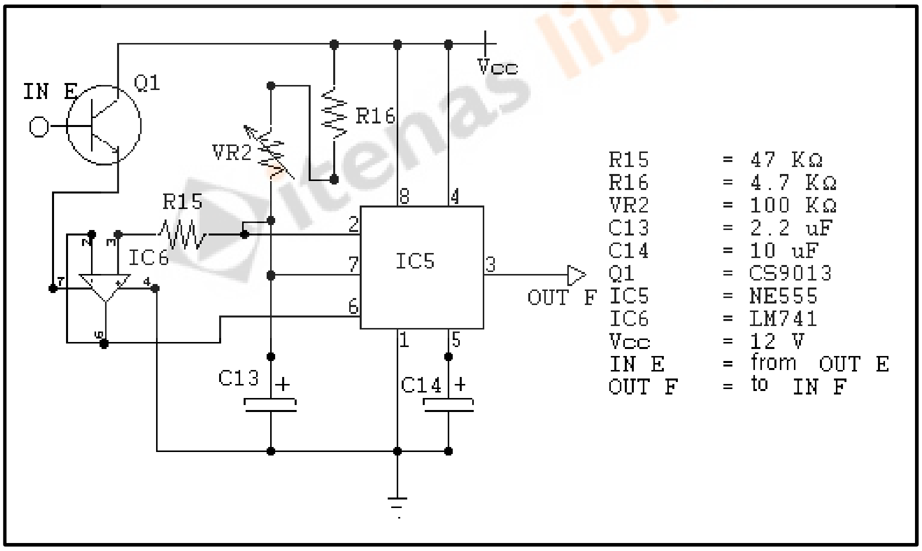


Figure 9 Electronic schematic of PFC.

When the transistor Q1 reads L signal, it break voltage supply for opamp IC6. As the result, pin 6 of timer intergrated circuit IC 5 cannot read the capacitor C13 voltage. Pin 2 of timer intergrated circuit IC 5 has read trigger signal before when the capacitor C13 empty, so the output F is H and the capacitor C13 is charged.When the transistor Q1 reads H signal, it passes power supply to opamp intergrated circuit IC6. The IC6 passes C13 voltage to pin 6 IC5. As the result, the timer intergrated circuit operates in astable configuration that produce repeated pulses. The PFC is expected to produce 10 - 100 Hz of L pulse when it reads H signal. The values of resistors R16, VR2 and capacitor C13 are determined by using the 555 astable operation equation in fairchild semiconductor corporation document [3]. Figure 10 shows theoritic signal from output F. The resistor VR2 is put at control panel and tuned by users to manipulate stimulus' pulse frequency. The 10 Hz of interval frequency determine by the resolution of the control panel.

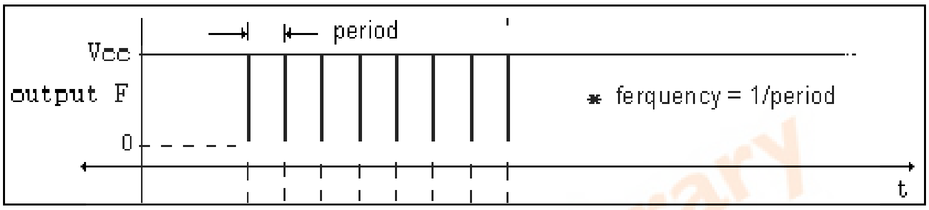


Figure 10 Ideal signal of output F when the pedal switch SW2 is pressed and release.

2.6 The Pulse Width Controller Circuit Module

The PWC uses low cost, reliable and 'easy to find' 555 series of timer intergrated circuit in monostable configuration to minimize size, additional external components and cost. The monostable operations of 555 series of timer intergrated circuit is explained in fairchild semiconductor corporation document [3]. Figure 11 shows positions and connection between electronic components of the PWC.

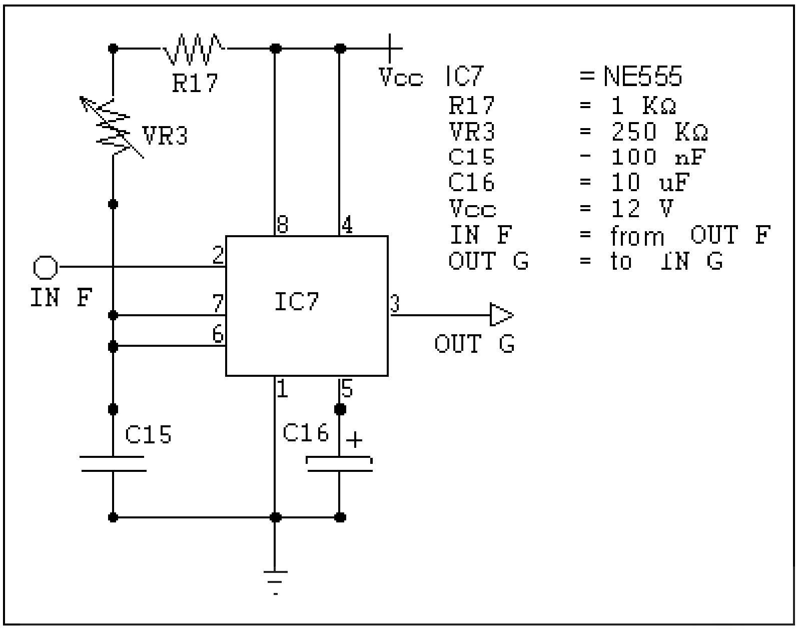


Figure 11 Electronic schematic of PWC.

When the timer intergrated circuit IC7 reads trigger signal from the PFC through input F, it will produce H signal through output G, as long as capacitor C15 is charged from 0 - 8 V through resistors R17 and VR3. After that output G returns to L signal and capacitor C5 is discharged to empty. The PFC is expected to produce 0.5 - 20 ms of H pulse when it reads trigger signal. The values of resistors R17, VR3 and capacitor C15 are determined by using the 555 monostable operation equation in fairchild semiconductor corporation document [3]. Figure 12 shows theoritic signal from output E. The resistor VR3 is put at control panel and tuned by users to manipulate stimulus' pulse width. The 0.5 ms of interval duration determine by the resolution of the control panel.

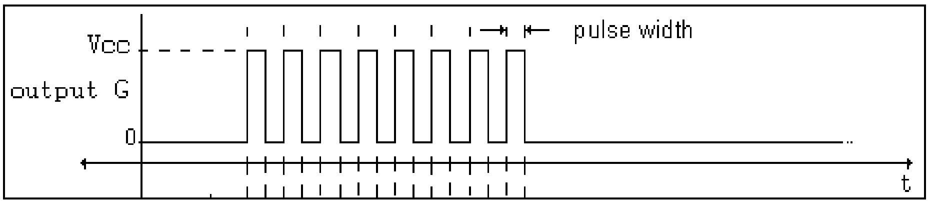


Figure 12 Ideal signal of output G when the pedal switch SW2 is pressed and release.

2.7 The Amplitude Modulator Circuit Module

The AM uses popular, high performance and low offset OP07 of opamp intergrated circuit in noninverting configuration to minimize size, additional external components and cost. Figure 13 shows positions and connection between electronic components of the AM.

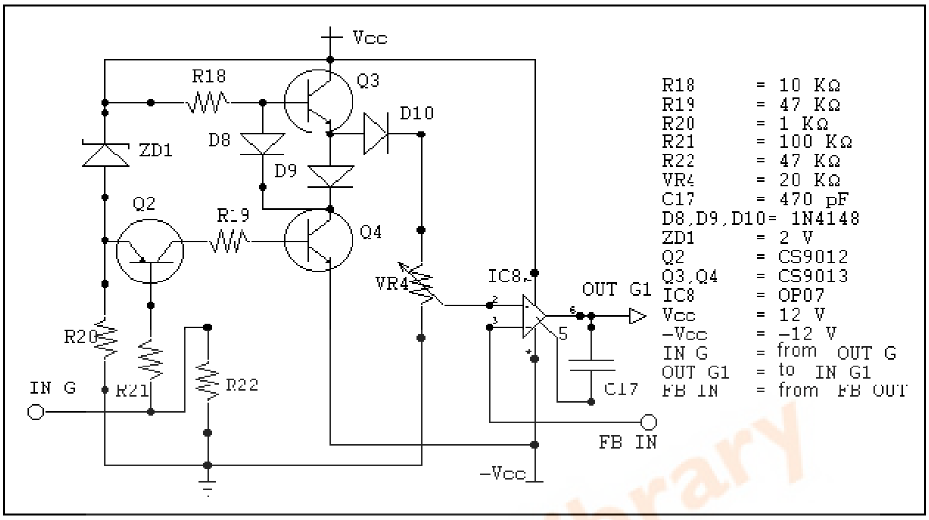


Figure 13 Electronic schematic of AM.

The transistor Q2 in common emitter configuration, resistors R20, R21, R22 and zender diode ZD1 are used to reconstruct pulses signal through input G. The transistors Q3, Q4 in totem pole push-pull configuration, resistors R18, R19 and diodes D8, D9, D10 are used to turn on and off voltage for resistor VR4 based on pulses signal through input G. The opamp intergrated circuit IC8 drives the converter circuit module through output G1, so that feedback signal from converter circuit through input FB is as equal as VR4 output signal. The VR4 modulates pulses signal through input G by potentio position of VR4. The expected value of FB input signal's amplitide is 0 - 10 V. The resistor VR4 is put at control panel and tuned by users to manipulate stimulus' ampltude.

2.8 The Converter Circuit Module

The converter circuit module uses popular, high performance and high voltage 2n3440 to minimize cost. Figure 14 shows positions and connection between electronic components of the converter circuit module.

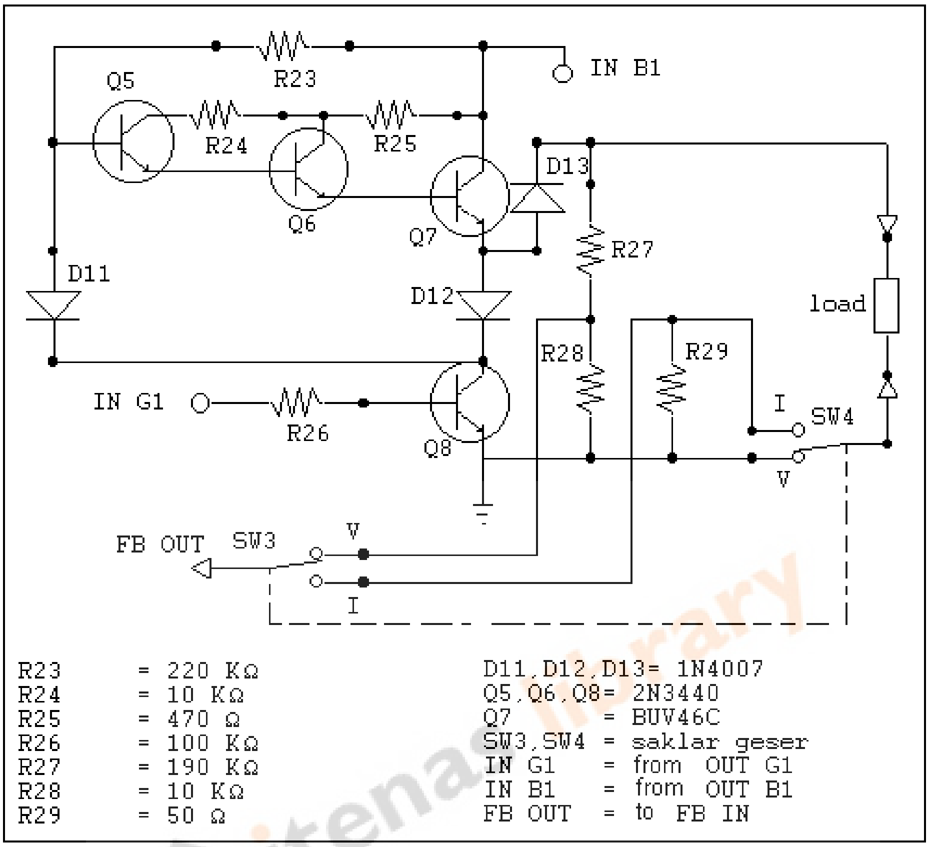


Figure 14 Electronic schematic of the converter circuit module.

The transistors Q5, Q6, Q7, Q8, the resistors R23, R24, R25, R26, the diodes D11, D12, D13 are configured in totem pole push-pull to amplify modulated stimulus signal from VR4. The amplified signal is sampled by the resistors R27 and R28 through output FB in voltage stimulus setting. For current stimulus setting, The amplified signal is sampled by the resistor R29. The converter circuit module is expcted to drive 0 - 200 V of stimulus' amplitude through the electrodes in voltage stimulus setting, or to drive 0 - 200 mA of timulus' amplitude in current stimulus setting. The output FB is expected to sample 0 - 10 V of stimulus' amplitude sample. Figure 15 shows theoritic signal from output FB.

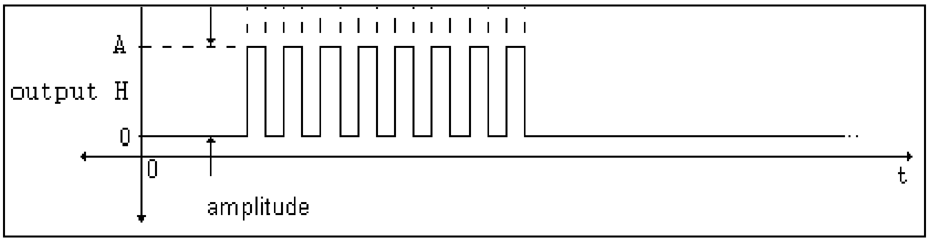


Figure 15 Ideal signal of output H when the pedal switch SW2 is pressed and release.

2.9 The Over Current Protector Circuit Module

The OCP uses low cost, reliable and 'easy to find' 555 series of timer intergrated circuit in monostable configuration to minimize size, additional external components and cost. The monostable operations of 555 series of timer intergrated circuit is explained in fairchild semiconductor corporation document [3]. Figure 16 shows positions and connection between electronic components of the OCP.

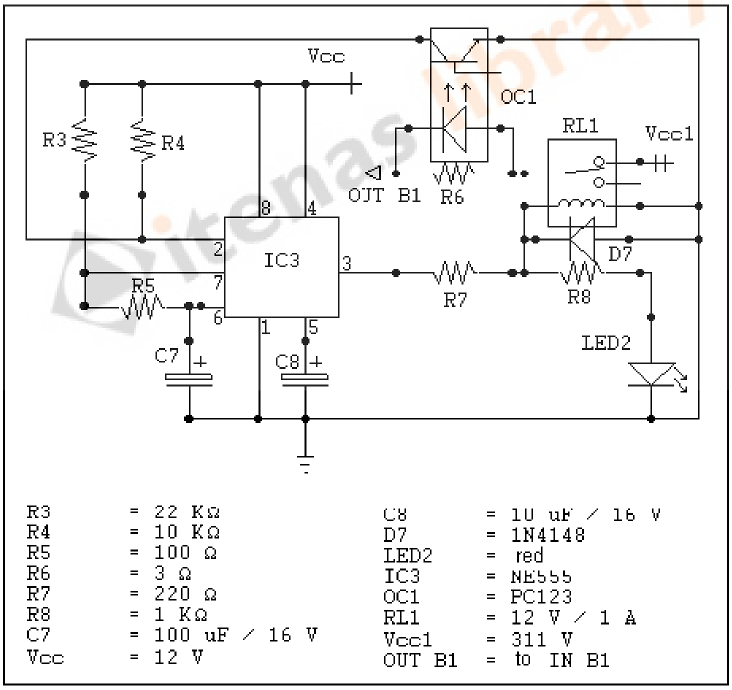


Figure 16 Electronic schematic of OCP.

When the current consumtion of the converter circuit module through the resistor R6 and LED in the opto coupler OC1 exceed 200 mA, the LED in the OC1 will light and activy the transistor in OC1. When the transistor in OC1 is activied, the timer intergrated circuit IC6 in monostable operation produce H signal that activy relay circuit breaker RL1 and light LED2 for about 2.43 s. If rhe RL1 is actified, it will break power supply from HVPS to the converter circuit module. After 2.43 s the RL1 will be reactivy if the cause of the over current is not removed. The values of resistors R3, R5 and capacitor C7 are determined by using the 555 monostable operation equation in fairchild semiconductor corporation document [3]. The OCP protects the HVPS and the converter circuit module from risk of over current.

2.10 The Under Load Detector Circuit Module

The ULD uses low cost, reliable and 'easy to find' 555 series of timer intergrated circuit in monostable configuration to minimize size, additional external components and cost. The monostable operations of 555 series of timer intergrated circuit is explained in fairchild semiconductor corporation document [3]. Figure 17 shows positions and connection between electronic components of the ULD.

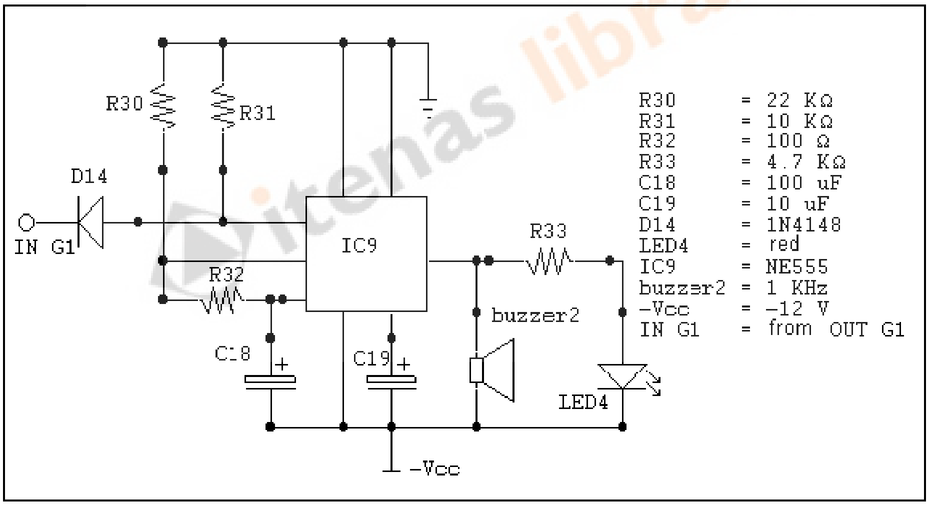


Figure 17 Electronic schematic of ULD.

Whwn the electrodes are not connected properly to the test animal and current type stimulation is conducted, the converter circuit modules and the AM will detect difference between modulated stimulus signal reference from VR4 and FB signal from the converter circuit module. This is because the converter circuit module can not get enough voltage from the HVPS to drive suffient current through the electrodes. In this case, the ULD will detect negative signal from output G1. The signal then trigger the timer intergrated circuit IC9. The ULD is expected to light LED4 and sound buzzer2 for about 2.43 s. The values of resistors R30, R32 and capacitor C18 are determined by using the 555 monostable operation equation in fairchild semiconductor corporation document [3]. The ULD tells the user that the stimulus' current amplitude can not reach as the control panel setting.

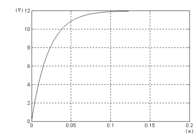
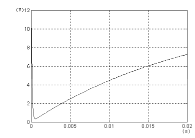
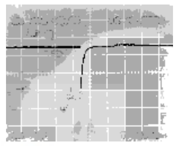
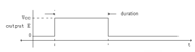
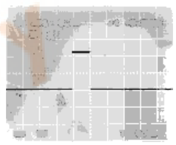
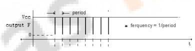
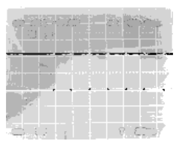
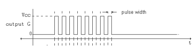
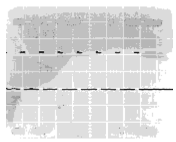
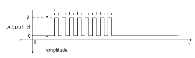
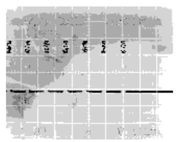
3 Experimental Results

The design of the electroconvulsive device is constructed in white plastic project box and then tested by using several instruments. Figure 18 shows the size and the shape of the constructed electroconvulsive device.

Figure 18 Photograph of the constructed electroconvulsive device.

The first testing is conducted to compared between the ideal values from calculations and simulations and the actual values from measurements. Each test points of input and outputs of the electroconvulsive device's mocule are tested with digital multitester and digital osciloscope. table 1 shows the comparation between ideal and actual parameters' values and signals' waveform.

Table 1 Ideal vs actual value and waveform.

Test Point	Parameter	Ideal		Actual	
		Value	Waveform	Value	Waveform
A	DC Voltage	+12 V, -12 V		+11.45 V. -11.4 V	
B	DC Voltage	289.15 - 311.13 V		305 V	
C	Response Signal				
D	Response Signal				
E	Stimulus Duration	0.52 - 1.15 s		0.1 - 1.2 s	
F	Pulse Frequency	6.26 - 139.53 Hz		8.9 - 166.7 Hz	
G	Pulse Width	0.11 - 27.58 ms		0.12 - 22 ms	
FB	Stimulus Amplitude Feedback	0 - 10.55 V		0 - 10.5 V	

Most of the test points' parameter value and signal's waveform comparation shows similiar result, except the actual waveform of stimulus amplitude feedback from the output FB which distorted with harmonic wave.

The second test is conducted to gauge the efficacy of the constructed electroconvulsive device to generate a sufficient stimulus to induce a maximal seizure in a test animal. Figure 19 shows the stimulation of a test animal.

(a) (b)

Figure 19 (a)Photograph of the test animal that was conected to the electroconvulsive device's corneal electrodes. (b)Photograph of maximal seizure in the test animal after electrical stimulating

The second testing confirms that the constructed electroconvulsive device is able to generate a sufficient stimulus to induce a maximal seizure in 20 - 22 gr of mice. The Stimulus parameters are: 0.2 s of stimulus' duration, 100 Hz of stimulus' pulse frequency, 0.5 ms of stimulus' pulse width and 25 - 35 mA of stimulus' current amplitude.

4 Conclusions

The constructed low cost and qualified electroconvulsive device has met the specifications, except the lack of resolution of 0.5 V of interval voltage amplitude or 0.5 mA interval current amplitude of control panel interface and the harmonic wave distorsion of stimulus' waveform.

The constructed low cost and qualified electroconvulsive device is able to generate a sufficient stimulus to induce a maximal seizure in 20 - 22 gr of mice.

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