Computer driven electro-therapy device

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ABSTRACT:

Since the 1960s, electric treatment on living tissue has become increasingly acceptable to medical public opinion. A new device has evolved whose parameters are changeable over a large spectrum, and which is controlled by computer and switchable constant current and constant voltage,and has the ability to generate either pulses or DC, with regard to electrical tools and parameters used by other authors.

The certain stabilization is provided through loading resistance between 0.01 ê to 1000 ê up to 40 mA, besides either pulses (f<238 Khz) or Dc. All electrical parameters (frequency, duration,inter pulse time, total charge, total treatment time) and reverse polarization time values are typed in by keyboard,then application is monitored,and put in a file for statistical purposes.

A simple and effective electro-therapy device is employed after calibration which is able to be constructed by the investigator. This device is named as AYDIN Apparatus.

Uncommercially, the detailed program list, detailed electronic diagrams, detailed connection configurations between the computer-tool can be suplied to the reader.

KEYWORDS: Computer , Elektroporation , Electric Treatment , Electrode Potential, Tissue Impedance, Electrical Parameters.

INTRODUCTION

Retrospective:

The early publications regarding the electricty began in 1600. Matteucci demonstrated the production of electrical current by injured tissue in 1791.Lund demonstrated that electrical potential could control the growth of tissue in 1947. Becker found that after amputation, the regenerating limb of the salamander produces a measurable current during the regenartion process [72]. Many investigators studied on fractures after Yashuda and Fukada showed that bone could produce piezoelectric caused by pressure . [109, 1, 127, 130, 2, 38, 114, 205, 206, 92, 189].

Literature has brimmed regarding electrical investigations, sampling retina, cornea, cochlea, brain, heart, dermal ulcer, spinal, cord, saliva glands , neuromusculer plaque , purkinje cells , testis, neoplastic tumor cells , genetic , bone , botanic, microbiology, renal tubulus, muskarin, 5HT,ATP, T3,T4,antiepyleptics, vazopressin, bacterial enzyms,histamin, asetyl colin recetors, lenfosits, adrenergic receptors, DNA and RNA relocations,hormones.

Since 1968, ischemic dermal ulcers and burn wounds have often been treated by either DC or pulsating current. [73, 74, 3, 39, 61, 19, 112, 191, 70, 6, 123]

MECHANISM:

Previously, knowledge of tissue response has been necessary to

understand the effect of electric current. When a wound is made in epithelium, the potential across the epithelium drives a current through the subepithermal legion and out of the wound (about 22 æA/cm2). The outer surface is negatively charged. This potential is named as SKIN BATTERY. Sodium ions migrate to subepidermal layer from outer surface through membrane-spanning segments S4 and S5. An average of frequency is 10^6 ion/sec^-1. [172] This voltage is a motor-power for healing, because it disappears after healing.
[193, 63, 72, 96, 16, 47, 24, 144, 57, 145, 50, 58, 100, 155, 152, 135, 55, 142, 88]

Biologic Effects of Electricity:
1) Ionic: An ion migration begins in either anode or cathode when the probes act as electrodes, either intercellular or intracellular liquids act as an electrolyte. The ions will stick on surface of electrodes and limit the current flow after a few times. This is an advantage for healing of bone fracture, but a disadvantage during therapy of soft tissue. Many authors noted that the poles interchanged during electric application, intermittently. [112, 200, 160, 2, 33, 160, 145, 101, 71, 72]
The control of probe reversal was given to computer on Serial Port#2.
2) Celullar: The epithel cells migrate to the point of negative polarity by galvanotaxic effect. Thus, cosmetic and faster epithelisation occurs without keloid tissue .[0180],101. The neutrophiles go to cathode [67, 52, 134, 56]. The macrophages migrate to both polarities [141]. The positive polarity inhibits the mast cells, hence, hystamine liberation is decreased [159, 197]. It is induced that, the electricity invites fibroblasts, synthesis of DNA rises by 20%, collogen synthesis increases to a maximum of 120% in negative polarity..[7, 13, 83, 46, 20, 60, 27, 76, 201, 114, 183, 99]. The negative polarity increases Calcium ions binding to external nerve cell membrane and neural regeneration accelerates. [21, 176, 95, 192]. Osteoblastic activity increases under negative polarity. In contrast, osteoclastic activity increases under positive polarity. This case has been used for healing bone fractures. [66, 125, 203, 32, 35, 109, 204, 206, 205]
3) Vascular: Edem reduces, because negative charged large molecules of proteins are repelled, thus, oncotic pressure decreases. Rich blood circulation occurs, by dilated vessels. Lipid peroxidation decreases, the granulation tissue is supported, debridement of necrotic tissue is facilitated. Thus, cathodal electric usable on flaps. [133, 158, 146, 161, 198, 169, 171, 86, 172, 71, 87, 53, 74, 172, 106, 107, 186, 11]. In contrast, the positive polarity pull the trombocytes into capillary vessels, hence it helps to stop the hemoragies, in surgery. [37, 170]
4) Antibacterial: The effect of both polarities is intense bacterisidal activity. [166, 165, 164, 111, 59, 25, 92, 91, 48, 84, 202, 4, 156, 69, 30].

In general review of the effects, acceptable electrical treatment acts as a trigger to electrophysiological reactants. [76] There is a potential voltage during the healing process. The electrical therapy can be applied if this potential disappeares or is reduced, but, not if it remains unchanged.

ELECTRICAL PARAMETERS

The electrical parameters are the directly dominant factor on the result of electrical therapy. It is very important that they are well obtained for ineffective or effective results even breakdown

beneath the electrodes. [65, 160, 60, 183, 102, 51].

Pain threshold has observed by Geddes and baker as 40 mA for noninvasive-coupled electrodes on living tissue. This limit has been chosen as a main target while building the device. Current of up to 20 æA is enough for invasive technique.

The tissue impedance is a more complex conception, because the electric current is compensated by tissue reactance and tissue resistance. This combination can act as an electrical system in which many capacitors and many resistors are connected by serial and/or paralell. The tissue electrolytes and water are good conductors . In contrast, the fats and skin and hard tissues are poor conductors of electrical current. Hence, cell membrane, which consist of a layer of nonconductive lipophilic material interposed between two layers of conductive protein molecules, are reactive elements that behave as capacitors when exposed to an electric current. Phase angle is simply the arctangent of reactance divided by resistance. This angle has been measured from 6.70ø to 10.9ø by Zarowitz in healthy bodies, and can increase or decrease during metabolic diseases or the hydration is broken. All variable information collected, tissue impedance has been calculated by Deuterium isotope Dilution, Densitometry, Anthropometry, Uriner Creatinine Excretion, Muscle Metabolites, Neutron Activation Analysis, Photon Absorptiometry,Computed tomography, Ultrasound, Nuclear Magnetic Resonance technics. In result, Segal et al reported it is 250 ê - 750 ê ñ %2 ê. VanLoan and Maycylin reported ñ 5 ê difference values on the same subjects during eleven days. [15]. The toleration range of 25% is aimed for by the AYDIN Apparatus (0.01 ê-1000 ê). But, it is known that, impedance will reduce when high frequency is applied.

The Electrodes can be distinguished as platinum, carbon, Ag, Ag+AgCl,Au Stainless Steel etc . Invasive technique entails the electrodes being inserted into tissue. But, the electrodes contact the tissue through skin gel (÷20 ê) by noninvasive technique. Finally, Electromagnetic methodes entail use of the conductor coil instead of electrodes. Besides, the operator has to consider the Offset Potential (Electrodes Noise) and Polarisation Impedance [97].

The tissue impedance can change for these reasons: 1) General hydration 2) Before and after Dialysis 3) False electrode placement 4) Corticosteroid Therapy 5) Cancer 6) Asidosis/Alcalosis 7) Cardio-Pulmoner diseases 8) Pregnant Women 9) New Born babies 10) Sex 11) Malnutrition 12) Body Temperature 13) Obesity 14) Age 15) Menstrual Sycle 16) Surgical Operations 17) Lassitude 18) Unknown factors. (The first nine are contraindication for electrical therapy)

Principally, the total charge represented by current per day, is the actual parameter, according to biospectral voltage on the tissue during electric therapy (Between 0.1 -2.0 Coulomb/day). This charge must be divided evenly throughouth maximum time per day.

$$\text{Total Charge} = \frac{I \; d \; T}{A}$$

I=Current (mA) per pulse
d=Puls duration (mSec)
A=Surface of electrodes(cm^2)
T=Total application time

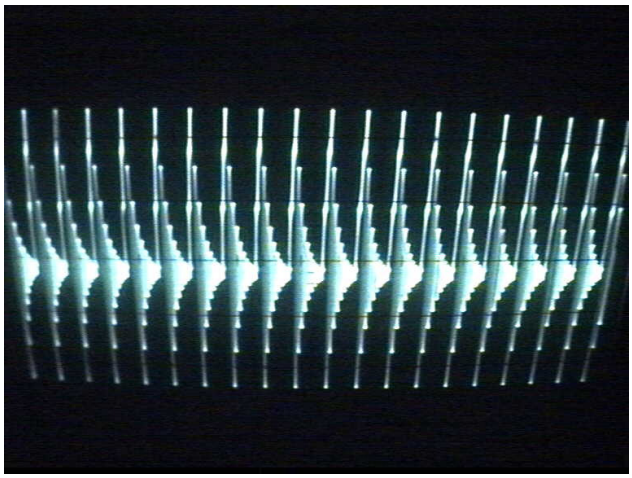
MATERIAL_METHOD

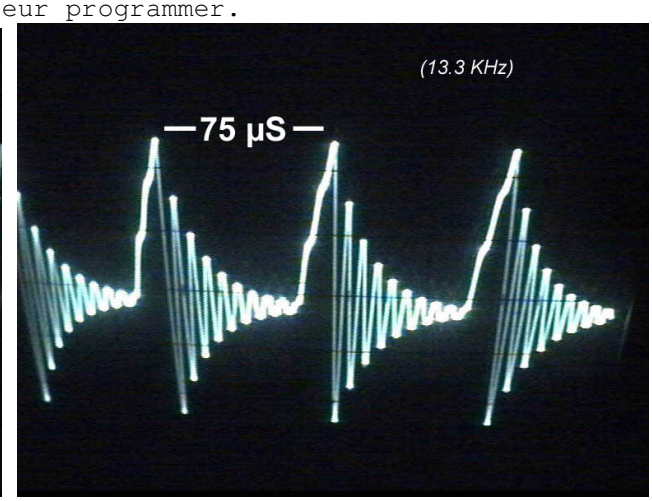
This tool consists of a computer signal generator and constant current and Voltage Source (CCVS) connected to the computer. Pulse parameters are made variable on the keyboard by typing and the pulses are sent to the tissue through CCVS.

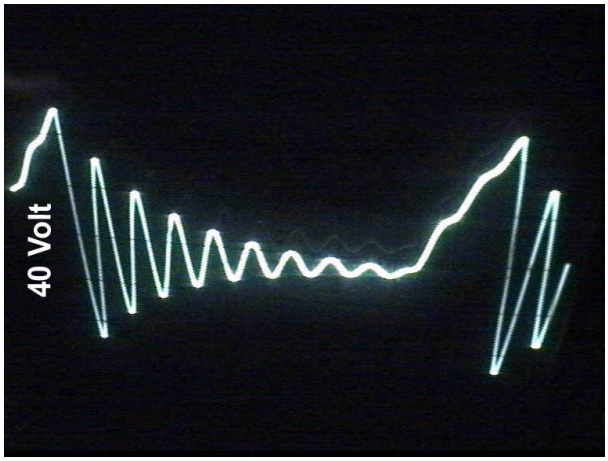
The present study, the configuration consists an IBM compatible

computer-based Pc-AT 286, 16 mHz, 4 Mb RAM SVGA, 89 Mb Hdd, 5¬ + 3« inch floppy. The floppy control card contained two serial output connectors, the first one with 9 pins, the other with 25 pins. (FCC ID:IZVBF 1590).

The Autoexec.bat and Config.sys files have no program for enlarging the memory, such as TSR. The software language is QuickBasic 4.0 (Microsoft Co.) and Turbo Assembler 2.0 (Borland). The time size was measured by Turbo Profiler. All measurements are with Kikusui Cor 5521u Oscilloscope. Fig.1 shows the program schematic diagram. Here, the activation to Serial Port(s) (SP) will be discussed because remaining segments can be prepared by any amateur programmer.







COMPUTER PROGRAM:

The computers have ability to intercommunicate through the serial ports from 2400 Hz to 16000 Hz, such as by modem or fax. These communications are made with data send bits either 1 or 0. On SP, pins are between +12 Volts or -12 Volts, between short time spaces during communication. A square wave already exists peak-to-peak 24 V, running and silent. At present, the purpose of the software program will be to generate a defined frequency signal along a defined time period by the user. Hence, the user can easily dispose either gate-on time (+12 V) (pulse duration = t1) or gate-off time (-12 V)(Interpulse time = t2) or total application time on keyboard. Output for SP#1 is on the seventh pin (Fig 2). (Notice: Remember that, the number of the pin can change particulary on IBM noncampatible machines)

The SP#1 connects to CCVS and the output signal reaches the tissue and SP#2 generates a trigger signal which is necessary for probe reversal. Accordingly, a minimum of two SP are necessary. The first generates a square wave, the second generates a reverse trigger signal. The user is able to change parameters of both signals over a large band. The fallowing piece of program can point to the SP adresses in Bios of

the individual computer from SP#1 to SP#4, if these exist.

```
'                  Serial port adresses
CLS : DEF SEG = 0: PORT = 0: FOR X = &H400 TO &H406 STEP 2
  PORT = PORT + 1
     PRINT "COM #"; PORT;
        IF (PEEK(X) OR PEEK(X + 1)) THEN
          PRINT " Serial Port active and adress= ";
        PRINT HEX$(PEEK(X + 1)); ":"; HEX$(PEEK(X)); "h"
      ELSE PRINT " No active"
   END IF
NEXT: DEF SEG : END
```

Generally, these two addresses are 1020,764. The addresses of the output gates of the ports are these numbers plus four. (1024,768) The seventh pin can take +12 Volts or -12 Volts values. The each one of ports will open when set to 1, or close when set to 3.

```
'              a simple square wave from SP # 1 pin 7
        DO: OUT &H3FC, 3: OUT &H3FC,1: LOOP UNTIL INKEY$ <> ""
```

This simple program produces an example square wave, t1 was measured at 25 æsec and t2=200 æsec from SP#1. Always t2 > t1 in any language except assembler. Assembler language is used to disengage from the interpreter delay and to obtain high speed.

```
                          ; Max speed for individual Computer
        MOV DX,03FC       ; Load to DX Gate Number SP#1
        MOV AH,0301       ; Open/Close command Ah=3/Al=1
        CLI               ; Stop interrupts,for retrenchment time
line:   OUT DX,AL         ; Open/Close ñ12 V to pin 7
        XCHG AL,AH        ; Change command
        JMP line#         ; Loop
```

This Assembler program generated t1=2.0 æsec, t2=2.2 æsec. There is a little difference between t1 and t2 even now. But these values are normal, because it can be explained by the clock delay of XCHG and JMP statements.

This case shows the highest speed for an individual computer (f>238 Khz).Although apparently enough, a faster computer or a frequency multiplier can be used if a higher frequency will be desired.

The 86'th subroutine of Int 15h (Casette and Extended Services) uses CX:DX long integer register and the IP waits up to the long integer time which is written on CX:DX as æsec. In other words, the flow of the program will stop until the end of CX:DX time (æsec), whereas, the 83'rd subroutine allows this waiting time to be used by the program counter (IP). Hence, either the time-trap works or the program continues.

Previously, the Int 15h 86h was conceived to limit t1 and t2 time, but it was rejected because:

1) Two Int 15h loops should not be used one inside the other.

2) There is an absence of true and determined values particularly in slight time portions. Afterwords, the BX:CX loop is preferred instead of Int 15h, during the preparation of t1 and t2. BX:CX long integer can represent maximum 4.294967 X 10^9 æsec. This is the adequate time for optimum electrical treatment.

```
     Proc Wait_Poz                ;puls duration (t1) loop
        Mov CX, Puls_PozLo
        Mov BX, Puls_PozHi
        cmp CX,0
        je Murat2
```

```
Murat1: Loop Murat1
Murat2: Dec BX
        Jnl Murat1
        Ret
     Wait_Poz EndP
```

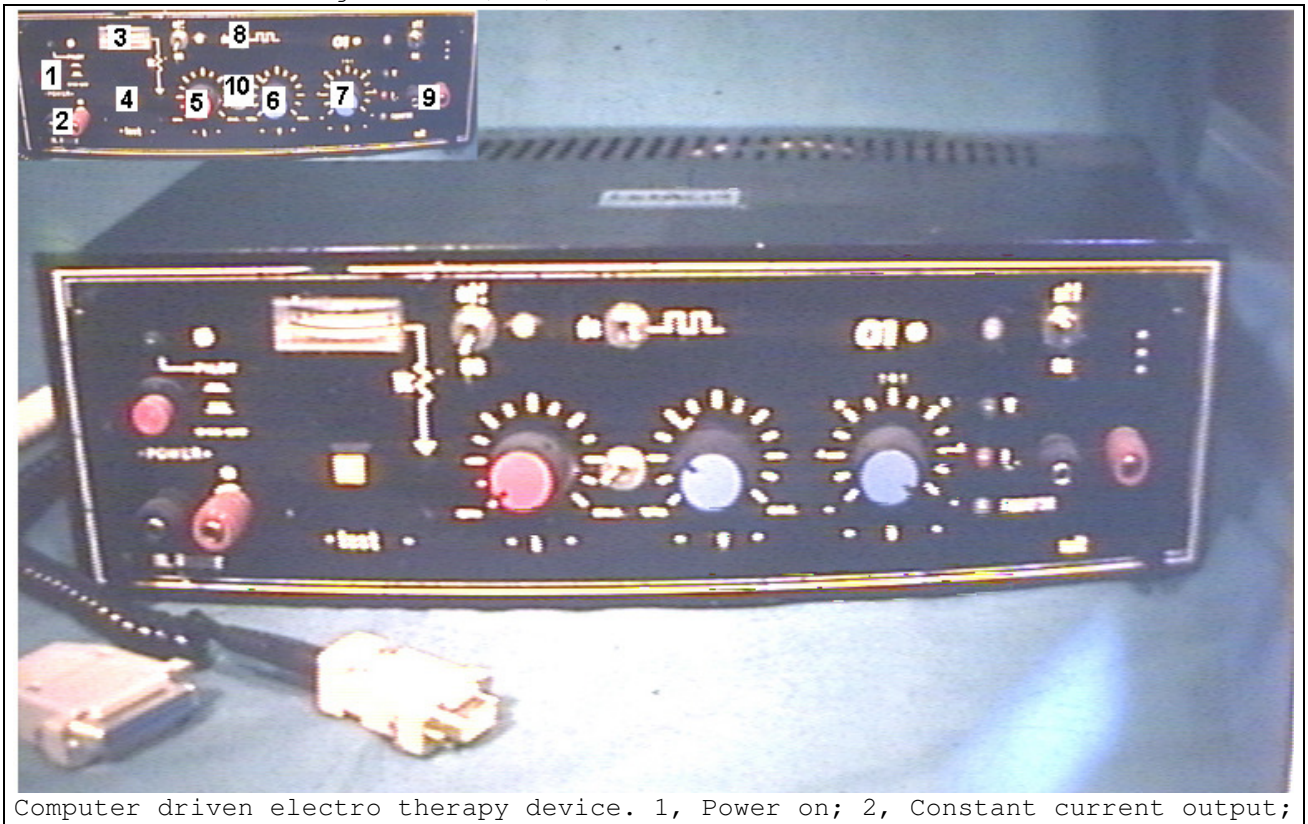
Indispensably , this condition entails only the initial calibration of the individual computer. Also, Int 15h 83h covers all segmets of the square wave generator program , to define the total therapy period (T). Hence, T value can divide little portions which occupy the pole reversal time (PRT) and the value is provided by SP#2. SP#2 gate is opened or closed for each step (T/PRT), along the therapy time(T). Finally, the assembler program is developed as in Fig 3.

During calibration, any TSR program must not exist in RAM or it has to stay always , although the software will warn the user, if it detects any RAM configuration changes after calibration. Clear RAM is ideal and preferable. In calibration, the program asks the user for 50 loop parameters for both t1 and t2 and collects these parameters in a file (CALIB). The BX:CX loop number determines the heterogen spaces and is chosen close to the loop number 255 and 65535 from 1 to 2 X 10^6, because the anticipated loop number-time curve may break near the rotated 16 bit (&H00FF, &HFFFF ...etc). However the curve has never broken (see Fig 4). This is just linear correlation. Hence, the program can easily calculate the loop number according to t1 and t2 time values input by user.

Finally, all program segments are compiled in a disk directory as EXE file

TOOL :

Tool consists of five parts: Power Supply, Voltage Regulator, Mixer, Pulse Amplifier, Current Stabilizer and mechanic relays for pole reversal. It has two switches on the front panel. The first switch controls DC/Puls;the second switch selects Constant Current Source (CCS) or Constant Voltage Source(CVS).



Computer driven electro therapy device. 1, Power on; 2, Constant current output; 3,current checker; 4, push button to checj actual current level; 5, current

level; 6,7, voltaj level; 8, SQW/DC switch; 9, constant voltage output; 10, constant current or constant voltage switch.

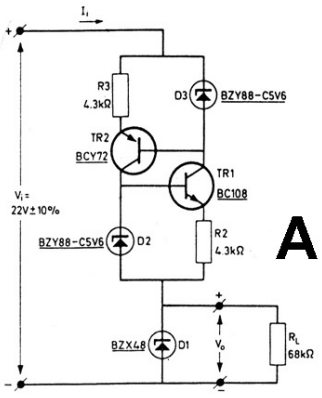
220 V is converted to 2 V, 22 V, 75 V ac voltage by transformer in the power supply stage. This potential is applied to LED diodes, mechanical relays, voltage regulator through the bridge diodes and capacitors (4 x 6800 æF/100 V Plessey Minican), respectively.

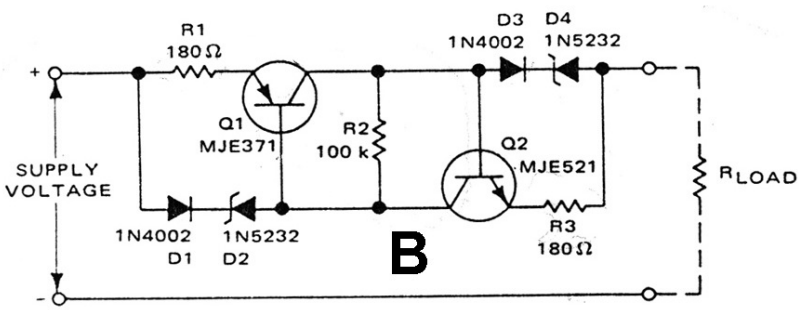
The Output impedance of voltage regulator is approximately 45 ê. Voltage output value is controlled from 6 V to 100 V by potentiometer which supports a second potentiometer with small resistance for sharp tunning (ñ 3,20 V). The tissue impedance is a maximum of 1000 ê and pain threshold is a minimum of 40 mA when the noninvasive technique is used. The reason for this is that, the tool must drive minimum of 40 V by the voltage regulator when switched to CCS. Hence, A mechanical relay cuts the connection between the voltage variable potentiometer, and voltage regulator, and puts a constant resistance in its place which allows 45 V, when the tool is set to CCS. Constant voltage gate can not vary above or below 45 V during this operation. By contrast, the voltage variable system appears when set to CVS. Constant voltage level is variable in this case but CCS gate turns to off, automatically.

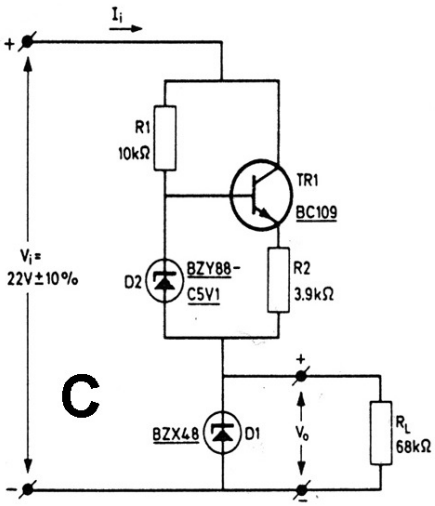
The tool has a mixer, which serves to overlap three independent signals (Input impedance ÷10 Kê). As a result, a composed single signal can be obtained as the chosen amplitude. This method is conceived as an advantage for investigation regarding two or three signals forming phase differentiations. Thus, the amplitute of input signal (peak-to-peak max 30 V) can increase or decrease in outport. Besides, this signal is selectable as CVS or CCS. A Large spectrum is useful for bioelectrical tests on tissue. Constant current is especially necessary , because live tissues require total charge instead of voltage. When switched to DC, the tool can workout variable voltage or variable current, but the mixer input gates are closed. The mixer stage drives the Pulse Amplifier.

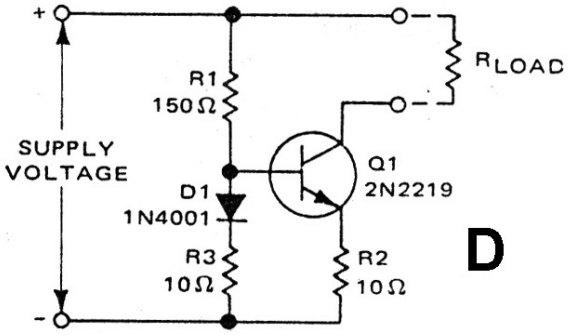
The Pulse Amplifier is designed fully with semi conductors with large band amplification. Capacitors are never prefered in the signal's path. Because they can distor the signal, particularly low frequency, during load time or store time. This circuit works with variable voltage which is produced by the voltage regulator. Hence, all component values are chosen to avoid voltages (above 100 V). The output of the amplifier is connected to the Current Stabilizer or to the device output through a switch.

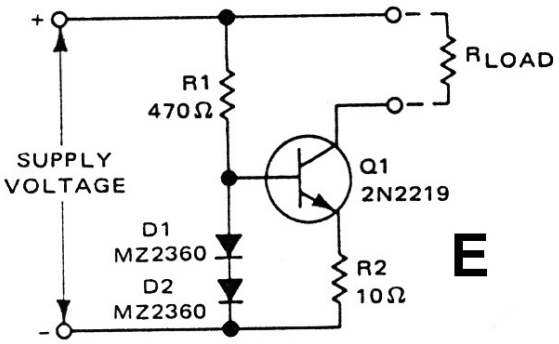
The Current stabilizer stage is essential for the entire tool. For true deliberation, this chapter has to discuss and select the successful design . Many alternatives are given in Fig 5 for the individual investigator to chose from.

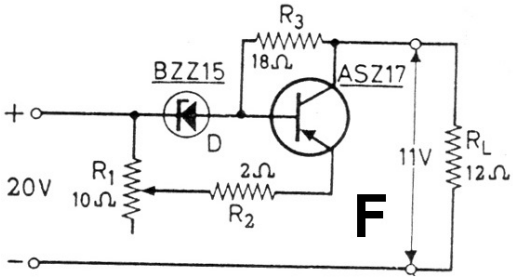


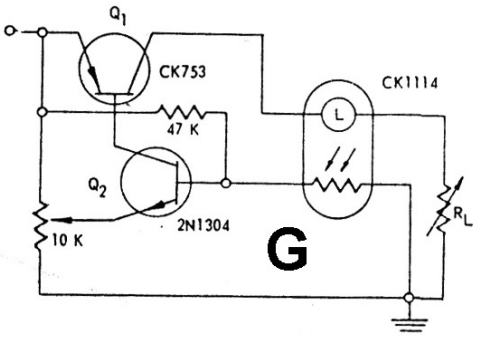


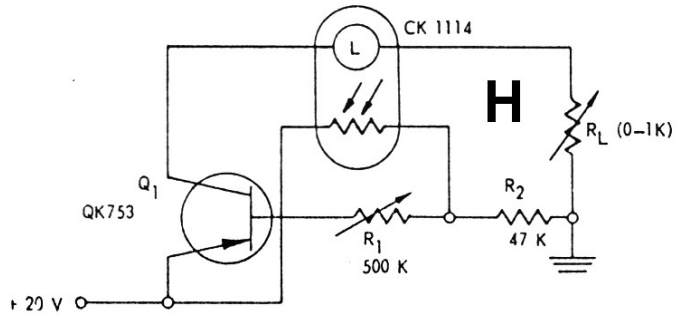












In Fig 5, the collective rule is base polarity remains constant while impedance alternates.

Fig.5A: The rule provides for drop voltage of double diodes (From Semiconductor,Power Circuits Handbook,Motorola,Phoenix, Ariz,1968,P3)

Fig.5B: The same rule applies to one diode. (From Semiconductor Power Circuits Handbook,Motorola,Phoenix,Ariz,1968,P3)

Fig.5C:A diode is used in serial with a zenner diode for more stability. R1 and R2 are operated by the same axle and limit range. Also R3 is a reostat, which provides balance. (Modified from Semiconductor Power Circuits Handbook, Motorola Phoenix,Ariz, 1968,p 3)

Fig.5D: A double zenner diode is used at the base for the same rule. This circuit works as shown in Fig 5C. Cross connected two transistors behave as a limit to current through them selves, because each ones's base polarity is equal to the other's collector polarity. (modified from Philips, Pub.Dept., Elcoma Div.Eindhoven The Neitherlands, No 331 1968)

Fig 5E: The characteristics of this circuit fits to our purposes.(T1= BD244C, R1=33 ê 3W, R2= 2 X 1K 3W pot.(parellel)=500 ê,D1=BZX85 5V6 1W) The zenner diode is the heart of this design. The BZX family is preferable. Under 45 Volts, the current-impedance curve includes a long plateau from 0.01 ê to 1000 ê and 0-40 mA. This plateau protected either DC or pulsation and no distortion to the square wave (delay angle>80). (modified from SCR Manuel 4th Edition, General Electric,1967 p166)

Fig.5F: The same rule is obtained by a zenner diode. (Modified from Philips,Pud Dept.Elcoma Div.,Eindhoven,The Neitherland No 331 1968)

Fig.5G anf 5I: This is the ideal configuration if either will not climb to high frequency or do not need to be above a few mA. Because optoelectronic properties have good sensitivity current flow and the ability to limit over a large spectrum by feed-back. But maximum 40 mA and high frequency behavior is dangerous to the optoelectronic instruments. Besides, the delay angle can decrase when optoelectronic instruments are prefered (< 45ø). This configuration allows a slightly smoother current. (From Raysistor Optoelectronik Devices, Raytheon, Quincy,Mass.,1967 P.23 and 24)

Fig.5H: Operational amplifier may be especially useful for current stabilization using feed-back system, but, in a range which is into stabilisation range , can decrease or increase the frequency. This is an unwanted case, whereas, in the present study, frequency is controlled exactly by the computer.

Some of above diagrams seemed stable over a small spectrum, or distor the signal except in Fig 5E.

Three mechanical relays are designed into the device . On controls the DC/Puls switch, the second controls the voltage variable potentiometers, the third reverses poles and is driven by SP#2. Besides, LEDs show the position of poles in front of panel. Other LEDs show probes on/off, and others tell DC/Pulses.

An ampermeter serves to show current flow with push-pull button on front panel.

Six adequate fuses put critical points for safety. LEDs show which fuse is broken if it collapses. All portions built into a 9.5 x 34.5 x 21 cm metal case and connected tightly to ground.

DISCUSSION :

The future of bioelectrical applications is a promising field. The concept of live tissue exposure to electricity is indeed an

alternative way to treat degenerative or infectious diseases. All of the above related responses of cells corroborate this notion.

Does it have any undesirable effects?, this question has to be replied fairly:

1) Soft tissue may ossify , [44]
2) Vesicules may appear because of opposite loading under cell membrane,
3) Endoplasmic reticulum may become rugged,
4) Membrane potential may break irreversibly,
5) Vacuolisation may arise in mitekondries,
6) The cell may turn 180 ø to electric downstream, hence the unity may be injured [195, 116, 36].
7) DNA stuctural abnormalites, cromosomal distortions may occur,
8) Serum proteins may be disturbed [162, 126, 132, 137, 79].
9) Becker and Esper induced high level negative charge on the surface of neoplastik tumor cells and increased fibrosarcoma cells in vitro in 1981. Lavine and Grodzinsky supported them in 1987.
10) Finally, Some authors said that "Electric cure is a quackery" [4800]

Hence, Electrical stimulation is not a magic wand. But, this fact is known that, the above list of adverse effects begin slightly and gradually when the tissue is exposed for overdose in long periods. This should not discourage further investigation into bioelectric treatment.In contrast, parameters and mechanisms have not been appointed accurately yet. Perhaps, all parameters must be reassessed. The all electrical parameters of the device have to be variable over a large spectrum which will be used during electrical therapy. Hence, the tool increases the investigator's ability regarding potential parameters on electric-treated tissue between variable values.

The nutralization is absolutely necessary by positive polarization for therapy instead of not attempting to cure, if there is a high negative charge on the surface of neoplastik cells. Besides, many investigations are necessary regarding the efficacy on viruses and some degenerative pathologies. More applications would be appeared in the medical arena, because many diseases can be explained by absence of or reduced voltage of tissue and have been labeled as "idiopathic", "spontane", "kongenital" or "essential" by medicine.

The present study shows that, the easily variable parameters entered by typing on keyboard, can be immediately filed; the computer offers precise control, monitoring, pole reversal time controling; universal standardisation (such as IBM). The tool can be provided cheaply and these are indeed advantages for each investigator.

In literature, the first ten devices already used by authors are considered and compared. Information about each one of these has been asked for by letter from their producer companies or from the authors. All replies are appreciated up to the current publication date. Mainly all rights have been sold to commercial companies, and the some of the companies wrote that "It is no longer manufactured or sold" etc.

Apparently, these tools can be difficult to provide to any investigator. The nonstandard parameters, and difficultly providing the tools are indeed obstructive factors for bioelectric studies. Accordingly, many experiments may be postponed or abandoned or a new standard will be born into the bioelectric arena by a new manufacturing. As a result, disputable standardisation parameters will produce adverse effects such as those in the above .

Present study accurately obtained these conclusions:

1) Universal Standardisation (after calibration to own PC),
2) The parameters are able to be input by the keyboard over a large spectrum,
3) Every investigator can easily build or be provided with the tool,
4) The immediate file system is automatic,
5) The parameters are open for statistical analyses,
6) It is cheap and noncommercial.

A further fact is that the electronic stages of AYDIN Apparatus can be evolved by more adept people or companies. AYDIN Appparatus must be thought of as a prototype for future models. Thus, noncommercially, I decided that any investigator, interested in either the program or electronic diagrams, may receive more information of AYDIN Apparatus.

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References:
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