

Computer Control of Electrical Brain Stimulation in the Rabbit

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Bernard G. Schreurs is a graduate student in the Iowa Conditioning Laboratories of the University of Iowa at Iowa City Ia. He expects his Ph.D. in 1983 under Dr. I. Gormezano in the area of the neural analysis of classical conditioning. An Australian citizen and a native of the Netherlands, Mr. Schreurs has extensive experience in the development of computer controlled electrical equipment and in the use of the First computer language. His undergraduate work was completed at the University of New South Wales.

The present report describes a computer-controlled (Apple II/FIRST),¹ independently programmable, eight-channel, constant-current electrical brain stimulation (EBS) system which can stimulate brain site combinations from one site in each of eight animals to as many as eight sites in a single animal.

Our development of a computer-controlled EBS system at the Iowa Conditioning Laboratories (cf.2-¹) has been guided by a desire to determine the neural basis of learning with the rabbit nictitating membrane response (NMR) preparation. Although a number of techniques have been employed to search for the neural substrates of learning (neural recording, lesions, histochemical labeling, autoradiography), one of our principal tactics has involved the use of EBS to determine the functional significance of structures comprising the neural pathways of the rabbit NMR. Specifically, the use of EBS permits the delivery of a discrete, well-defined stimulus to a localizable group of cells in an intact, behaving animal. Moreover, use of the rabbit NMR preparation offers the benefits of a well-understood behavioral response system in which a number of neural pathways, including the final common pathway, have been delineated. Accordingly, EBS can be used to activate identified groups of cell bodies along the anatomical pathways of the rabbit NMR (e.g., pars oralis of trigeminal spinal nucleus) and, thus, has the potential to determine whether such stimulation can: (1) serve as a conditioned stimulus (CS), (2) elicit the NMR, and (3) function as an unconditioned stimulus (UCS) to support classical conditioning of the NMR. Consequently, by using EBS we are in a position to determine more precisely the CS-CR and UCS-UCR pathways of the rabbit NMR and identify specific neural structures that are involved in

conditioning.

For the purposes of exposition, the EBS system, as seen in Figure 1, can be divided into three stages: (1) control, (2) timing, and (3) isolation. The control stage consists of components used for generating data and address signals that are transmitted to the timing and isolation stages. The timing stage is composed of a counter and eight programmable timers each of which can generate timing signals. The counter is used to split the 1-MHz Apple II clock into signals which the timers independently modify into timed pulses. Next, the isolation stage receives the timed pulses and, via digital-to-analog (D/A) converters, the computer-generated specifications of the pulse amplitude. The isolation stage then produces either a monophasic or biphasic pulse train which is transmitted to a constant-current device which, to minimize potential signal distortion, is secured as close as practicable to the site of stimulation. The constant-current device consists of a 100-kohm "sense" resistor and an operational amplifier which are employed together to detect and compensate for any potential impedance changes at the electrode site.

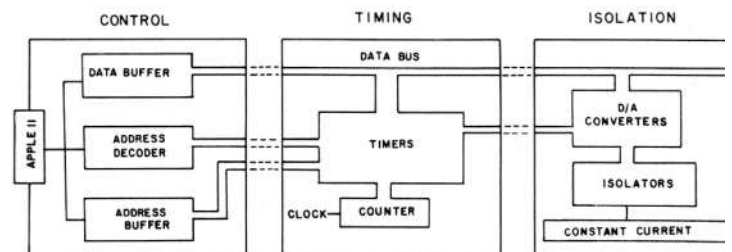


Figure 1. Block diagram of the EBS system.

To operate the EBS system, computer-generated binary values are loaded into the timers and D/A converters which are then activated within a timing loop. The frequency of the pulses and duration of the pulse train are controlled by establishing an appropriate delay between pulses and repeating the timing loop a given number of times. A separate timing loop and individual timers and D/A converters allow for independent control of either monophasic or biphasic pulses for up to eight subjects. Of course, all eight brain sites can be stimulated with the same pulse characteristics simply by programming the same set of binary values into each set of timers and D/A converters.

Once the EBS system is programmed, the experimental procedures are the same as those for any conventional EBS experiment. In our experiments, electrodes constructed of insulated (Epoxy-lite) 00 insect pins were stereotaxically implanted using a Kopf 1760



Editor's Column

this is written. issue is mailed, year will be well and in spite of George looks like it could year. It is also winter in Christmas time set a new cool minus 10 degrees F. It is a weather. We hope that all of the Carrier readers have had a very nice Holiday season and are now happily back in the work spirit. The article in this issue of the Carrier outlines a computer controlled brain stimulator which can activate up to eight brain sites in one animal or one site in up to eight separate subjects. The power of the microcomputer is certainly making itself known. Obviously, this is only the start of the changes to be brought about by these machines. The ability to use and understand microcomputers is rapidly becoming a necessary part of the neuroscientist's skills.

As we mentioned in the previous Carrier, we will publish questions and comments sent to us at the address below. One such question which recently was asked by a Carrier reader had to do with the availability of special stereotaxic equipment from the Kopf company. The reader asked if there was a headholder available for the Golden Hamster. As with a number of such pieces of equipment, the answer was yes. Kopf has specially designed a Hamster headholder as well as a number of other special purpose pieces. Information can be obtained by writing to the company or to the Editor, who will transmit inquiries to the appropriate people at Kopf.

In addition to these special instrument services, Kopf Instruments has published a list of Stereotaxic Atlases. This list is available by writing to the Editor at the address below or by writing direct to Kopf Instruments. We would like to update this list and ask that you inform us of any additional atlases that you know about which are not on the list or which have been recently published. Please send this information to the Editor.

If you have comments or questions about material in the Carrier, please send them to the Editor at the address below. Also, if you would like to write an article for the publication, let us know about it. We will be pleased to discuss any ideas with you and give help in any way we can in preparing the manuscript. We will publish articles of general interest to the Neuroscience community, including short commentaries, and questions and answers when appropriate.

We hope you are having a good start in this especially auspicious New Year,

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Computer Control (Continued)

manipulator in conjunction with a Kopf 1275 collet electrode holder. Once in place, each electrode was cemented to two stainless-steel screws which had been threaded into the skull. When the cement was dry, a female Amphenol pin was secured to a length of stainless steel wire previously soldered to the electrode. A second female Amphenol pin was connected to a length of wire attached to a stainless-steel screw which was threaded into the nasal bone and served as the indifferent electrode. The two female Amphenol pins were then inserted into an assembly consisting of an Amphenol connector and a Plexiglas block. The entire assembly was then cemented to the skull to form a platform upon which the constant-current device and an NMR transducer could be mounted.

In order to document the capabilities of our EBS system, we undertook an examination of the functional significance of pars oralis of the trigeminal spinal nucleus (TRIG). The examination consisted of stimulating TRIG with a range of values from each of the stimulation parameters provided by the EBS system (pulse amplitude, pulse width, frequency, and pulse train duration) and measuring a number of dependent variables of the NMR (amplitude, area, latency, frequency). For purposes of illustration, we have chosen to discuss the NMR amplitude data.

Panel a of Figure 2 reveals NMR amplitude to be an increasing function of pulse amplitude (25,35,50,60, 70, 80, 90,100 microA) and train duration (10, 20, 40 msec) at a pulse width of .1 msec and frequency of 1,000 Hz. Panels b and c of Figure 2 show, for pulse amplitudes of 35 and 70 microA, respectively, that at a train duration of 20 msec, NMR amplitude is an increasing function of frequency (250, 500,1,000 Hz) and pulse width (.1, .2, A msec). Clearly, the data indicate that the NMR varied systematically over an extensive range of each of the stimulating pulse characteristics manipulated.

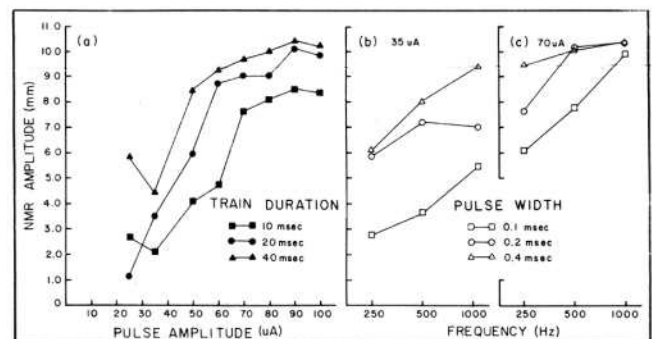


Figure 2. Panel a presents NMR amplitude as a function of pulse amplitude and train duration at a .1-msec pulse width and frequency of 1,000 Hz. Panels b and c present NMR amplitude for pulse amplitudes of 35 and 70 microA, respectively, as a function of frequency and pulse width.

In sum, our EBS system allows us to stimulate independently up to eight animals and manipulate values along the dimension of pulse amplitude, width, frequency, and train duration. Consequently, a number of sites can be concurrently stimulated while the characteristics of the stimulation are under complete software control.

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New Products

The 980 Rat Spinal Unit is shown in Fig. 3.

This instrument features a new 24" x 12" x 1" slotted base plate. One end of this plate contains the hole pattern necessary to mount a Model 900 Small Animal Stereotaxic Instrument.

The new unit will include: Seven #982 Adjustable Base Mounts with Post and Clamp, one pair #985 Hip Spikes, one #986 Vertebrae Clamp, one pair #987 V-Notch Spikes, and one pair of #988 Retractors. Optional accessories include: #982 Calibrated Bar and Brackets, that will accept 1760 or 1460 Series manipulators. Please specify bar size when ordering.

This new Rat Spinal Unit is available at no increase in cost to our customers.

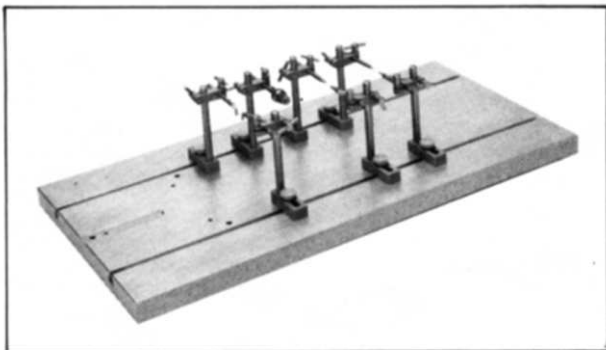


Figure 3. 980 Rat Spinal Unit.

Platinum-Iridium Heater Filaments -VS- Coils

It is easier to control the heating of a pipette with a ribbon filament than with a heater coil. Approximately 180° of the coil has one turn more than the other 180°, resulting in uneven heating of the pipette.

A proper filament will allow one to form a glass pipette at lower current and will result in more concentric heating of the pipette.

Two conditions that affect the pipette are the width of the filament and the proximity of the filament to the pipette. A wide element gives longer taper than the narrow element. The major control factor in forming pipettes is heat.

The "U" of the filament needs to be deep enough to allow even heating of the glass (approximately 10mm deep). The glass should be positioned approximately 1/3 of the way into the loop and equal distance between the two sides of the filament. See Fig. 4.

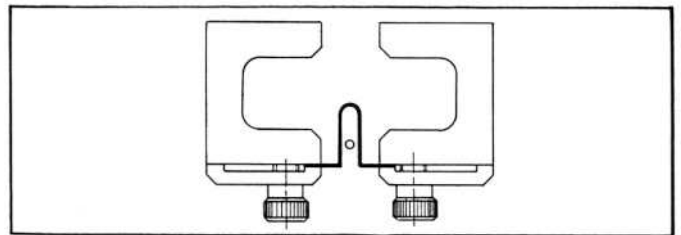


Figure 4. Drawing of Pipette Placement in Platinum Filament shown in Heater Bracket No. 706.

Forming Tool

Allows one to form their own platinum iridium filaments from sheet stock and is a quick' easy way to properly form filaments purchased from David Kopf Instruments. See Fig. 5.

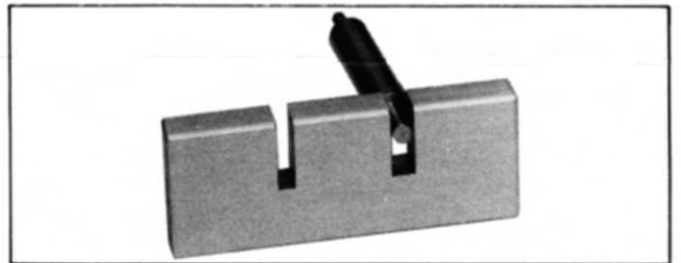


Figure 5. Forming Tool No. 702.

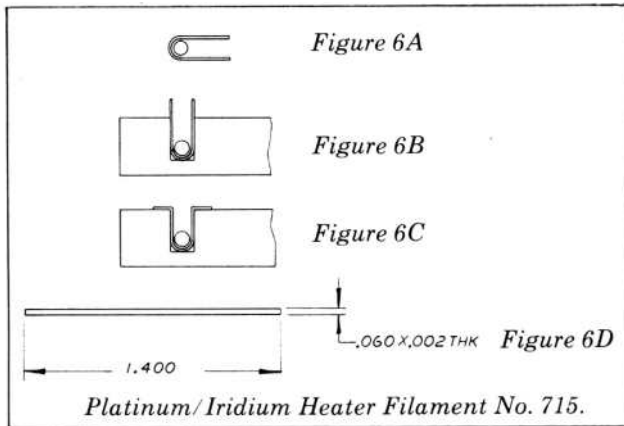
How To Use The Forming Tool:

The forming tool is a flat plate with two different size slots and an arbor with diameters turned to fit these slots. A pre-cut platinum-iridium filament 1.400" long is formed into a "U" shape over one of the diameters of the arbor (Fig. 6A) and inserted into the proper slot (filament must be formed so the two ends are equal). Fig. 6B. While the filament and arbor are in the slot, bend the ends sticking up out of the slot flat against the edge of the forming tool. Fig. 6C. The filament may now be picked up with forceps and placed carefully in the heater bracket making sure the filament sides are centered, and as parallel as possible.

Cont. Back Page

Forming Tool (Continued)

Platinum-iridium heater elements are available in 1.5 x 35.6mm and 3.0 x 35.6mm widths. Sheet stock is also available. Sheets are .002" x 1.400". Minimum order length is 1.5".



New Products (Continued)

700D-CK-A

This kit allows one to install a plastic cover on any 700C Vertical Pipette Puller. Kit is complete with hinge, smoked acrylic cover, magnetic latch, epoxy, necessary hardware and instructions. To install a cover on your 700C puller, it will be necessary to drill two holes in the metal hood. Tools needed are (Vv,") drill, screwdriver and pliers.

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