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AN ANALOG COMPUTER MECHANIZATION OF THE HODGKIN-HUXLEY EQUATIONS

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Application of Information Theory to the
Nervous System

H.D. Landahl
Principal Investigator

AN ANALOG COMPUTER MECHANIZATION OF THE HODGKIN-HUXLEY EQUATIONS

By

Hugo M. Martinez

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The University of Chicago

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ABSTRACT

The Hodgkin-Huxley equations describing the action potentials for giant squid axons have been mechanized on the University of Chicago analog computer (Beckman EASE 2132) for the purpose of simulating a variety of experimental situations. The mechanization is described together with the following results: 1) response to constant currents ranging from theshold to saturation, 2) response to a 100 cps sinusoidal current at two amplitudes and two phases, and 3) the effect of removing the potassium current term.

I. Mechanization of the Hodgkin-Huxley Equations.

The Hodgkin-Huxley equations (1952) describing the relation between membrane current I and membran potential V (measured from resting value) are given by

$$-C_M \, dV/dt = \bar{g}_k n^4 (V - V_k) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_L (V - V_L) - I$$

$$dn/dt = \alpha_n - (\alpha_n + \beta_n) n$$

$$dm/dt = \alpha_m - (\alpha_m + \beta_m) m$$

$$dh/dt = \alpha_h - (\alpha_h + \beta_h) h$$

$$\alpha_n = 0.01 (V + 10)/ \left[\exp(\tfrac{V+10}{10}) - 1 \right]$$

$$\beta_n = 0.125 \exp(V/80)$$

$$\alpha_m = 0.1 (V+25)/ \left[\exp(\tfrac{V+25}{10} - 1 \right]$$

$$\alpha_h = 4 \exp(V/18)$$

$$\beta_h = 1/ \left[\exp(\tfrac{V+30}{10}) + 1 \right]$$

where

V = membrane potential (mv) measured from resting value

C_M = membrane capacity (μ f/cm^2)

I = membrane current (μ amp/cm^2)

V_k = potassium Nernst potential (mv) measured from membrane resting potential

V_{Na} = sodium Nernst potential (mv) measured from membrane resting potential

V_L = equivalent leakage potential (mv) measured from membrane resting potential

$\bar{g}_K$ = potassium conductance constant (m mho/cm^2)

$\bar{g}_{Na}$ = sodium conductance constant (m mho/cm^2)

$\bar{g}_L$ = leakage conductance constant (m mho/cm^2)

m,n,h = dimensionless variables with values between 0 and 1

α_n, β_n, α_m, β_m, α_h, β_h = rate constants which are membrane potential dependent.

Time t is in milliseconds.

The following values of conductance and potential were chosen:

$\bar{g}_k$ = 36 | V_k = 12

$\bar{g}_{Na}$ = 120 | V_{Na} = -115

$\bar{g}_L$ = 0.3 | V_L = -10

The initial mechanization of the above equations on the University of Chicago analog computer proved to be unstable as was indicated by repetitive firing when the membrane current I was set equal to zero. A stability analysis of the equations was accordingly conducted, showing that optimum scaling and programming would have to be achieved in order to obtain stability and reliable results in the presence of the inherent noise and error of the computer. The consequent mechanization, especially designed for minimizing the principal error due to non-linear components and noise yielded and required stability and solutions matching those of digital computers. In particular, the table of threshold excitation current vs. duration as obtained by Cole, Antosiewicz and Rabinowitz (1955) on the SEAC computer was reproduced to within three significant figures.

Shown in Fig. 1 is the computer mechanization with the pertinent nomenclature and details. Fig. 2 is the action potential obtained for an excitation current pulse of 1500 μ amp amplitude and 10 μ sec duration. The time scale chosen was 1 msec real time = 1 sec machine time.

2. Response to constant currents.

Figs. 3a through 3r show the membrane potential in response to a series of constant current pulses ranging in magnitude from 1.220 to 200 μamp/cm^2. Fig. 3a corresponds to 2.220 μamp/cm^2 and, as seen, no action potential is generated for this magnitude of stimulating current. A single action potential is generated at 2.230 μamps/cm^2 (Fig. 3b), three action potentials at 6.100 μamps/cm^2 (Fig. 3e), and then repetitive firing occurs for currents of from 6.300 to 160 μamps/cm^2 (Fig. 3f to Fig. 3p). At currents of 180 μamps/cm^2 and above the response is that of single action potential followed by a series of damped ones. At this stage the response is very much like that of an overdamped 2nd order system.

Other than the qualitative features shown by these responses it is possible to abstract the relation between amplitude of constant current and frequency of firing. This frequency may be taken as corresponding to the time between the first two action potentials or the time between successive action potentials in the steady state of repetitive firing.

3. Response to Sinusoidal currents.

From the response to constant currents, sinusoidal responses may be expected to exhibit a sensitivity to the amplitude and phase of the driving sinusoidal current. A frequency corresponding to approximately 100 cps was used to indicate this sensitivity. Fig. 4a shows the response to sine wave of 100 cps of rms amplitude equal to 6.2230 μamps/cm^2. After an initial transient condition repetitive firing occurs at every other cycle. In Fig. 4b the amplitude of the driving sine wave has been increased to five times that of Fig. 4a. Now firing occurs at every cycle. Figs. 5a and 5b show the analogous response to a cosine wave.

It is planned to make a more extensive study of sinusoidal responses in the frequency range of from 50 to 1000 cps in order to obtain an empirical relation between response frequency vs. driving frequency, phase and amplitude. Anticipated at large amplitudes is a response corresponding to an overdamped 2nd order system.

4. Effect of Removing the Potassium Current Term.

Upon removal of the potassium current term the system sought a new equilibrium value for V of approximately 35 mv, but it was in general unstable. Stability was recovered by increasing the leakage conductance coefficient $\bar{g}_L$ to ten times its normal value and the equilibrium value of V returned to zero. This would not be accomplished by a change in the sodium Nernst potential. Moreover, it was necessary to consider the term $\bar{g}_L (V - V_L)$ in the form $aV - bV_L$ and let $a = 10 \bar{g}_L$ and $b = \bar{g}_L$, with $\bar{g}_L$ its normal value. This is a combination that worked and it was possible to generate an action potential with a current pulse of 2000 μamp/cm^2 and 0.01 msec duration. This response is shown in Fig. 6. For values of a less than 10 $\bar{g}_L$ an action potential could still be produced but V could not be made to return to its initial value.

Action potentials in the absence of internal and external potassium have been reported in the literature, T. Narahashi (1963). It was with the intention of attempting to simulate the results in this article with the Hodgkin-Huxley equations that this extreme and simplest case was investigated. The indications thus far are that a change in the leakage conductance term will play a dominant role. Planned is a series of computer runs corresponding to various ratios of internal and external potassium concentrations.

We would like to gratefully acknowledge the very able assistance of Mr. George Angwin of the Analog Computer Lab., Dept. of Radiology, and also the encouragement and cooperation of Dr. L. S. Skaggs, Director of the Laboratory.

LIST OF FIGURES

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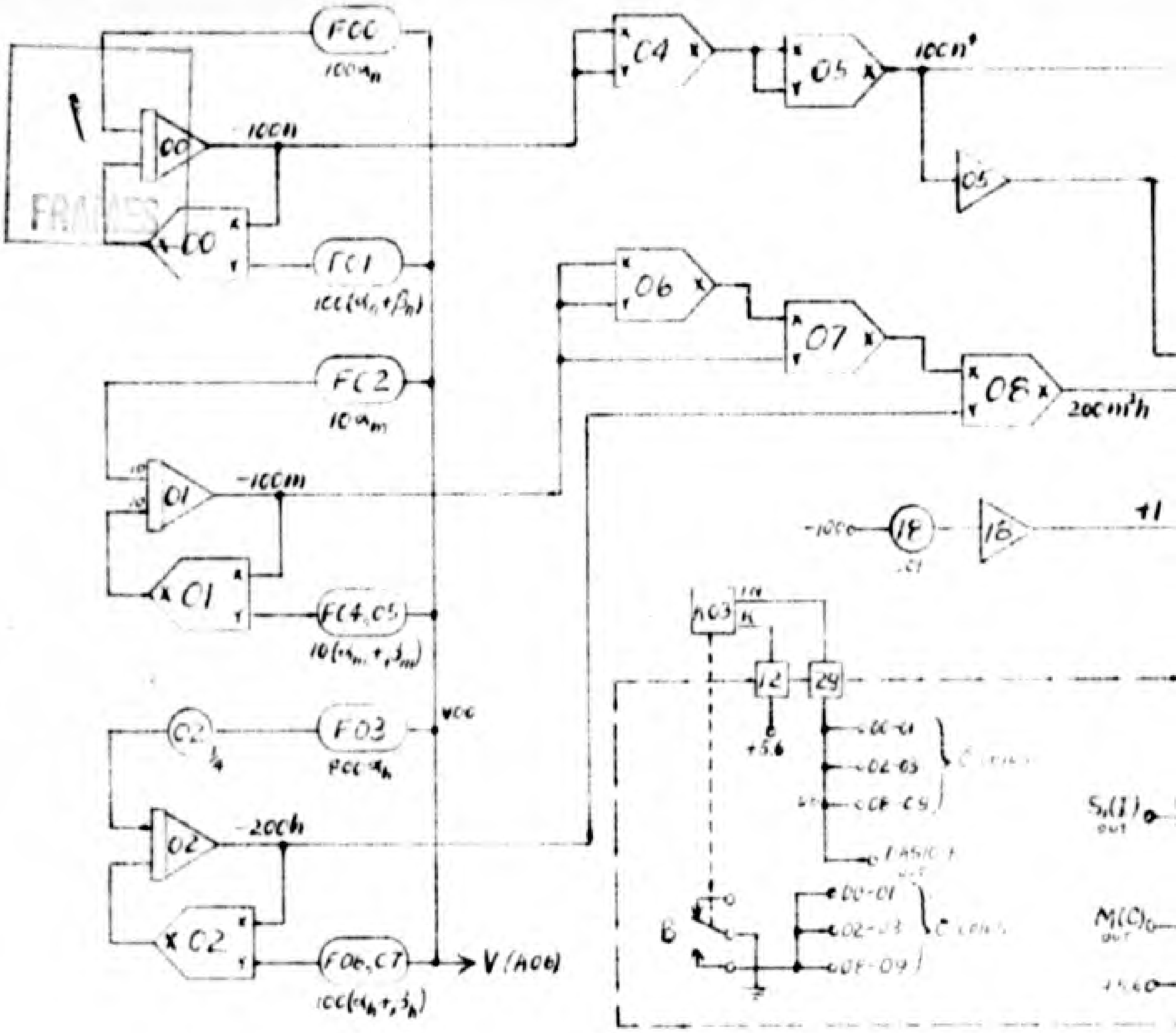
Cole, K.S., H.A. Antosiewicz and P. Rabinowitz. 1955. "Automatic Computation of Nerve Excitation". Jour. of the Society for Industrial and Applied Mathematics, 3, 153-172.

Hodgkin, A.L. and A.F. Huxley. 1952. "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve." Jour. Physiol. 117, 500-544.

Narahashi, T. 1963. "Dependence of Resting and Action Potential on Internal Potassium in Perfused Squid Giant Axons." Jour. Physiol. 169, 91-115.

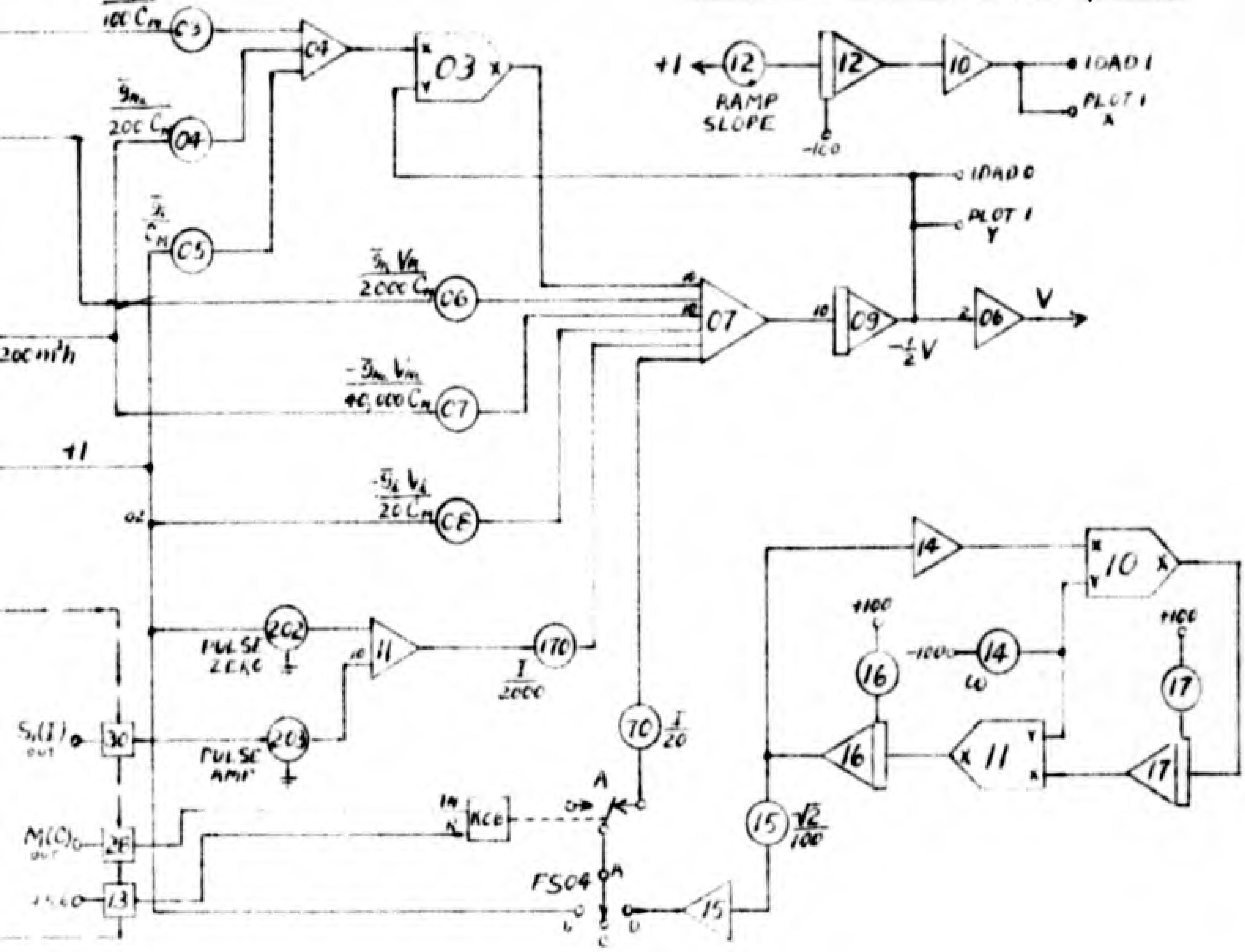


NOTES: 1. IDACAS settings:

	M	S_1
I	01	(pulse period) - (pulse duration)
H_I	01	ZERO
C	EXT coin	pulse duration
H_C	01	ZERO
START MODE	C	C

2. Integrators 00, 01, 02 and 09: hold their voltages in POT SET an
are computing in all other modes.
The $\bar{C}$ coils are closed in POT SET to provide loading for the po
K03 opens the C coils in POT SET to prevent grounding the grids

FIGURE 1 - HODGKIN-HUXLEY EQUATIONS



tion)

SET and HOLD;
modes.
the potentiometers.
e grids of the amplifiers.

3. To set P 202 and P 203: adjust P 202 for OV out of All in STANDBY;
   switch S_1 C COIN to EXT and adjust P 203 for 100 V out of All in COMPUTE;
   repeat.
4. FS04: UP - constant current (zero P 170)
   CENTER - pulses
   DOWN - sine wave current (zero P 170)
5. K06 applies the signal selected by FS04 to the circuit during COMPUTE

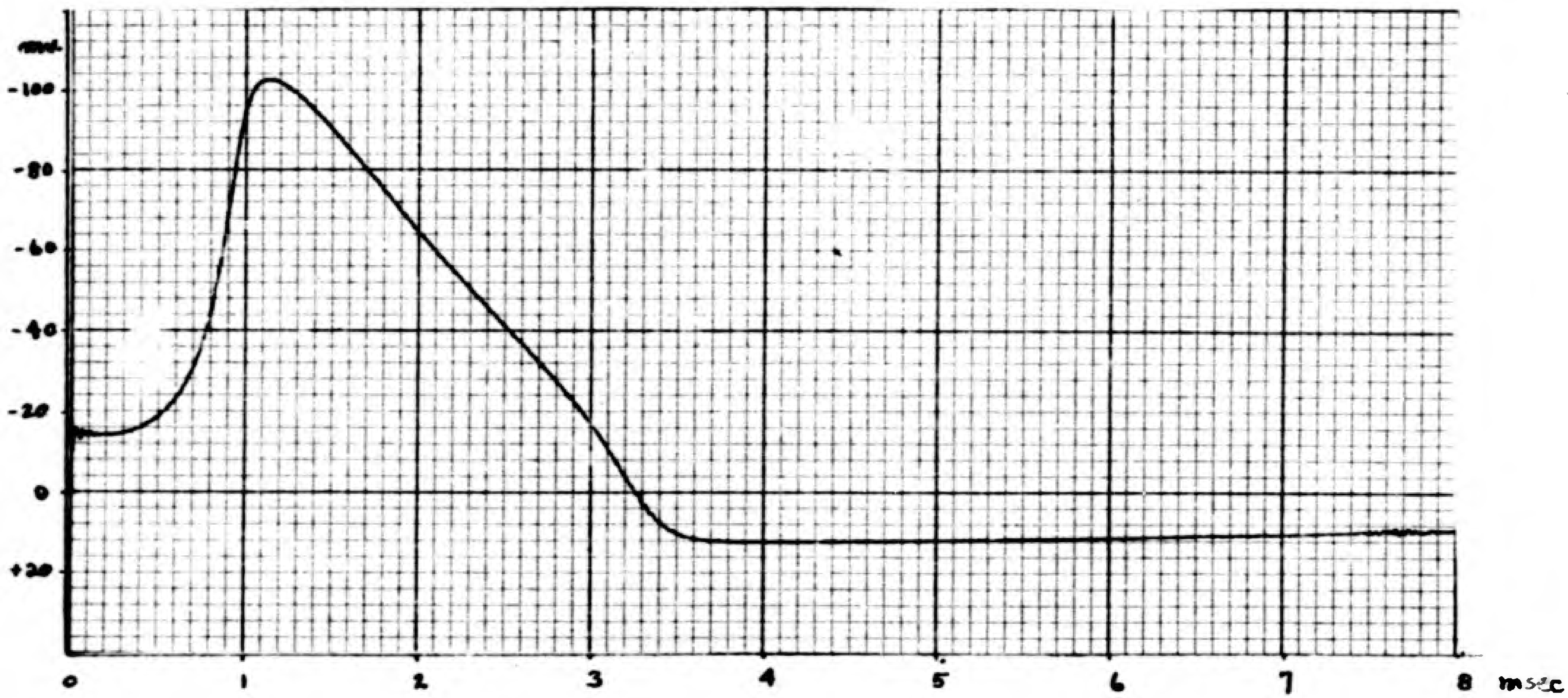


FIGURE 2

FIGURE 3a

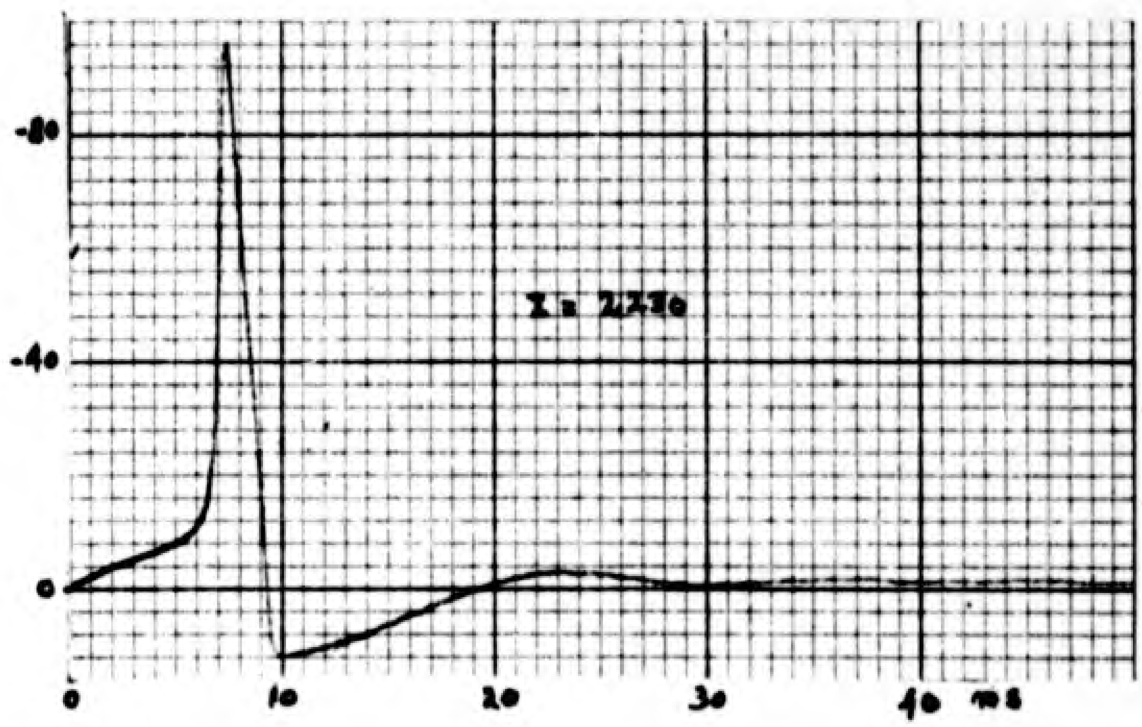


FIGURE 3b

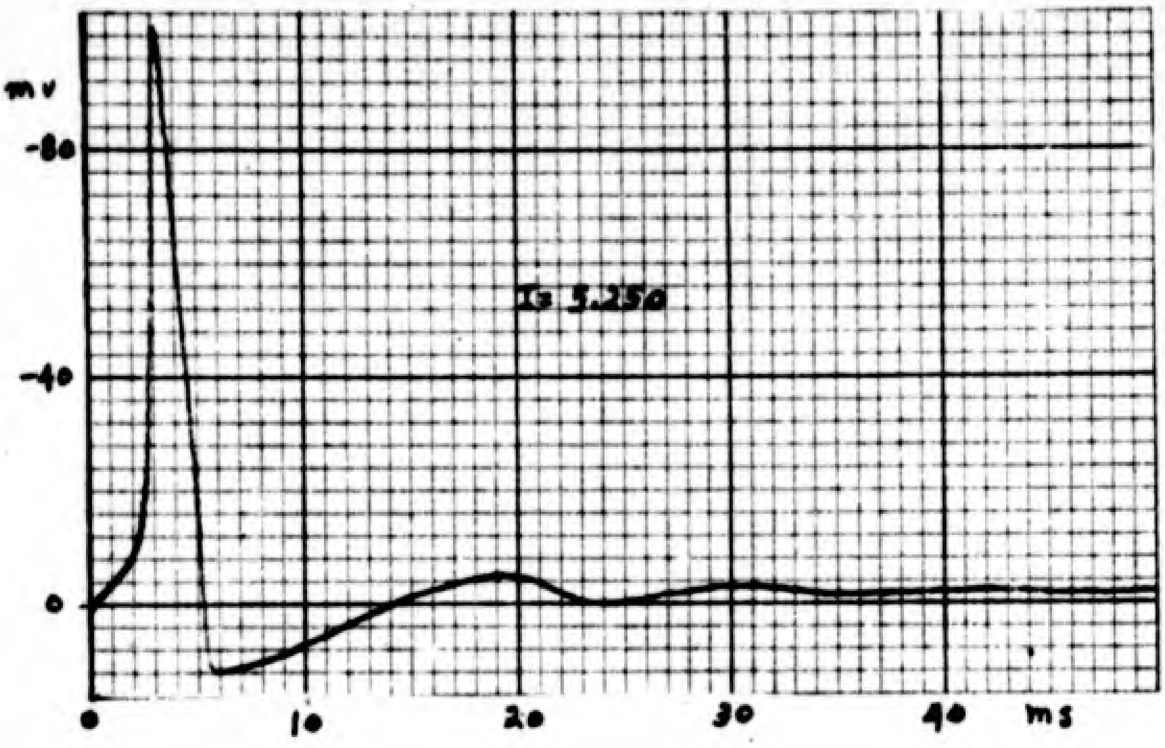


FIGURE 3c

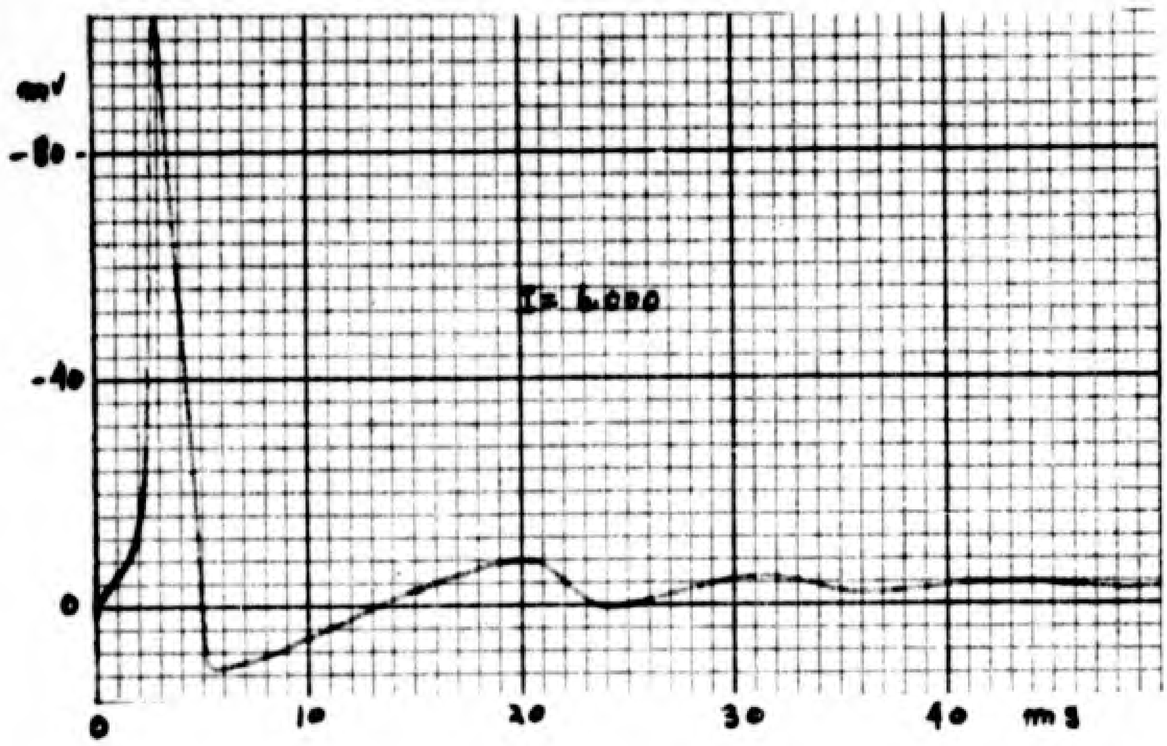


FIGURE 3d

FIGURE 3e

FIGURE 3f

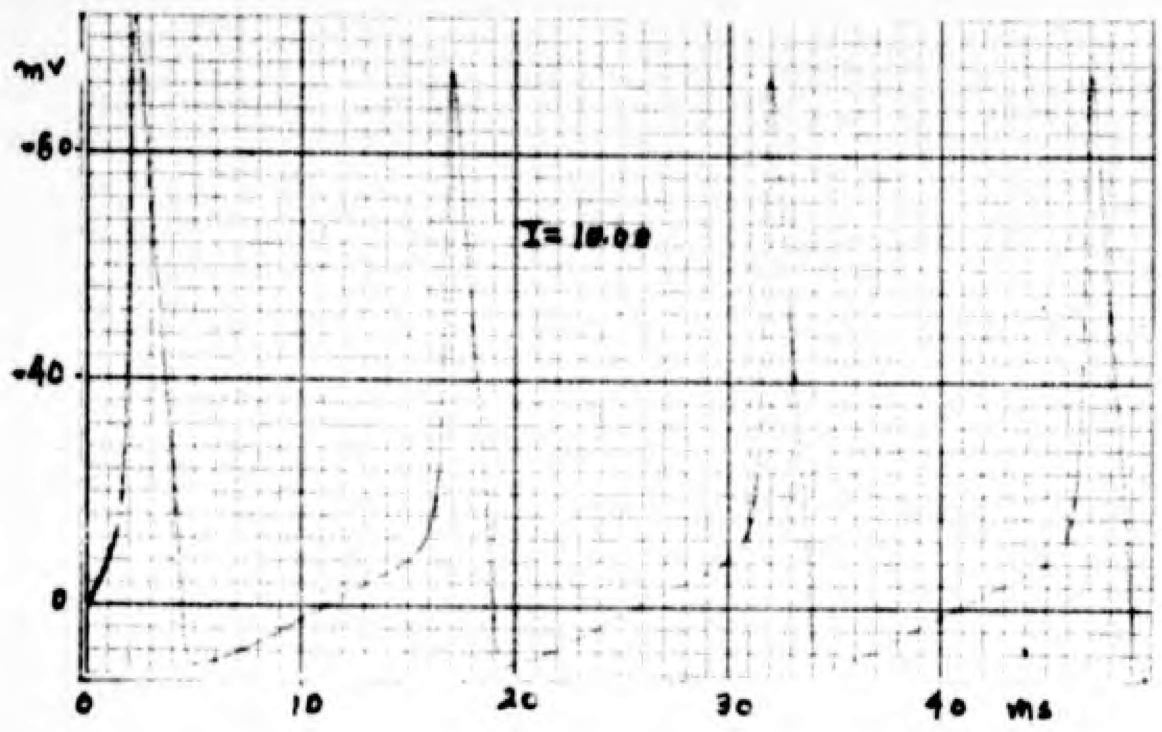


FIGURE 3g

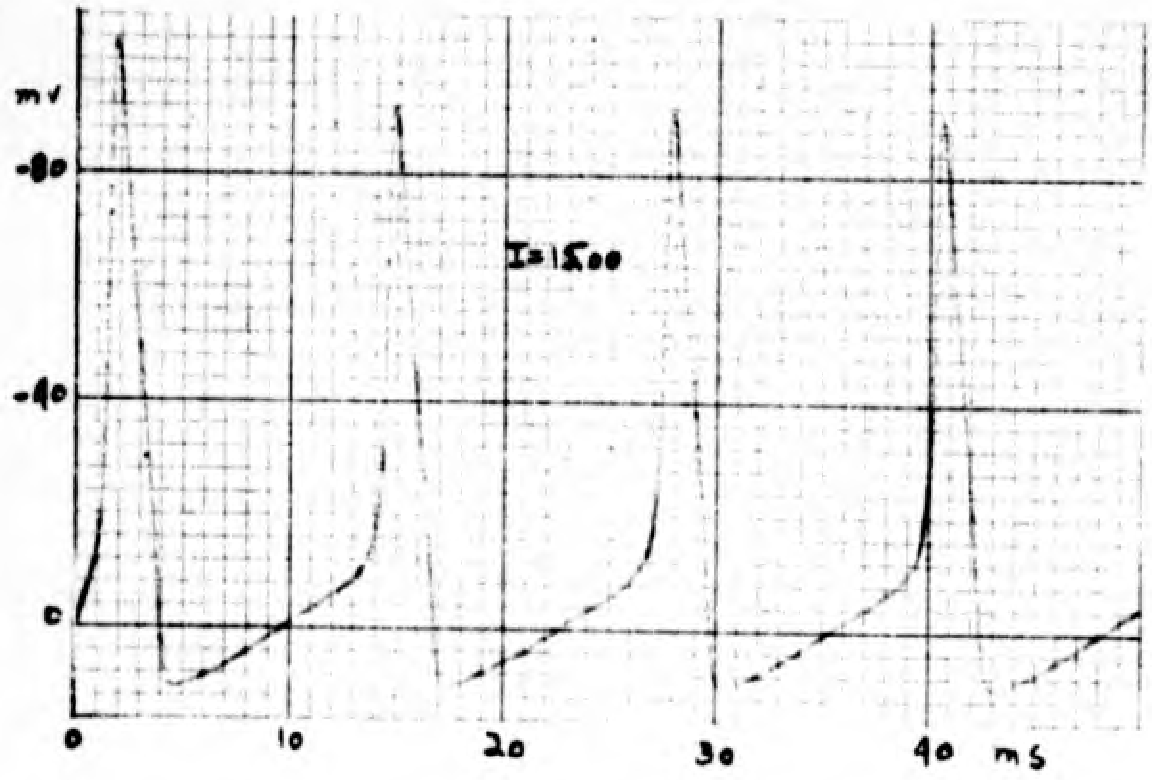


FIGURE 3h

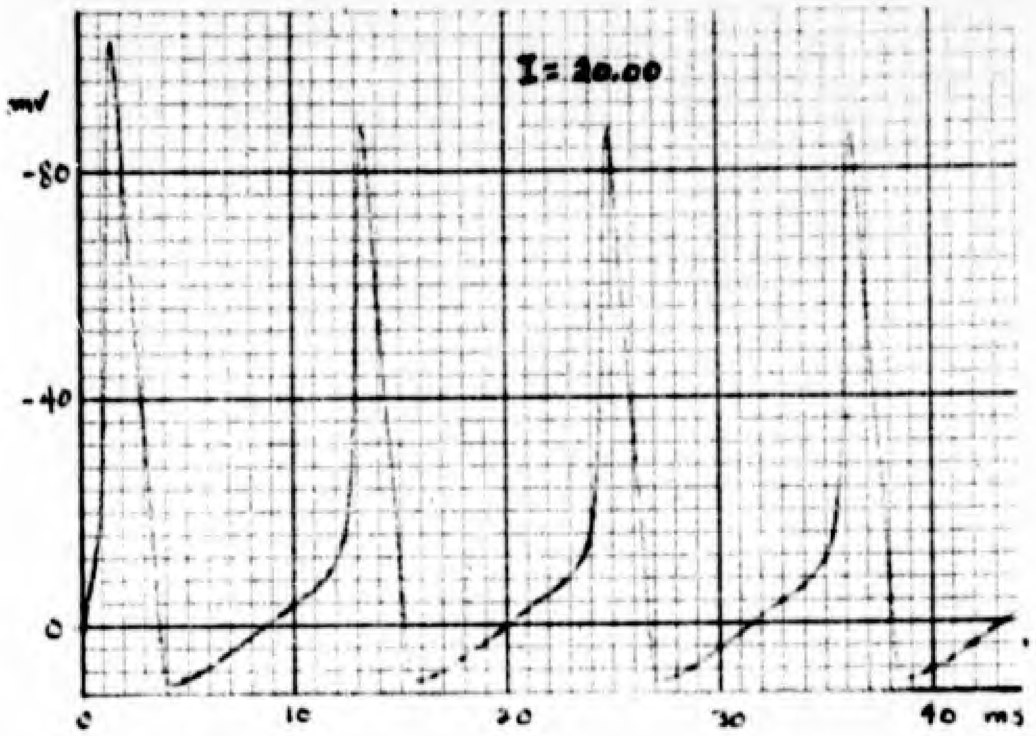


FIGURE 3i

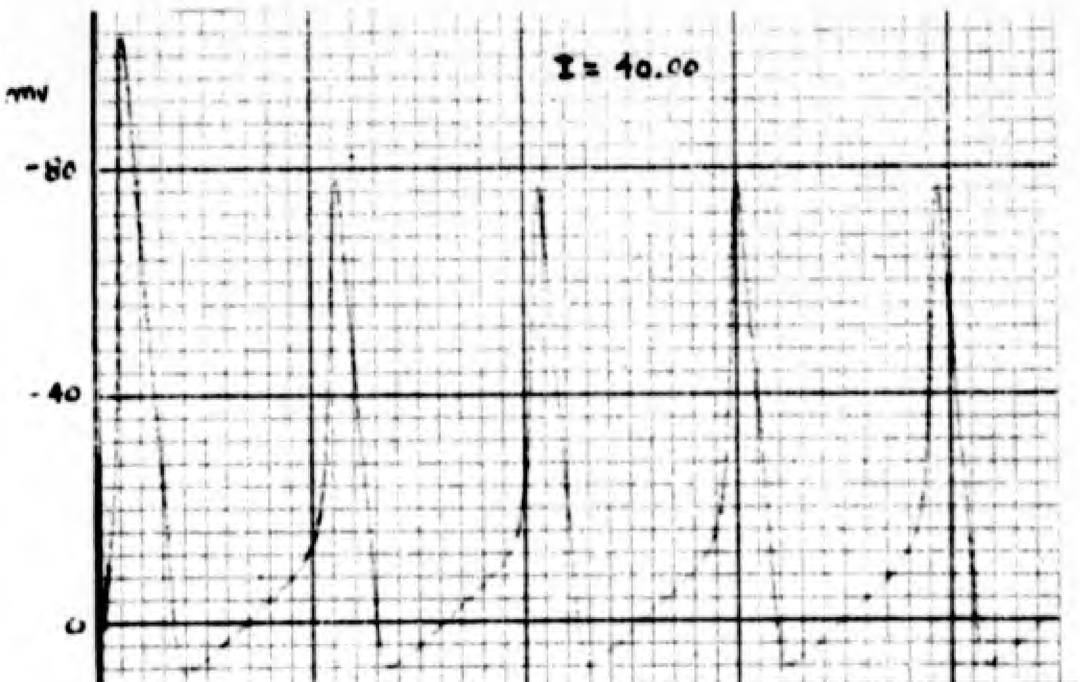


FIGURE 3j

FIGURE 3k

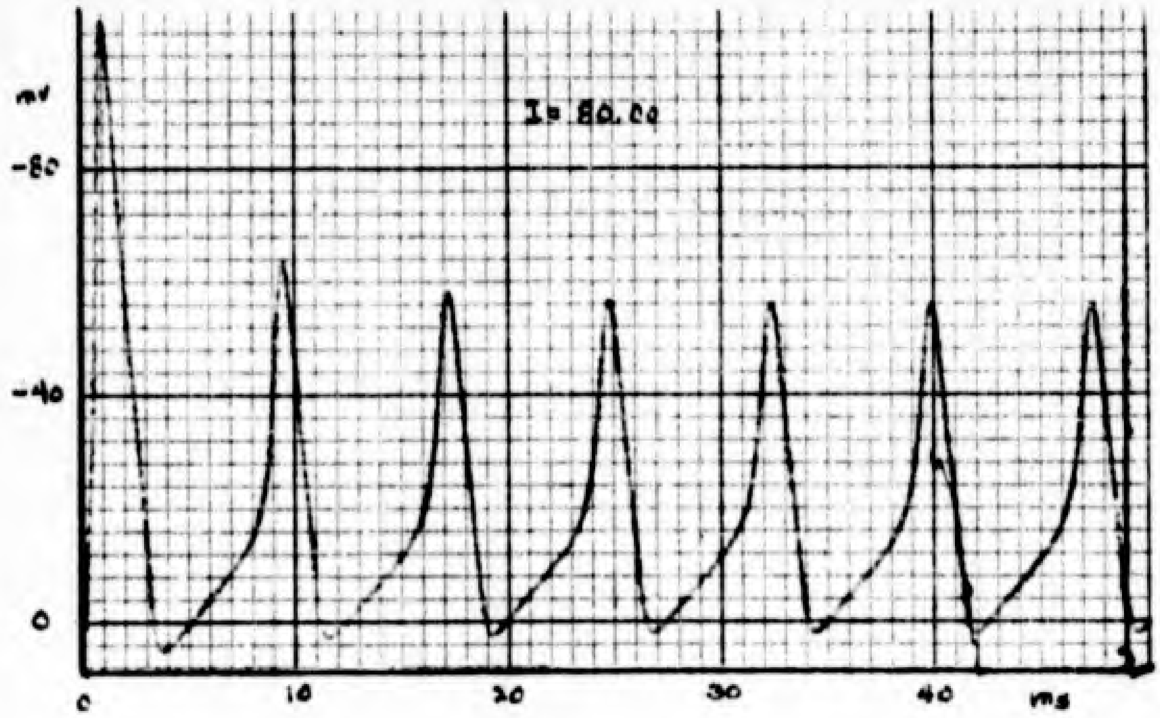


FIGURE 31

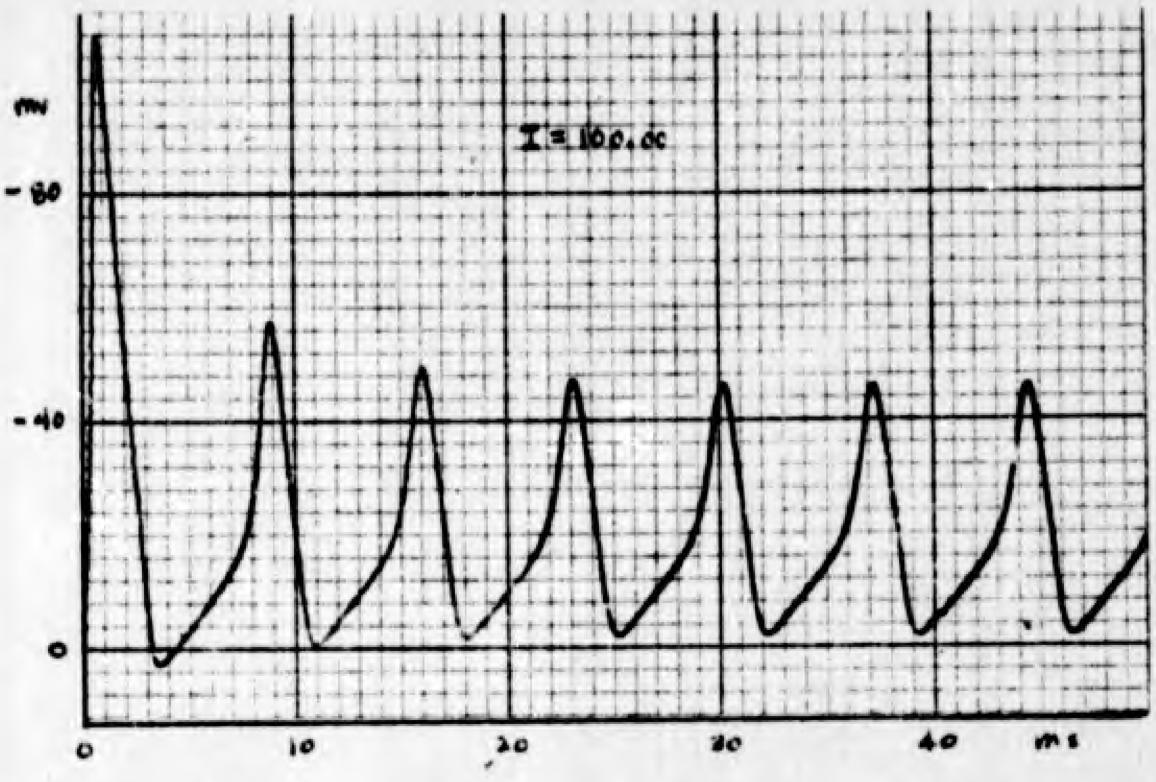


FIGURE 3m

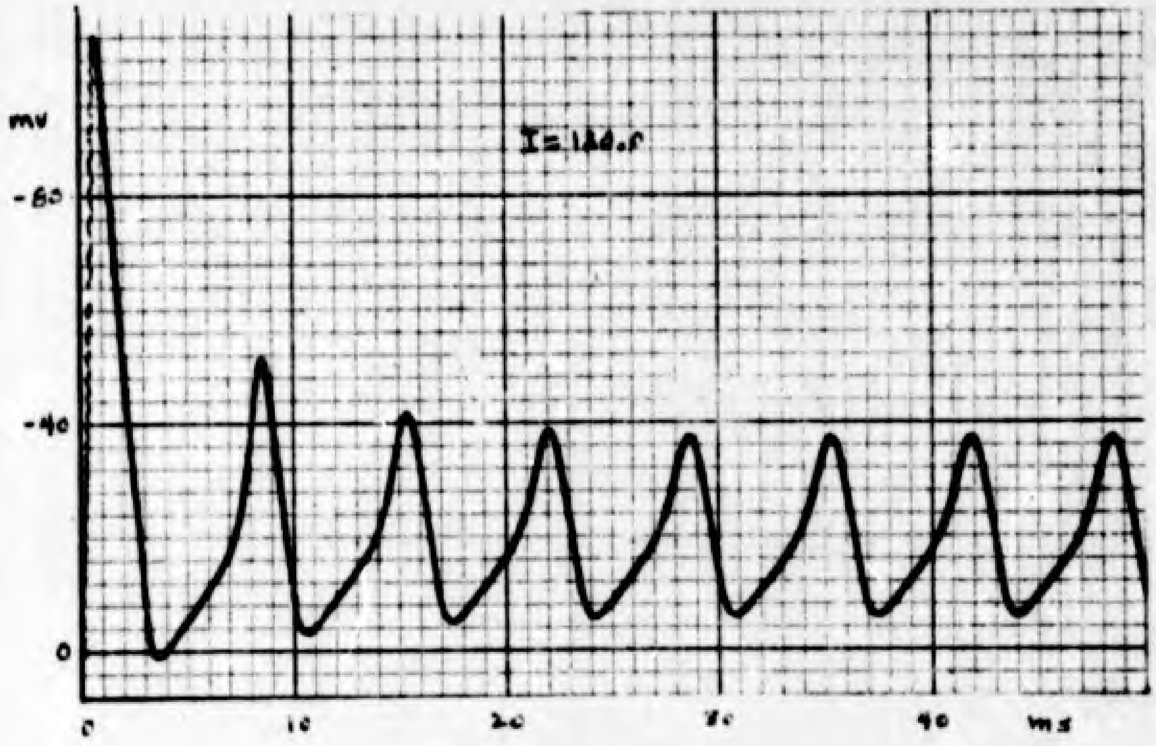


FIGURE 3n

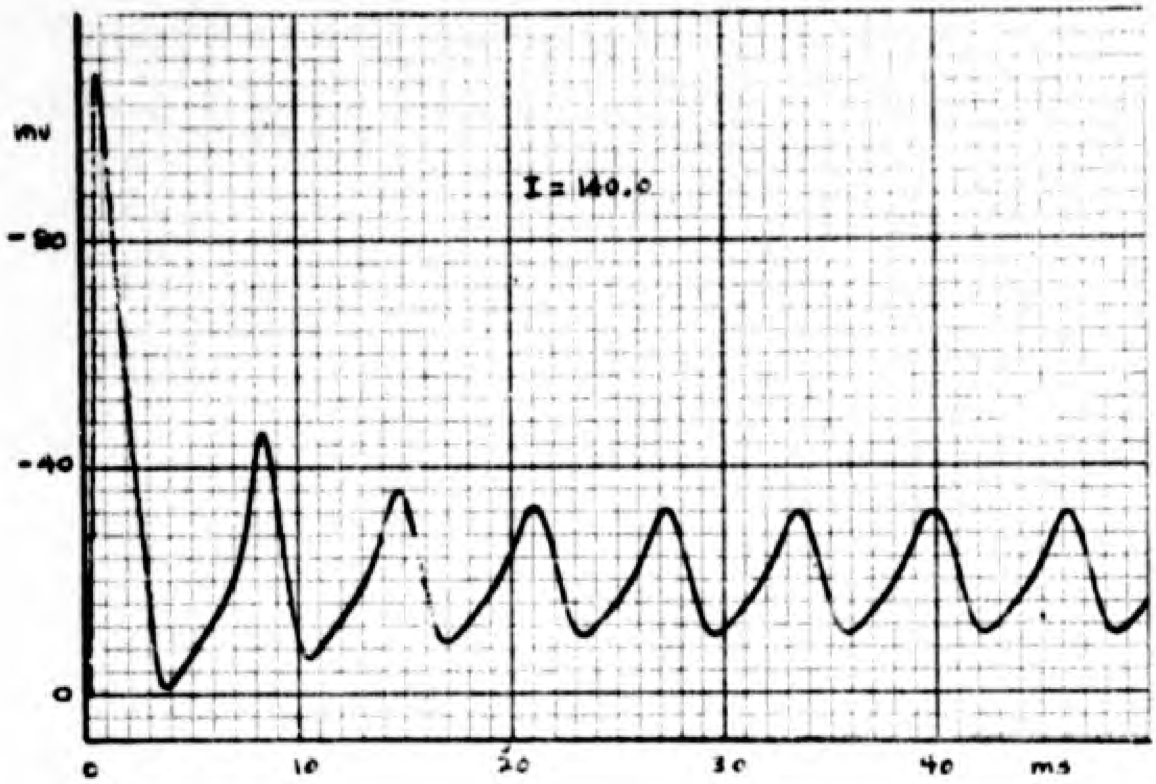


FIGURE 3o

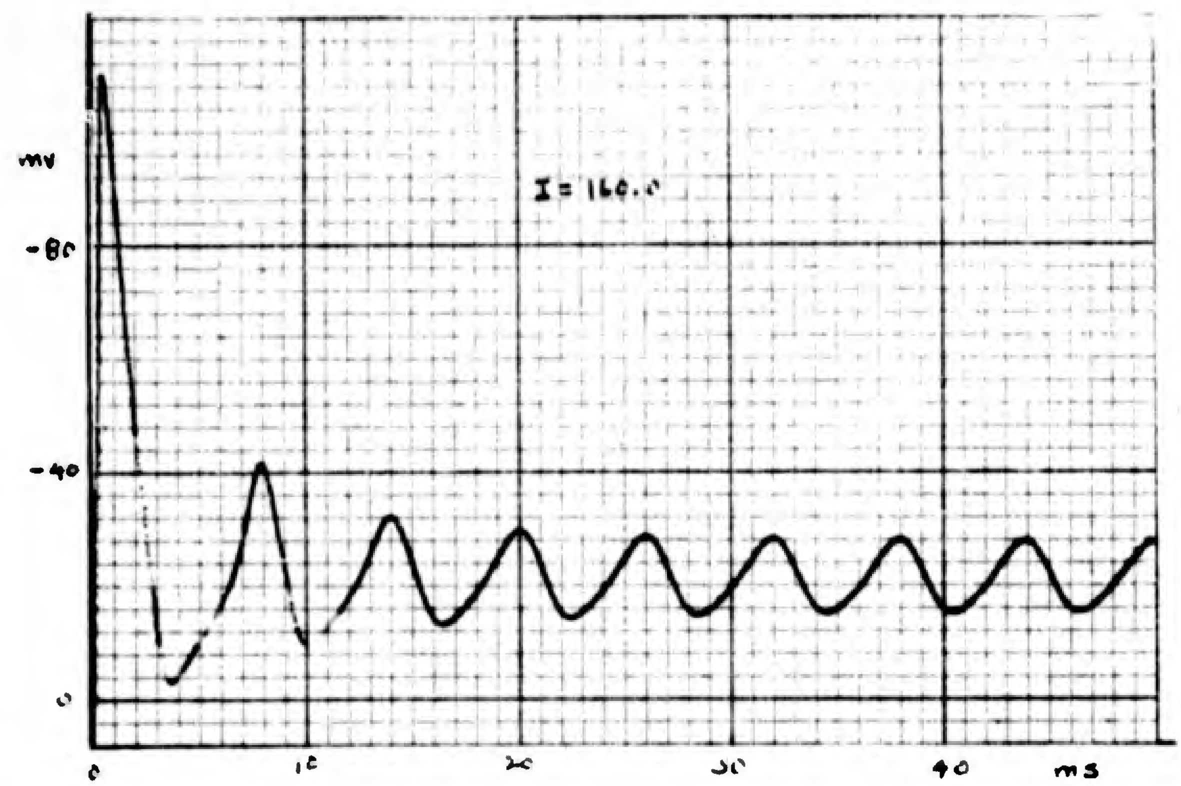


FIGURE 3p

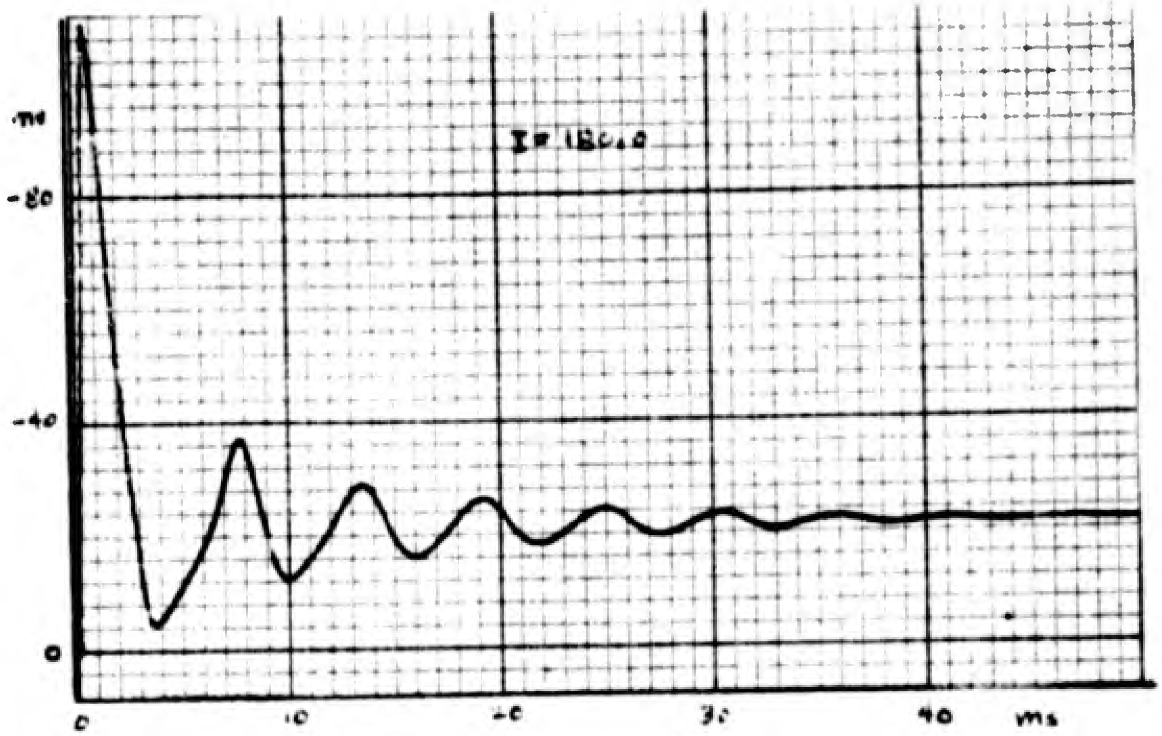


FIGURE 3q

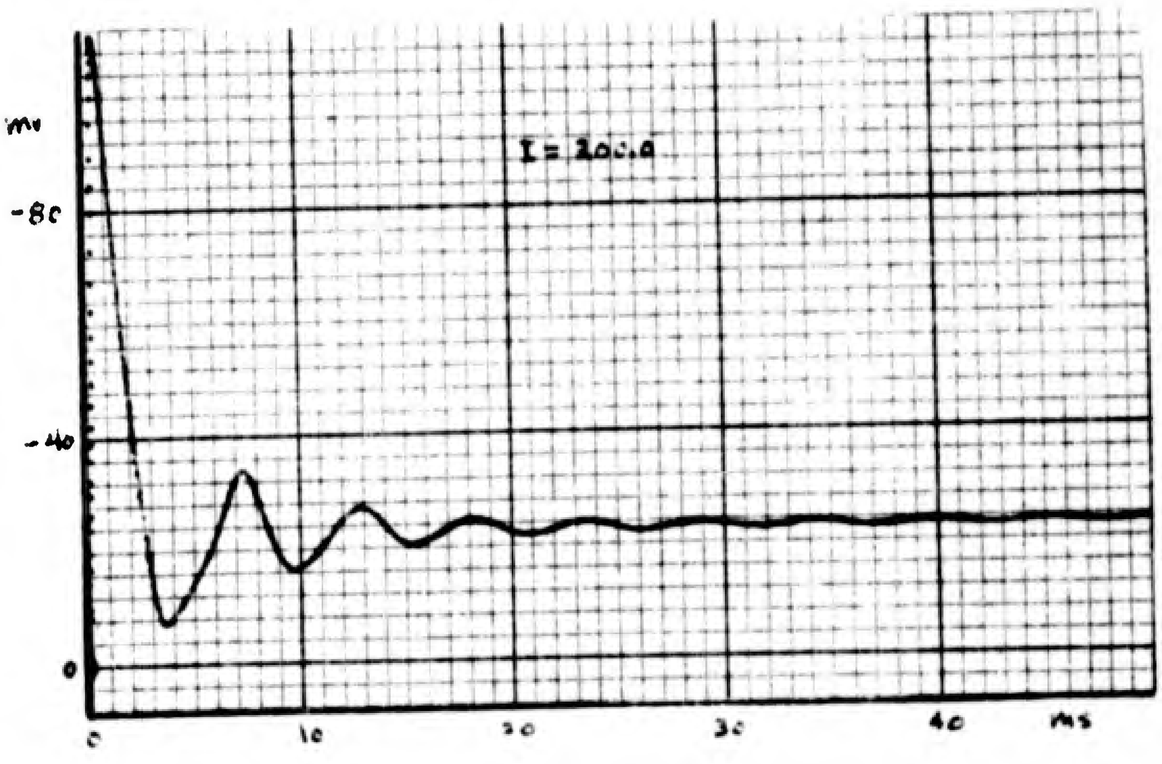


FIGURE 3r

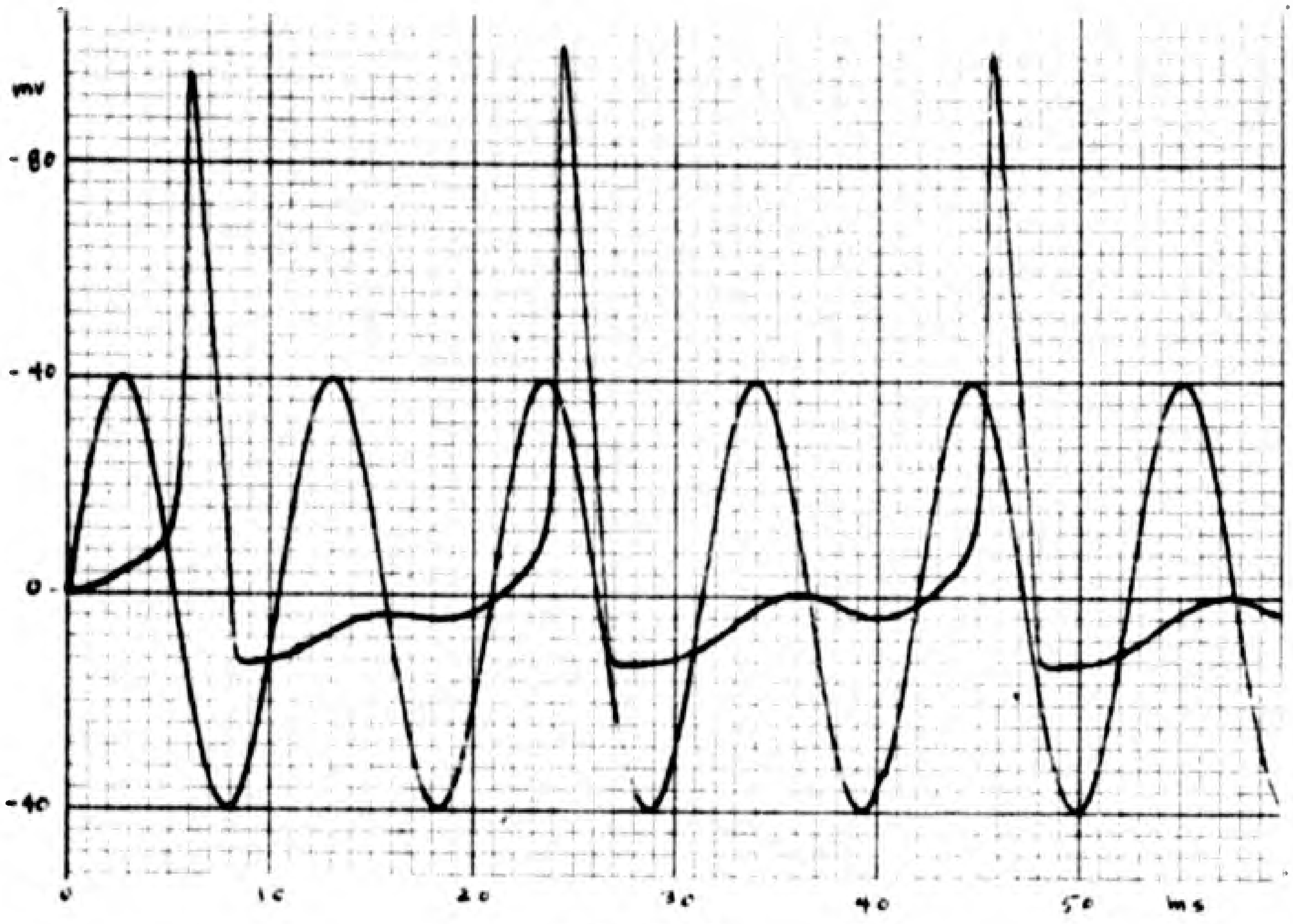


FIGURE 4a

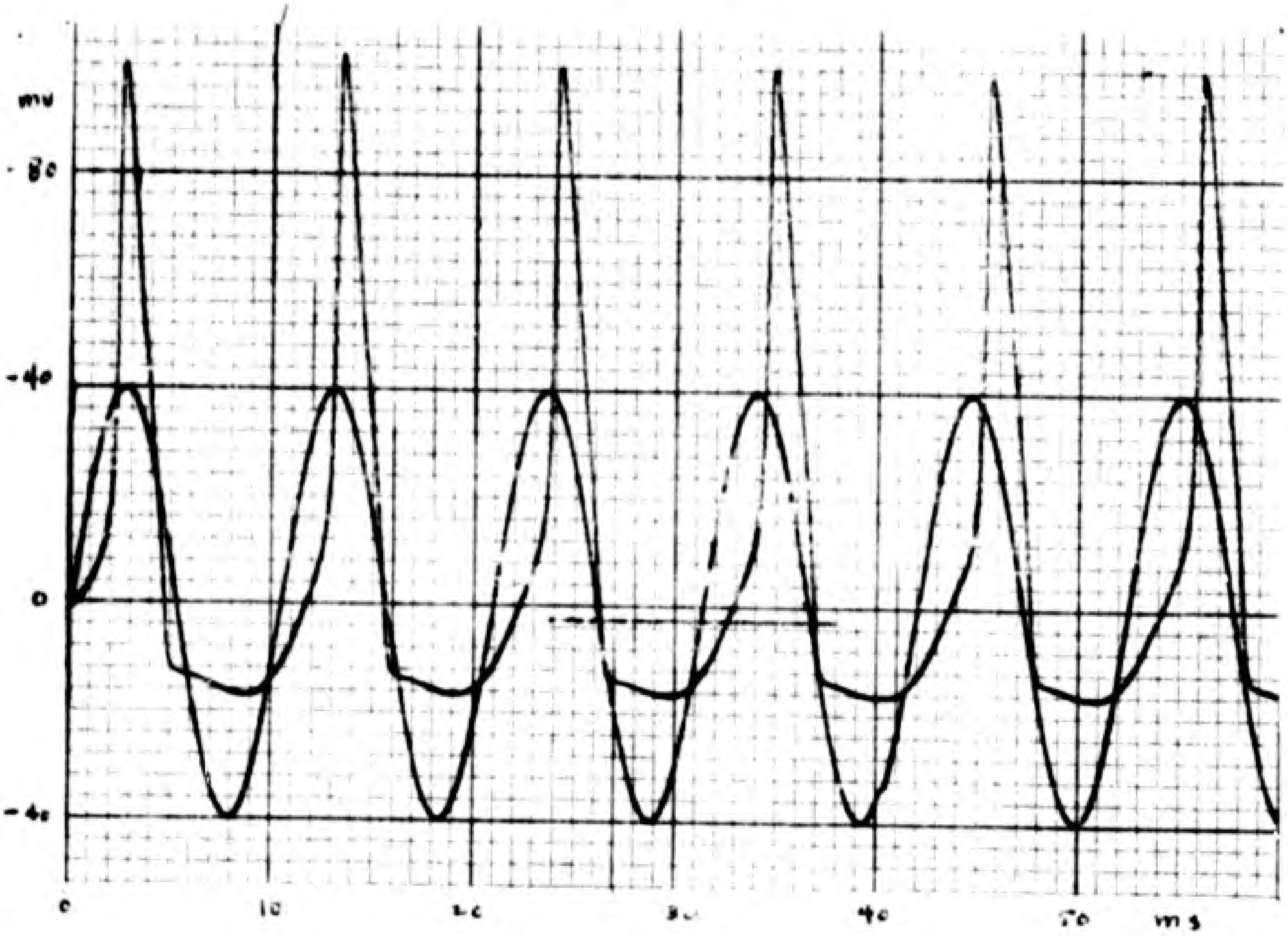


FIGURE 4b

FIGURE 5a

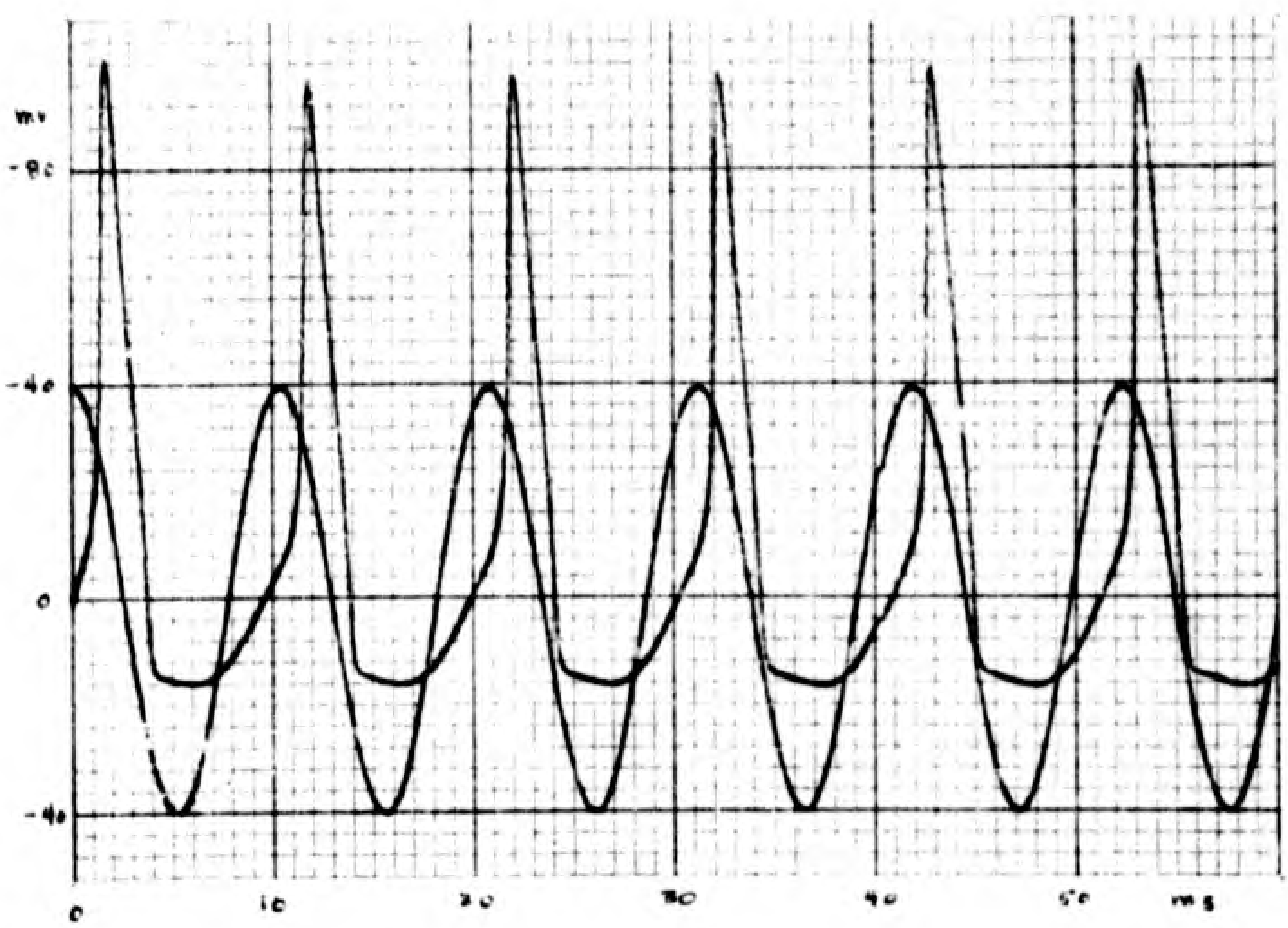


FIGURE 5b

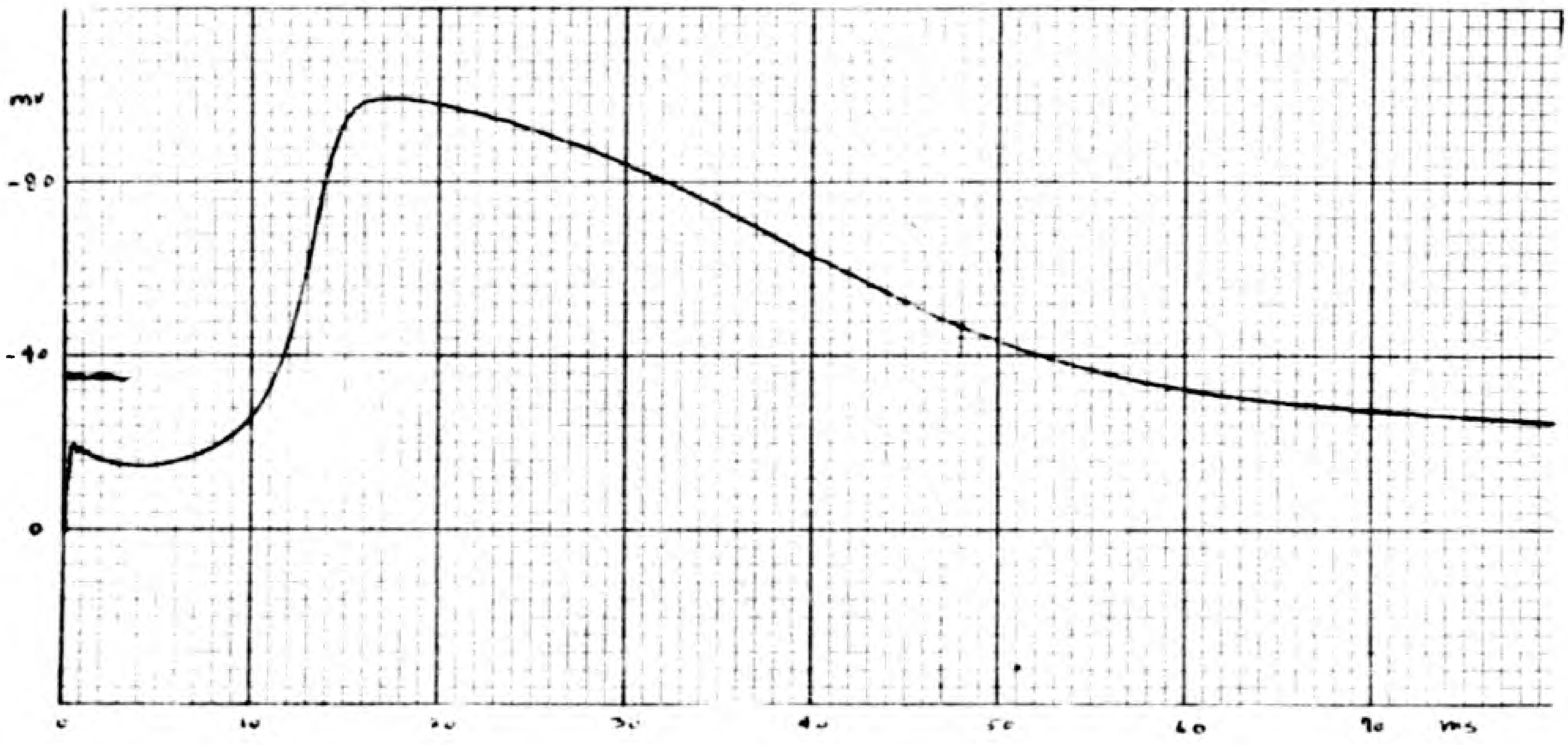


FIGURE 6

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