The CLOOGE: a simple device for interspike interval analysis

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The pattern of discharge as well as changes in average impulse activity of a neurone can be represented by plotting successive interspike intervals against time. Because sequential pulse intervals vary widely, from a millisecond to minutes, a linear representation on the ordinate unduly compresses brief intervals in order to show long intervals on the same scale.

We present here a device which generates a log compression of intervals between spikes and displays each interval *seriatim* on an oscilloscope. One of us (J. Y. L.) originated the device initially, and many versions of it now exist. The circuit diagram of one such device, called a CLOOGE (acronym for Continuous Log Of On-Going Events), is shown in Fig. 1 A. The core of the device is based on the principle that the time course of voltage change across a capacitor (C), when allowed to discharge in the forward direction through a p-n junction, approximates a logarithmic function. If a back-biased matched diode is in parallel, the course of voltage may be expressed as

$$-\frac{dV}{dt} = \frac{I_s}{C}e^{V/V_T},\tag{1}$$

where I_s is the reverse saturation current, and $V_T = kT/q$, which, at 20° C is 25·2 mV. Integrating equation (1) and evaluating the integrals between V at t and V_i at t_i,

$$\tau(e^{-V/V_T} - e^{-V_i/V_T}) = t - t_i,\tag{2}$$

where $\tau = V_T C/I_s$. After a brief initial delay of $t_i = \tau e^{-V_i/V_T}$, equation (2) becomes

$$V/V_T = -\ln(t/\tau).$$

The initial delay, after which the time course of voltage change follows a logarithmic function, depends on the magnitude of V_i and on the value of I_s. For V_i of 350 mV and I_s of 10^{-10} A, the delay is approximately 0·21 msec. In practice the CLOOGE is calibrated empirically. R_1 in Fig. 1 A is adjusted such that changes in input frequency by each decade produce constant changes in the output voltage. If the drop in output voltage produced by switching between intervals of 1 msec to 10 msec is smaller than for switching between 10 msec and 100 msec, then the duration of the input pulse should be shortened (or V_i raised by lowering R 1). If the drop

A

20 K

T 2

+12 V

D 1

T 3   T 6

T 5

In

T 1   20 K   2 K   T 4   ×10   300 pF   T 8

−10 V

Out

<1 msec   100 K   R 1   1 μF   T 7

T 9

20 K

−12 V

T 1 T 7 T 8   2 N 5163
T 2 T 5 T 9   2 N 3565
T 4   DUAL NPN (TD 101)
T 3 (T 6)   DUAL PNP (TD 401)
D 1   1N 4001
OP AMP   FET OPA

B   (a)   (b)   (c)

10^2

10^0

3   6   4   8   5   10

Inter-pulse interval (msec)

(d)   (e)   (f)

10^4 10^3

10^2 10^1

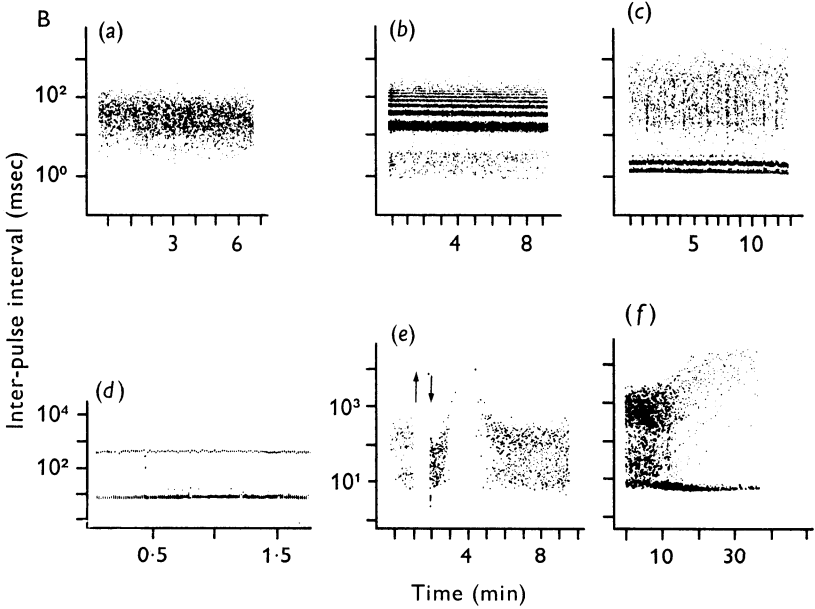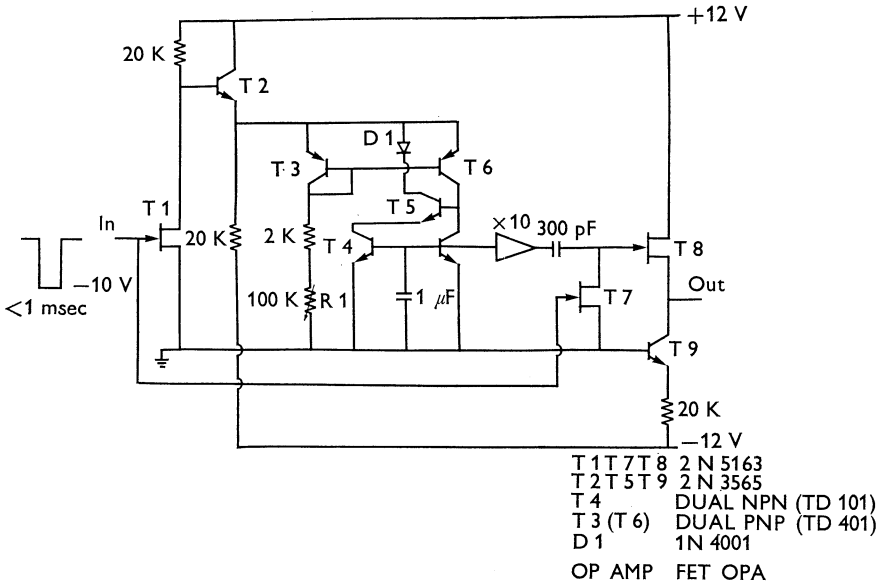0·5   1·5   4   8   10   30

Time (min)

Fig. 1. For legend see opposite page.

is larger for the first decade than for the second, the duration of input pulse should be lengthened.

Samples of records obtained by using the CLOOGE are shown in Fig. 1 B. To generate the records, each peak of the square-wave output from the CLOOGE is brightened to give a dot, and a slow time base, when needed, is obtained by a motor-driven potentiometer supplied with a constant voltage source. A band-limited noise exceeding an arbitrarily chosen threshold voltage produces clusters of dots with well-defined upper and lower limits of intervals in the CLOOGE record (a). When noise is superimposed on a fixed frequency sinusoidal wave, a pattern reminiscent of interference fringes emerges (b). Such bands of preferred and forbidden interspike intervals are frequently encountered in endogenous activities of neurones in the central nervous system (c). Rhythmic bursts of impulses (d), when presented in the form of the CLOOGE record, reveal the inter-burst interval as well as the range of interspike intervals within each burst. Finally, an oscillatory variation in frequency of discharge (e) and a slow alteration in the rate and pattern of discharge (f) can conveniently be depicted by the CLOOGE records.

Legend to Fig. 1.

Fig. 1. (A) The circuit diagram of the CLOOGE. Each nerve impulse is arranged to generate a negative voltage pulse of adjustable duration. This pulse is used to intensify the scope beam and to trigger the CLOOGE. At each spike the CLOOGE output voltage will jump from a d.c. level (which depends on the characteristics of T 8) by an amount that is propor-tional to the logarithm of the interval between the trigger pulse and its predecessor. R 1 is used to set the magnitude of V_i (see text). Input leakage of the operational amplifier must be less than 10^{-9} A.

(B) Samples of records obtained by using the CLOOGE. (a) Band-limited noise. (b) Noise superimposed on a sinusoidal wave. (c) The endo-genous discharge of a neurone in the pigeon's ectostriatum. (d) Rhythmic bursts of a retinal ganglion cell of *Xenopus*, previously given a prolonged exposure to stroboscopic illumination. The record shows that bursts of several impulses occur at fixed intervals. The interburst interval is repre-sented by the upper band, whereas the broad lower band shows the range of interspike intervals within each burst. (e) 'Off' responses of a 'dimming' fibre from *Rana pipiens*. The endogenous activity is suppressed when the background illumination interrupts the darkness (upward arrow). Upon cessation of illumination (downward arrow), the fibre discharges actively for a minute and goes into a period of inhibition before the resting level is regained. (f) Responses of a 'dimming' fibre from *Rana pipiens* to slowly brightening illumination. The intensity of illumination is slowly increased from threshold to four log units above threshold in 40 min.