

## Repetitive Subthreshold Synaptic Excitation and Transmitter Depletion

Consider the simple equation for somatic nerve membrane depolarization  $V(t)$ ,

$$\frac{dV}{dt} + \frac{V}{\tau} = \frac{I(t)}{C}, \quad (1)$$

where  $\tau$  is the time constant,  $C$  is the capacitance and  $I(t)$  is the input current. Use of this lumped circuit picture means that  $I(t)$  represents the current seen at the soma due to synaptic sources which may be located on the dendrites.

From equation (1) the current pulse has been deduced (Curtis & Eccles, 1959) which gives rise to an *epsp* resulting from a single afferent volley to a cat spinal motoneuron when group Ia fibers are stimulated. This current pulse can be well approximated by a triangular one, though other equally suitable pulses have been postulated. We are interested in the effect of repetitive subthreshold excitation, so we set:

$$I(t) = \begin{cases} Jt/a, & 0 \leq t \leq a, \\ J - J(t-a)/2a, & a < t \leq 3a, \\ 0, & 3a < t \leq T, \end{cases} \quad (2)$$

with  $I(t+T) = I(t)$  and  $3a \leq T$ .

In response to the periodic train of pulses,  $V(t)$  builds up to a steady state with maxima and minima of magnitudes:

$$V_{\max} = J\tau \left( 3 - \frac{t_2}{a} \right) / 2C, \quad (3)$$

$$V_{\min} = J\tau t_1 / aC, \quad (4)$$

where:

$$t_2 = \tau \log [(2 - 3e^{a/\tau} + e^{-T/\tau} e^{3a/\tau}) / (e^{-T/\tau} - 1)], \quad (5)$$

$$t_1 = \tau \log [(2e^{T/\tau} - 3e^{a/\tau} + e^{3a/\tau}) / 2(e^{T/\tau} - 1)], \quad (6)$$

as may be verified, for example, by using Laplace transforms.

Let the amplitude of an *epsp* elicited from rest ( $V = 0$ ) be  $\varepsilon_{\max}$  and define  $\varepsilon = V_{\max} - V_{\min}$ . We seek the ratio  $r = \varepsilon / \varepsilon_{\max}$  as a function of  $T$  as this was experimentally determined. This ratio was computed with  $J = 3.3 \times 10^{-8}$  A,  $a = 0.5$  ms,  $C = 5 \times 10^{-9}$  F and  $\tau = 5$  ms, which are appropriate values for cat spinal motoneurons undergoing submaximal Ia excitation

(Eccles, 1957). This gives  $\varepsilon_{\max} = 4.3$  mV. The calculated values of  $r$  for values of  $T$  down to 1.5 ms (when overlap of the current pulses starts to occur) are shown as the solid line in Fig. 1. Note that  $r$  does not depend on the choice of  $J$  or  $C$ . Also shown in the figure are the experimental points at various  $T$  for the terminal responses of the membrane potential of cat gastrocnemius motoneurons under repetitive synaptic excitation for 170 ms (Curtis & Eccles, 1960).

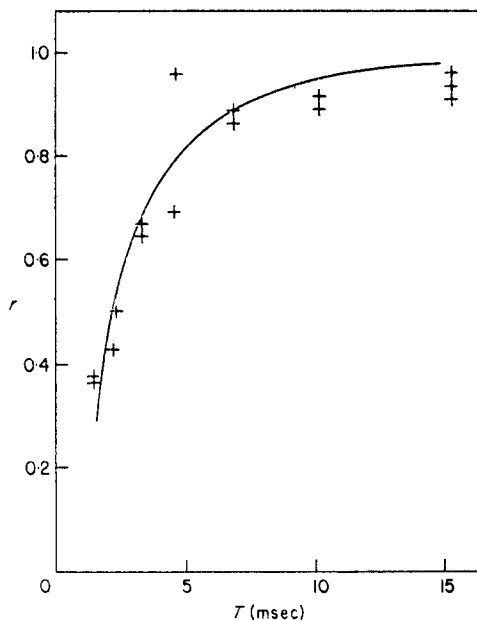


FIG. 1. A plot of the ratio  $r$  vs.  $T$ . The solid line was obtained from the calculations for the model neuron described in the text. The crosses are experimental points (Curtis & Eccles, 1960).

It can be seen that the calculated ratio stays fairly close to unity for  $T$  much greater than 10 ms. For faster rates of stimulation the ratio declines quite rapidly. It is apparent that the simple model we have employed predicts the experimental points quite well, especially for small values of  $T$ . The qualitative dependence of  $r$  on  $T$  is relatively independent of the exact pulse shape, as was found when we employed square waves rather than triangular ones.

In the interpretation of the decline of  $r$  for small  $T$  it was assumed that there was an underlying decrease in the amount of available transmitter substance. We feel that our calculations indicate that no part of the observed

decline can be attributed to transmitter depletion and that the drawing of a straight line through the experimental points for  $T$  less than about 5 ms is probably not justified. If one assumes that the magnitude,  $J$ , of the current pulse is decreased due to transmitter depletion, then the decline of  $r$  would be faster than that obtained experimentally. In fact, since our calculations, based on uniform pulse size agree so well with experiment, we are tempted to conclude that there was an insignificant diminution of available transmitter in the experiment we have mentioned.

Transmitter depletion was questioned in another experiment (Kuno, 1964, 1971) where the postsynaptic responses after a failure to respond had the same distribution of *epsp* amplitudes as those after a successfully elicited *epsp*. Furthermore, when an *epsp* quickly follows one that has been elicited from resting potential, then the *epsp* amplitudes are not proportional to their respective current pulses. In particular, a facilitated *epsp* (Kuno & Weakly, 1972) corresponds to an even larger current pulse than that deduced from a proportionality argument.

We thank Dr Hugh McLennan for his comments on an earlier version of this.

*Department of Mathematics,  
University of British Columbia,  
Vancouver, B.C., Canada*

JOHN B. WALSH  
HENRY C. TUCKWELL

(Received 13 June 1977, and in revised form 23 August 1977)

#### REFERENCES

- CURTIS, D. R. & ECCLES, J. C. (1959). *J. Physiol., Lond.* **145**, 529.  
CURTIS, D. R. & ECCLES, J. C. (1960). *J. Physiol., Lond.* **150**, 374.  
ECCLES, J. C. (1957). *The Physiology of Nerve Cells*. Baltimore: Johns Hopkins.  
KUNO, M. (1964). *J. Physiol., Lond.* **175**, 100.  
KUNO, M. (1971). *Physiol. Rev.* **51**, 647.  
KUNO, M. & WEAKLY, J. N. (1972). *J. Physiol., Lond.* **224**, 271.