

## LOW AMPLITUDE FITZHUGH-NAGUMO NERVE PULSES

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### Abstract

Low amplitude pulses have been observed in a FitzHugh-Nagumo nerve model. These pulses only occur as members of pulse trains, and cannot propagate as solitary waves. They can be described conceptually in terms of the current-voltage characteristics of the tunnel diodes used as nonlinear elements in the analogues. Computations indicate that pulses of variable amplitude can also be generated by nonlinear elements that have the same general dynamical properties as the tunnel diodes, a class of "devices" that would include nerve cells.

### 1. Introduction

In a previous paper (Luzader, 1984) we described multiple pulse propagation in a FitzHugh-Nagumo neuristor of the type shown in Fig. 1. The interstage resistance used in that circuit was  $1000\ \Omega$ , which gives an effective "decay length" of less than one stage. This means that a subthreshold input is attenuated to less than  $1/e$  of its original amplitude by the second stage. To increase the decay length and thus have a model which is a better approximation of an unmyelinated axon, the interstage resistance was changed to  $100\ \Omega$ . When experiments were begun with the modified circuits, a new type of pulse with "subnormal" amplitude was observed. This phenomenon was deemed worthy of further study before continuing with the multiple pulse experiments.

Examples of the small amplitude pulses are shown in Fig. 2. The inputs are short pulses at the indicated frequencies. At low driving frequencies, the response of the neuristor is a series of propagating pulses at the input frequency, as one would expect. At very high frequencies, the propagating pulse train has a frequency which is a sub-multiple of the driving rate. But at intermediate frequencies, small propagating pulses are seen.

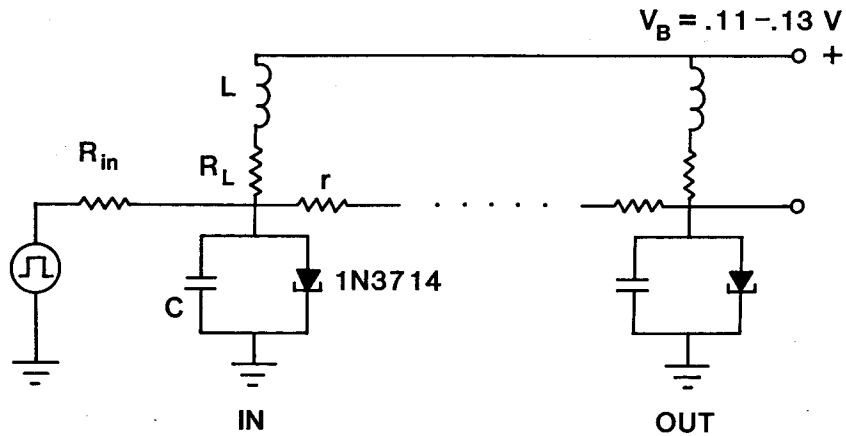


Fig. 1. A schematic diagram of the FitzHugh-Nagumo neuristor. The component values for this report are  $L=1\text{ mH}$ ,  $C=.01\text{ }\mu\text{F}$ ,  $r=100\text{ }\Omega$ . Current stimulation is provided by connecting a pulse generator to one end of the circuit through a large resistance  $R_{in}$ .

## 2. Single stage studies

In an effort to understand the origin of these low amplitude pulses, we studied the behavior of a single stage of the neuristor (Fig. 3). It was found that the amplitude of the "action potentials" generated by the analogue depended on the bias voltage  $V_B$  and the inductance  $L$ . The bias voltage controls the threshold for pulse production (increasing  $V_B$  decreases threshold), and  $L$  controls the duration of the model nerve pulses (increasing  $L$  decreases pulse width). Fig. 4 shows the dependence of peak amplitude on  $L$  and  $V_B$ . We see that low values of  $L$  and  $V_B$  tend to yield low amplitude pulses, with an abrupt transition to large amplitude at some critical bias voltage.

The variation in pulse amplitude can be understood by considering the current-voltage characteristic for the tunnel diode, shown in Fig. 5. For a simple circuit like the one in Fig. 6, the "resting" state  $Q$  of the diode is given by the intersection of the load line with the characteristic (Nagumo *et al.*, 1962). The load line intersects the  $I$  axis at  $V_B/R$  and has a slope of  $1/R$ . As  $V_B$  increases, the resting point  $Q$  moves upwards along the  $IV$  curve toward the peak at  $P$ . If the diode is biased at  $Q$  (below  $P$ ), then a positive input signal  $V_{in}$  has the same effect as increasing the bias. When the diode's state reaches  $P$ , a transition occurs and the diode voltage switches to a higher value at point  $A$  on the load line. Thus the circuit has a switching threshold, and the value of the input required to reach threshold is determined by the bias voltage. Increasing the bias reduces the size of the positive voltage pulse needed to get the diode to point  $P$ . Once the diode is on the steeply rising branch of its characteristic,

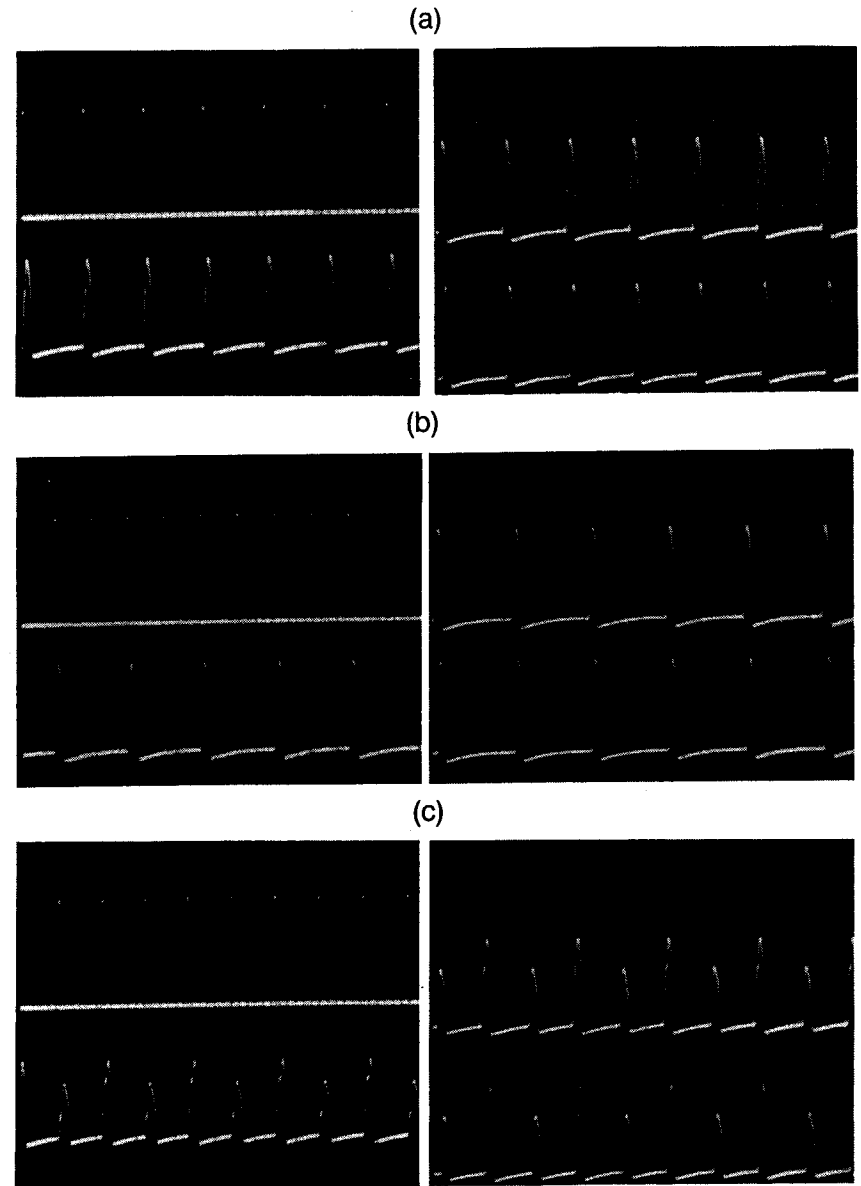


Fig. 2. Response of the neuristor to repetitive stimulation. The inputs are  $5\text{ V}$ ,  $1\text{ }\mu\text{sec}$  pulses fed through  $5\text{ k}\Omega$ . In each picture, the top left trace shows the input pulses, and the bottom left, top right, and bottom right traces show the diode voltage at stages 1, 5, and 11.  $V_B=0.100\text{ V}$ . The driving frequency is (a)  $13.4\text{ kHz}$ , (b)  $22\text{ kHz}$ , (c)  $18.7\text{ kHz}$ . The vertical scale for the diode voltage is  $0.2\text{ V/div.}$ , and the time scale is  $50\text{ }\mu\text{sec/div.}$

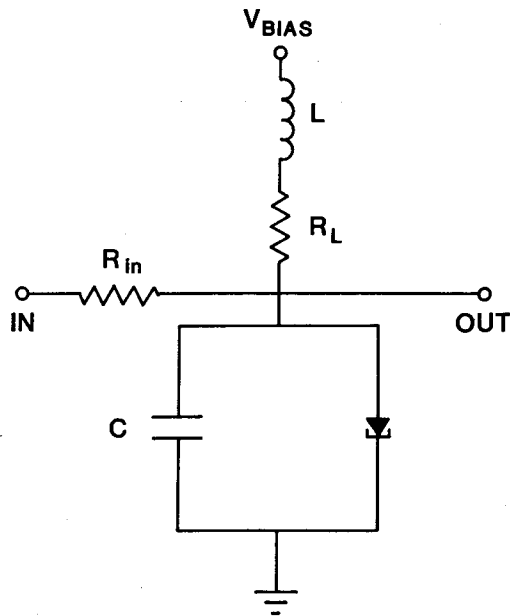


Fig. 3. A single stage neural analogue. The component values are the same as in Fig. 1.

further positive inputs will have little effect on its voltage, since the slope of the  $IV$  curve is so steep that the voltage is nearly constant. Negative values of  $V_{in}$  can move the diode's state point downward along the curve until it reaches the left end of the flat valley, whereupon the diode switches back to a low voltage state. By reducing  $R$  and  $V_B$ , the load line can be changed so that the high voltage state of the diode is shifted to point  $A'$  in the valley, resulting in a low value for the "ON" voltage.

In the FitzHugh-Nagumo model, the load line analysis is more complex, because the circuit contains reactive elements. The slope of the load line is controlled by the inductance, whose impedance depends on the instantaneous rate of change of the inductive current. If the instantaneous load line has a relatively large slope (as in the line  $QA'$  in Fig. 5), or if the bias voltage is set at a low value, then the load line will pass through the valley portion of the diode's  $IV$  characteristic, resulting in a low amplitude pulse. In order to produce a "normal" high amplitude pulses, the instantaneous load line must pass through the steeply rising part of the characteristic.

A glance at Fig. 4 shows that the dependence of peak amplitude on bias voltage reflects the shape of the diode's  $IV$  characteristic. Decreasing  $L$  lowers the impedance, raising the instantaneous slope of the load line and shifting point  $A$  down into the flat part of the  $IV$  curve. Lowering  $V_B$  shifts point  $A$  down towards the origin, again moving point  $A$  into the valley. We can also see how large pulses can be produced even at low  $V_B$  or high  $L$ . A large stimulus can force the diode onto the steep part of the characteristic, resulting in a normal high value for the "ON" voltage.

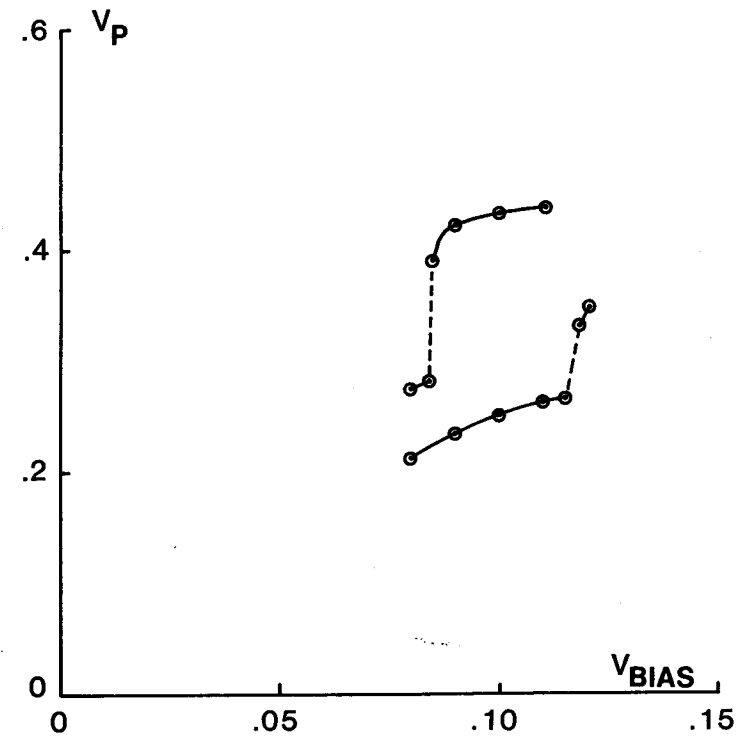


Fig. 4. A graph of peak pulse amplitude for different bias voltages for the single stage circuit. The inductance used is noted on the graph.

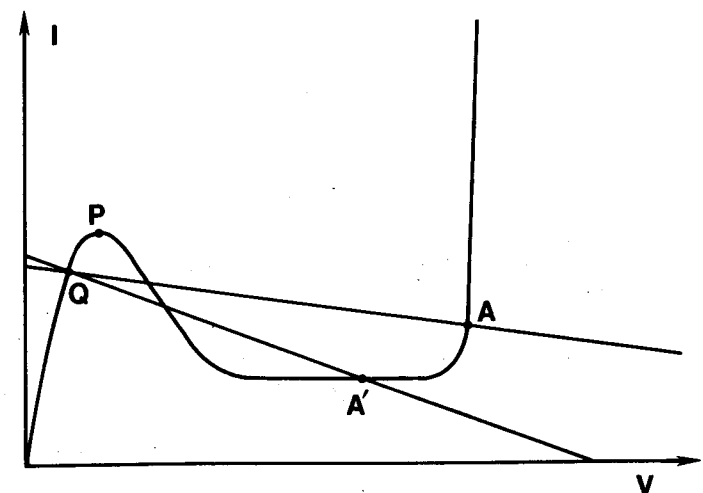


Fig. 5. A sketch of the  $IV$  characteristic for the tunnel diode.

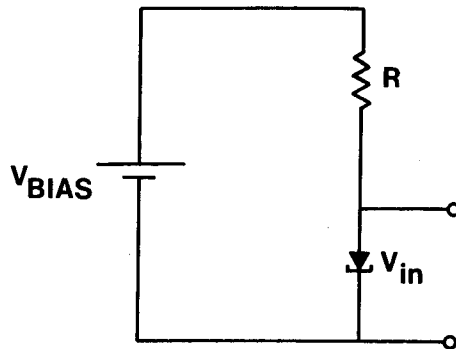


Fig. 6. A simple tunnel diode circuit which shows threshold switching behavior.

The question then arises of whether low amplitude pulses could be obtained for a current-voltage characteristic which did not have a sharp corner. We integrated the dimensionless FitzHugh-Nagumo equations (see Luzader, 1984)

$$\dot{V} = -F(V) - W + I_0(t)$$

(1)

$$\dot{W} = \epsilon V - bW$$

for a cubic  $F(V)$ :

$$F(V) = V(V - \theta)(V - 1)$$

where the dot denotes differentiation with respect to time. The term  $I_0(t)$  represents an externally applied driving current. The relationship between the circuit component values and the parameters in Eq. (1) is the following: the recovery parameter  $\epsilon$  is inversely proportional to the inductance  $L$ , and the threshold parameter  $\theta$  is controlled by the bias voltage — increasing  $V_B$  decreases  $\theta$ . So we would expect that peak amplitude in solutions to Eqs (1) will decrease with increasing  $\epsilon$  and  $\theta$ . Some results are shown in Fig. 7. We see that the peak value of  $V$  does indeed decrease in the predicted manner. The main difference between the computed pulses and the behavior of the electronic model is that the neuristor shows fairly abrupt transitions from small to large amplitude pulses, owing to the sharp corner and steep slope in the diode's  $IV$  characteristic. The mathematical model, on the other hand, displays a continuous variation in pulse amplitude, since  $F(V)$  is a more slowly varying function of  $V$ .

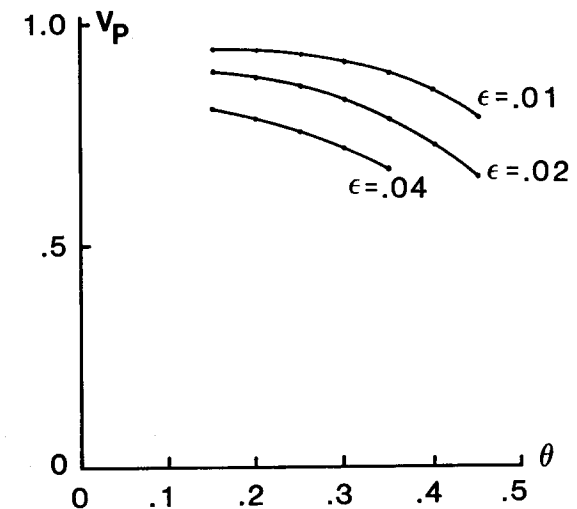


Fig. 7. A plot of the peak value of  $V$  as a function of  $\theta$  for different values of  $\epsilon$ . The peak values were found by integrating Eqs (1) using a rectangular pulse for  $I_0$  of amplitude 1 and duration 0.5. For these curves,  $b=0.02$ .

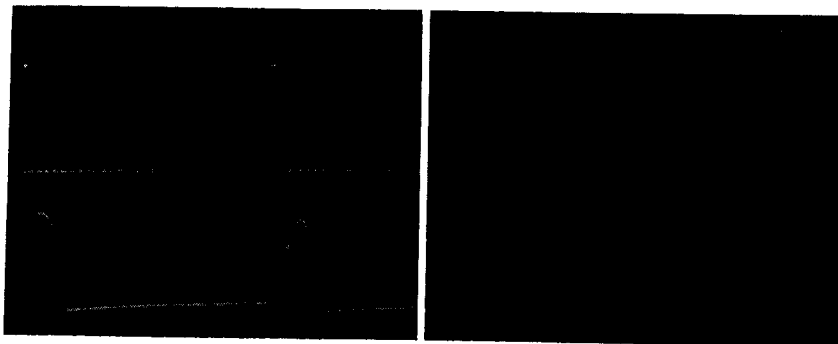
### 3. Propagating pulses

The situation for the propagating pulses is a bit more difficult to understand than the single stage case. In an extremely simplistic view of the entire neuristor, we can think of each stage as being driven or stimulated by the previous stages. Thus we expect that *propagating* pulses should display a true "all-or-none" behavior — all having the same shape and amplitude. This is obviously not the case shown in Fig. 2. To understand this unusual behavior of propagating pulses, we carried out some experiments with pairs of pulses.

For an input consisting of two closely spaced pulses, the response of the model was (a) only one propagating pulse; (b) a normal pulse followed by a low amplitude pulse; or (c) two normal pulses. Examples are shown in Fig. 8. If the interval between the stimuli was too short, the second stimulus failed to elicit a response because of refractoriness, while large interstimulus intervals resulted in two normal responses. Intermediate intervals gave a normal pulse followed by a low amplitude pulse.

Following a suggestion by J. Rinzel, we checked to see if the small pulses could be forced to propagate singly. To do this, a pair of propagating pulses was launched and a negative current pulse was injected at a stage far from the input to extinguish one member of the pair (Fig. 9). Killing the trailing small pulse had no effect on the leading pulse (to no one's surprise), while extinguishing the leading pulse always resulted in the small pulse growing to full size. Thus we see that the small pulses are unstable and cannot propagate as solitary waves.

(a)



(b)

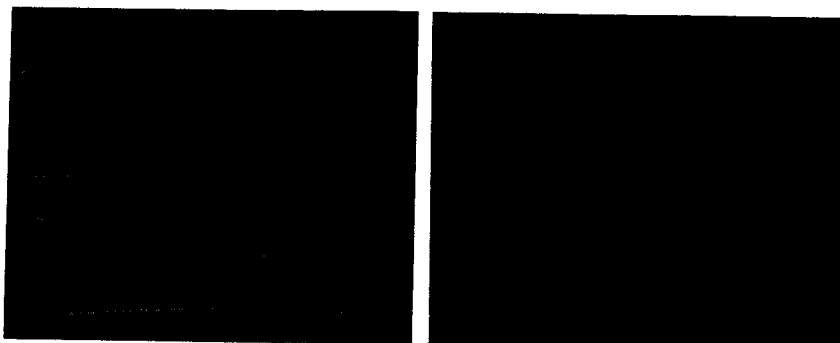


Fig. 8. Response of the neuristor to paired inputs. In each picture the top left trace shows the stimulus pulses, and the bottom left, top right, and bottom right traces show the diode voltage in stages 1, 11, and 20. The bias voltage was 0.100 V. The interstimulus interval is (a) 64  $\mu$ sec and (b) 56  $\mu$ sec.

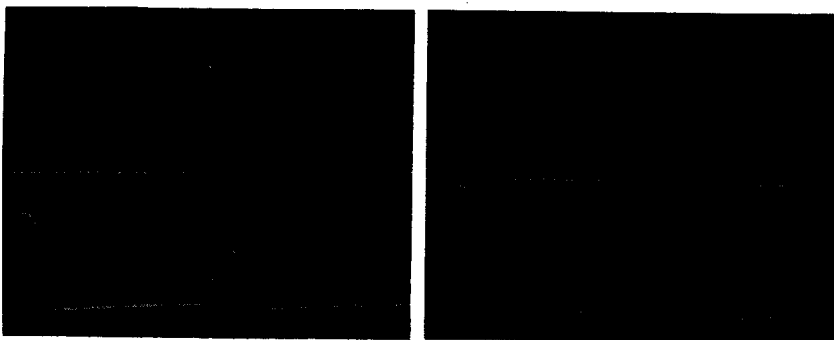


Fig. 9. Effect of injecting a negative pulse at stage 10 to kill one member of a propagating pair. All conditions are the same as in Fig. 8 except that the top right trace shows the diode voltage at stage 10. The negative input is a  $-5$  V pulse fed through 1 k $\Omega$ . The time scale is 10  $\mu$ sec/div. Extinguishing the leading pulse at stage 10 results in the trailing pulse growing to full size by stage 20.



Fig. 10. Decrease in speed as the small member of a pulse pair propagates. The vertical scale is 0.1 V/div., and the time scale is 2  $\mu$ sec/div. The left trace shows the diode voltage at stages 5 (top) and 10 (bottom), indicating a 5 stage delay of about 4  $\mu$ sec. The right traces show the pulse at stages 10 (top) and 15 (bottom); the 5 stage propagation time has increased to about 9  $\mu$ sec.

Another experiment showed that the normal-small pulse pair does not constitute a true travelling wave system, since the leading large pulse travels at a higher speed than its trailing companion. Fig. 10 shows the increase in propagation delay of the small pulse as the pair moves along the neuristor, which means that the small pulse travels at a lower speed than the leading large pulse. It was also noted that even when propagating behind a normal pulse, the small pulse tended to be unstable and would occasionally drop out or grow to full size as it approached the unterminated end of the circuit.

#### 4. Discussion

The response of the neuristor to pairs of stimuli can be understood in terms of refractoriness. In the FitzHugh-Nagumo model, refractoriness is related to the value of the recovery variable  $W$  (FitzHugh, 1961, 1969; Scott, 1977). When  $W$  is high, the effective threshold for pulse generation increases. As we have seen, high threshold allows the possibility of small pulse generation. In a uniform and relatively noise-free environment, such as a mathematical model or a carefully constructed electronic analogue, it is possible to generate action potentials of different amplitudes in response to changes in threshold, etc. (FitzHugh, 1961, 1969).

In the neuristor, the propagation of these pulses depends on the interstage coupling resistance. If that resistance is high, then little longitudinal current flows from stage to stage; it is this longitudinal current that is responsible for the propagation of pulses along the circuit. When the longitudinal current is low, then small amplitude pulses generated by the first stage in response to some input will fail to propagate because they cannot deliver sufficient current to subsequent stages to get above the effective threshold established by the residual effects of previous activity. When the interstage resistance is lowered, these small pulses can deliver sufficient current, but only

enough to maintain the stage-to-stage production of low amplitude pulses. When the pulse train contains only two members, the trailing low amplitude pulse has a low speed because of its effective high threshold, so its separation from the leading pulse increases as the pair propagates along the circuit. Eventually the second pulse would find itself in an environment where it can grow to full size and propagate as a normal pulse. While it is in this precarious small state, however, it is unstable and can be extinguished by encountering irregularities as it propagates. For instance, increasing the interstage resistance to  $1000\Omega$  between two stages will destroy the pulse.

For the periodic pulse trains shown in Fig. 2, the behavior can be understood in light of what we have illustrated above. At low stimulation frequencies, the circuit recovers sufficiently between stimuli that it is able to propagate pulses successfully in response to all inputs. At high frequencies, the neuristor is absolutely refractory during some stimuli, and frequency division occurs. At intermediate frequencies, however, the recovery variable has raised the effective threshold to the point that while pulses can be produced, they tend to be low amplitude pulses. When the interstage resistance is high, the small pulses are unable to stimulate downstream stages, and some pulses fail to propagate. The result is the kind of patterned pulse trains reported in a previous paper (Luzader, 1984). At low interstage resistance, some small pulses are able to propagate, but again they are always moving into a region with a high effective threshold, so they continue to occur as low amplitude pulses. Their relative stability is maintained by the fact that they are "surrounded" by other pulses. However, they are not absolutely stable and have been observed to fail when they encounter nonuniformities in the circuit. (For instance, we have noted their disappearance at a point where a cold solder joint was subsequently discovered. Repairing the faulty connection resulted in successful propagation of the pulses.)

It is also worthwhile to note that these pulses do not satisfy the conditions for other types of small pulses that have been predicted to exist for FitzHugh-Nagumo (Rinzel and Keller, 1973; Luzader, 1979; Levi, 1981; Sleeman, 1982). Unstable low amplitude solitary waves have been calculated, but they differ from normal pulses in that they have very low propagation speeds and very narrow pulse widths (Luzader, 1979), characteristics not shared by the observed pulses. Sleeman (1983) has predicted the existence of low amplitude periodic travelling wave solutions to the FitzHugh-Nagumo equations, but those solutions involve oscillation about an elevated potential and not about the resting potential. Low amplitude oscillations about an elevated potential have been observed (Luzader, 1984), but only for a single stage of the circuit. They have not been seen to propagate along the entire neuristor. Levi (1981) has described small amplitude oscillations for the van der Pol equation, of which the FN equation is a special case. However, his solutions are for the ordinary differential equation with periodic forcing, which is physically different from the situation described in this paper.

## 5. Physiological implications

Since the generation and propagation of low amplitude pulses require carefully controlled conditions, they would not be expected to occur very frequently in real physiological settings. Two-pulse experiments similar to those described here have been carried out on squid fibers (Donati and Kunov, 1976); these show velocity variations for the second pulse, but no huge amplitude differences. However, the analysis described here indicates that the origin of these pulses lies in the current-voltage characteristic of the nonlinear element in the model. Thus we would expect that such pulses may occur in nerves, which have qualitatively similar characteristics. For example, it may be possible for such pulses to appear and travel for short distances before either failing or developing into full-grown action potentials. Thus they may be of significance in short-range signalling between neurons, or for information processing within a single nerve cell by means of dendritic spikes.

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