

## Frequency of firing of Stein's model neuron with application to cells of the dorsal spinocerebellar tract

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We present here the results of some exact calculations of the expected firing rates of neurons which receive random synaptic excitation or randomly arriving intracellularly injected short lasting current pulses. The assumptions of the model<sup>27,28</sup>, insofar as it is used here are: (a) arrival of an EPSP or current pulse causes the membrane depolarization to increase by  $\varepsilon$  mV, (b) the individual EPSPs arrive according to a Poisson process whose mean rate is  $\lambda$  per second, (c) between occurrences of EPSPs the depolarization, which we denote by  $V(t)$ , decays to zero (resting level) according to the equation

$$\frac{dV}{dt} = -\frac{V}{\tau},$$

where  $\tau$  is the time constant of decay (d), when the depolarization first reaches or exceeds a (fixed) threshold level  $\theta$  mV, an action potential is generated. The depolarization is then re-set to zero after an absolutely refractory period  $T_R$ .

There will of course be neurons and conditions of stimulation and firing for which this model will be more appropriate than others. The model assumes that the depolarization at a small region of membrane is critical in determining how close the neuron is to the threshold for spike initiation. This seems a valid approach when the neuron has a 'trigger zone', the existence of which has been fairly well established for cat spinal motoneurons<sup>4</sup> and also dorsal spinocerebellar tract (DSCT) neurons<sup>8</sup>. The model ignores the afterpotentials following a spike (delayed depolarization, afterhyperpolarization, late afterdepolarization) which vary from cell to cell, but have been found important in relation to bursting and the rates of repetitive firing in response to steady intracellularly injected currents<sup>13,16,17,25,26</sup>. If, however, the post-spike potentials have become negligible throughout most of the interspike interval then the model should be good as a first approximation. A neuron firing in the 'occasional spike mode'<sup>3,4</sup> would meet these requirements. Furthermore, if the neuron is excited from resting level, then these afterpotentials will not influence the time to the first spike, so that the model should perform best in determining the statistics of the first interspike interval.

Another consideration is that the waveforms of small EPSPs (such as are obtained by activation of a single synaptic knob or single afferent fiber in some cases) are not, at least as depicted by recordings made with an electrode at the soma, always of the shape of a step-up followed by a clear exponential decay<sup>1,21</sup>. This may of course be due to a limitation of recording techniques for very small EPSPs. Nevertheless, it is usually the case that when spatial summation makes the EPSP amplitudes larger as several synapses are more or less simultaneously activated<sup>1,6,7,9</sup>, or when large unitary EPSPs are involved<sup>10,11,20</sup>, the shape of the EPSP is able to be much better represented by a step followed by exponential decay. We note too that the finite rise times of actual EPSPs can be handled with Stein's model by replacing the EPSP amplitude with an effective step increase in depolarization<sup>31</sup>. Larger effective step increases result for longer rise times which leads to different firing rates for EPSPs originating from synapses at the distal dendrites in comparison with those originating from somatic or proximal-dendritic synapses because the former have longer rise times as well as larger initial time constants of decay<sup>22</sup>.

The firing rate will also be affected by such factors as facilitation of EPSPs and summation of negative after-currents. At low firing rates, however, these effects and those mentioned above, should be relatively unimportant so that one expects the model to be appropriate for experimental Poisson excitation by Ia fibers of cat lumbosacral motoneurons (particularly those with predominantly tonic responses) where several bundles of primary afferents were simultaneously stimulated<sup>23</sup>, or in cases where random afferent inputs give rise to large unitary EPSPs. The latter is the case for DSCT neurons with Ia input where the ratio of threshold to EPSP amplitude is usually quite small, and most often less than five<sup>2,10,11,15,19,20,32</sup>. These neurons, however, are believed to have a pacemaker-type spontaneous steady depolarization<sup>32</sup> which causes them to emit about 10 impulses/sec in the absence of afferent input. This feature can also be incorporated in Stein's model by assuming a steady depolarizing current, but it is expected to have a greater effect on the variance of the interspike intervals than upon the mean firing rates which are the object of the present study. We note that computer simulations have been carried out for Stein's model<sup>28</sup> and modifications thereof<sup>32</sup>. To summarize, the present calculations should be applicable for relatively strong synaptic (or intracellular) excitation of a neuron which possesses a trigger zone and is firing in the occasional spike mode.

Of the 4 parameters  $\theta$ ,  $\varepsilon$ ,  $\lambda$  and  $\tau$ , two can be replaced by one. The reason for this is that the time between action potentials has been shown to depend on  $\theta/\varepsilon$ , rather than the absolute magnitudes of these potentials<sup>29</sup>. Thus we will set  $\varrho = \theta/\varepsilon$  in the following. The aim is then to find, for given values of  $\lambda$ ,  $\varrho$  and  $\tau$ , the average firing rate of the neuron. Let us denote this latter quantity by  $f$ , which is related to  $T$ , the expected time at which the depolarization first exceeds threshold starting from resting level, by

$$f = \frac{1}{T + T_R}.$$

In the tabulated results we will give the values of  $T$  in units of the time constant  $\tau$ ,

so that they may be used for any neuron satisfying the requirements to make the model valid.

The calculations of  $T$  are algebraically rather lengthy and details have been presented elsewhere in a number of cases<sup>29-31</sup>. In brief we have that if  $T(x)$  is the expected time for the depolarization  $V(t)$  to exceed threshold for the first time, given that  $V(t)$  was initially  $x$ , then  $T(x)$  is found by solving the differential — difference equation

$$-\frac{x}{\tau} \frac{dT(x)}{dx} + \lambda T(x+1) - \lambda T(x) = -1,$$

with  $T(x) = 0$  for  $x \geq \varrho$  and  $T(x)$  a continuous function of  $x$ . The time to the action potential is then identified as  $T = T(0)$ .

It has proven convenient to perform the calculations at selected values of the mean frequency of stimulation,  $\lambda$ , which bear a definite relation to the time constant,  $\tau$ . We have performed calculations at  $\lambda = 1/4\tau, 1/2\tau, 1/\tau, 2/\tau, 3/\tau$  for values of  $\varrho = 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 5$ . The results for the last two values of  $\varrho$  were obtained by extrapolation at a given input frequency, and for  $\varrho > 2$  the input frequencies  $1/4\tau$  and  $1/2\tau$  were not considered as the firing rates become exceedingly small. As an example of the analytic results obtained, we have, when  $\varrho = 2$  and  $\lambda = 1/\tau$ , then<sup>29</sup>

$$T = \left[ 2 + \frac{1}{1 - \log e^2} \right] \tau$$

which gives a number close to that obtained for computer simulation studies<sup>28,32</sup>.

In Table I we show the values of  $T$  for a Stein model neuron for the above values of input and neuronal parameters. A dash in the table indicates an extremely large  $T$  value or a very low firing rate (less than about 1/sec for DSCT neurons or spinal motoneurons in cats). It is noteworthy that the expected interspike intervals increase

TABLE I

Expected interspike intervals,  $T$ , in units of the time constant of decay,  $\tau$ , for various values of  $\varrho$ , the ratio of threshold to EPSP amplitude, and for various mean input rates  $\lambda$ . The refractory period is to be added in all cases. Dashes indicate very large values of  $T$ .

$\varrho \downarrow$	$\lambda =$				
	$\frac{1}{4\tau}$	$\frac{1}{2\tau}$	$\frac{1}{\tau}$	$\frac{2}{\tau}$	$\frac{3}{\tau}$
1.00	4.00	2.00	1.00	0.50	0.33
1.25	17.40	5.92	2.32	1.04	0.67
1.50	26.96	8.14	2.84	1.15	0.71
1.75	46.00	11.98	3.70	1.38	0.83
2.00	109.96	20.64	5.26	1.82	1.09
2.50	—	67.30	9.80	2.53	1.36
3.00	—	462.62	20.75	3.80	1.86
4.00	—	—	156.02	9.49	4.06
5.00	—	—	—	33.12	10.49

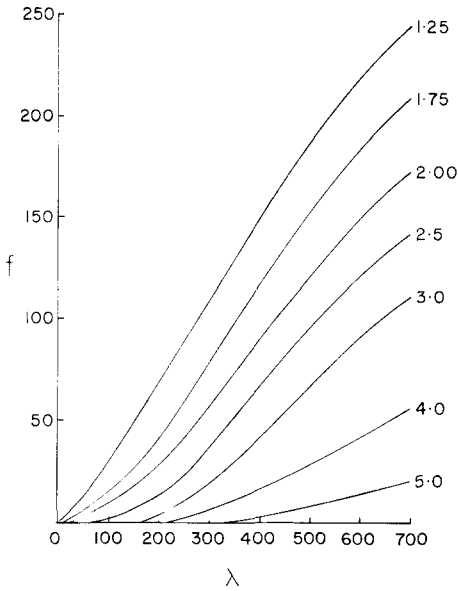


Fig. 1. Showing the variation in mean output frequency,  $f$ , versus mean rate of arrival,  $\lambda$ , of EPSPs. All units here are  $\text{sec}^{-1}$ . The values of  $f$  are as calculated with Stein's model using values of the parameters appropriate for DSCT neurons;  $\tau = 4.4$  msec,  $T_R = 1.2$  msec. The numbers to the right of each curve are the ratios of threshold to EPSP amplitude,  $\rho$ .

rapidly as  $\rho$  increases and become very large even for fairly high frequencies of stimulation when this parameter becomes much larger than 2.

In the many experiments on intracellular current injection into spinal motoneurons or in experiments with varying afferent stimulation of DSCT neurons, the results are often presented as firing rate versus input current or strength of stimulus. In Fig. 1 we show the results of our calculations of the expected firing rate as a function of mean frequency of stimulation for Stein's model. With DSCT neurons in mind we have set  $\tau = 4.4$  msec<sup>20</sup>, though the results are not qualitatively different if we use the value  $\tau = 5.8$  msec, which would be more appropriate for Ia excitation of spinal motoneurons<sup>14</sup>. Indeed, the results for DSCT neurons are very similar in magnitude to those obtained in computer simulations which assumed  $\tau = 3.0$  msec, with  $T_R = 1.2$  msec<sup>32</sup>, this value for the absolute refractory period also being employed in our calculations. (One should, to make a proper comparison, add about 10 imp/sec to our results in order to allow for the spontaneous discharge of the DSCT neurons). We note that the values of  $\rho$  for DSCT cells are<sup>11,32</sup> within the range of values at which our calculations have been done, whereas for motoneurons undergoing natural Ia excitation (as opposed to controlled multi-fiber activation<sup>23</sup>), the  $\rho$  values will usually be higher<sup>1,2,5,19</sup>.

It can be seen that over a fairly large range of input frequencies, the relation between mean input frequency and mean output frequency of spikes is nearly linear, with a somewhat noticeable change of slope at  $\lambda = 1/\tau$  (see particularly the curves for  $\rho = 2.5$  and  $\rho = 3.0$ ). This linearity can be compared with the separate linear ranges

(primary, secondary and tertiary) obtained for frequency versus current in experiments on repetitive firing of spinal motoneurons in response to steady intracellularly injected depolarizing currents<sup>5,12,16,24,25</sup>.

The kind of results shown in Fig. 1 would correspond most closely with those expected for a neuron which had a short-lasting afterhyperpolarization and no recurrent inhibition, both of which have been reported for DSCT neurons. This leads to the idea that these neurons probably function primarily as 'relaying' neurons rather than as 'integrating' neurons. The effects of a more pronounced afterhyperpolarization and recurrent inhibition, which are present in motoneurons, will be to increase the value of  $\rho$  as the firing rate increases. This will decrease the rate of increase of output frequency with respect to input frequency, which has been found to be the case for strong synaptic excitation of cat spinal motoneurons according to a Poisson process<sup>23</sup>. There will also be the effect of output frequency on the difference between the 're-polarization' potential and the threshold for spike initiation<sup>18</sup>. Thus there are separate considerations for different neurons which must be included before one can extend the results to higher input frequencies.

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