Research Reports

IMPULSE SEQUENCES OF THALAMIC NEURONS — AN ATTEMPTED THEORETICAL INTERPRETATION

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INTRODUCTION

Interval distributions of thalamic neuron discharges in unanaesthetized monkeys, reported by Poggio and Viernstein[4], could not easily be characterized by the two classes of distributions commonly encountered as statistical references in neurophysiology.

These are: (a) the monomodal distribution, above all the Gaussian distribution, preferably used when a more or less regular discharge is at stake; (b) the exponential distribution, convenient for action potential sequences in which a preponderance of short intervals is present and longer intervals occur less frequently. Some of the published interval distributions of thalamic neurons have shown a combination of these two characteristics. The impression is gained that this feature is especially present during stimulation, whereas spontaneous activity is, in general, characterized by the absence of short intervals. *E.g.* during spontaneous activity of neuron 19–3 most intervals have durations between 20–80 msec with a strongly favoured duration of 30–38 msec. When peripheral stimulation is constantly maintained, the majority of intervals is shorter than 40 msec, and the interval histogram has an exponential-like character with only a small peak in the neighbourhood of 30 msec. The gradual change from a nearly monomodal distribution during spontaneous activity into one of the mixed type of distribution under driven circumstances is still better observable in neuron 39–2 where the stimulation has increased in strength by three successive steps. In addition, another property of distributions was sometimes encountered, namely multimodality, which further complicated an attempt to fit the observed distributions with theoretical known functions. We propose a model that accounts for most of the peculiarities mentioned, and that is surprisingly simple both in concept and as to its numerical evaluation. These requirements have to be imposed upon any model in order to generalize experimental results.

Nevertheless, we would not have gone into the matter had not another statistic of the discharge pattern been measured, and published, by the said authors. We

refer to the expectation density function, shortened to $E(t)$ hereafter, that is, but for a multiplicative factor, equal to the better known autocorrelation function. $E(t)$ is defined as follows: $E(t) \cdot dt$ equals the expected ratio of occurrences of an event within a time interval $(t, t + dt)$ following a known occurrence at $t = 0$.

This measure provides information about the temporal ordering of impulse series. For an adequate description of an impulse series, $E(t)$ is a necessary item. In fact, neuron modelling is sometimes discredited by its non-unique solutions. These have to be restored largely to the point that no sequential aspect of events is taken into account in theory. Otherwise stated, neural impulse series are often assumed recurrent and the durations of the intervals independent of each other. Only when this is true, is the interval distribution alone an adequate substratum of the underlying mode of activity.

The systematic search for interdependency between interspike durations has led Poggio and Viernstein[4] to the conclusion that in many instances a deviation from randomness exists in nervous discharge patterns. As this feature is also present in the proposed model, we have, besides the interval distribution $p(t)$, included the expectation density function $E(t)$ in the investigation. Upon comparison with experimental observations, elements of agreement were found. An elegant method to visualize deviation from recurrency has been demonstrated[4] by comparison of $E(t)$ of intervals in the order as these have been recorded, and $E(t)$ of the same population of the intervals after being rearranged in a new order with the use of a random number generator (shuffled sequence). As pointed out by Poggio and Viernstein, the latter $E(t)$ will represent only those structural characteristics of the time series which depend on the composition of the available intervals, that is on $p(t)$. Consequently, the difference between $E(t)$ of the original time series and that of the shuffled one is a selective measure of that component of the periodic pattern which is due to the specific sequential structure of the impulse train.

THE MODEL

Consider impulses via two separate channels impinging upon a (thalamic) nerve cell, and each of these, from whatever source, giving rise to a response. The interval durations between two impulses in channel (a) are monomodally distributed in the first instance. We assume the intervals to be independent of each other. This restriction is not essential and may be omitted if so wished. Channel (b) carries impulses with exponentially distributed intervals. These, too, are independent of each other and thus constitute a Poisson process. Again, they may have an arbitrary interval distribution, and in the DISCUSSION we shall mention an example of such a generalisation. If the mean frequency in (a) is much larger than in (b), the output impulses will mainly consist of those of the first process and will have an interval distribution almost the same as these, *i.e.* a single-peaked distribution. In the reverse case the output interval distribution will, for the same reason, have an exponential-like character. If the mean frequencies in the two channels are of the same order of magnitude the resulting interval distribution will have a shape between those of the two input distributions.

Multimodality of distributions which for thalamic neurons is mostly restricted to two equally spaced modes, can be envisaged by a simple mechanism which has been dealt with in full elsewhere[8], and is briefly described here. Suppose the impulses in (a), with a mean interval duration of m_φ, are subjected to a simple mode of inhibition, such that impulses are occasionally deleted. Intervals of double duration (mean $2.m_\varphi$) will sometimes occur, and also of triple and larger duration. In the same way distributions with a long tail may be simulated to some extent.

From the foregoing considerations the main thesis of this communication is to identify increasing intensity of stimulation with an increase of irregularly occurring impulses superimposed on the more or less regular resting discharge of neurons. Furthermore, the discharge pattern of spontaneous activity remains essentially unchanged at present but becomes submerged by a massive bombardment of impulses from another source.

As already mentioned, after pooling two recurrent processes, the resulting process is no longer recurrent. Qualitatively this can be recognized as follows. The more or less equal intervals in channel (a) are, owing to impulses from channel (b), split into two or more parts. If, for instance, an interval is cut in two, either the smaller part is followed by the larger part, or the reverse holds. This means that the duration of an interval is at times determined by its predecessor in such a way that, when restricting ourselves to this measure, the first order serial correlation coefficient r_1 has a negative value. The effect increases to a maximum if the number of Poisson impulses in channel (b) increases in relation to those in (a).

For still larger mean frequencies of impulses in (b), these will dominate the output impulse pattern in turn and, being of a recurrent nature, will counteract the tendency for negative correlation. Ultimately, the output intervals will again be almost independent of each other. Had the monomodally distributed series of events in (a) been positively correlated, the same argument would hold that r_1 will diminish in absolute value, will eventually become negative, and upon severe distortion by the Poisson series in (b) will reach zero. Poggio and Viernstein found that during spontaneous activity the intervals were almost always (but for two) positively correlated, and that negative correlation was present in samples of driven activity only. These findings are in accord with the properties of the model if stimulation is considered to be an influx of non-regularly occurring impulses brought into the resting discharge.

METHODS — EVALUATION OF THE MODEL

We shall mention in outline the analytical tools used, define the parameters needed to characterise the interval distributions encountered, and indicate how these can be estimated from experimentally observed distributions. In the APPENDIX formulae are given; their derivations are described elsewhere[8,9]. For the monomodal interval distribution $\varphi(t)$ we have used the Gaussian distribution*. If the time series

* Since the time interval t in $\varphi(t)$ is a positive number it is, strictly speaking, incorrect to use the Gaussian function since it is not zero for $t \leq 0$. In the examples given the spread is several times smaller than the mean, and the error is negligible.

of impulses is recurrent, the process is completely defined by the mean m_φ and the spread or standard deviation σ_φ. These can be obtained numerically from experimental distributions by conventional methods.

If not one, but two (*cf.* Fig. 3a) or more (*cf.* Fig. 9) equidistant peaks are present we have assumed that this has been brought about by annihilation of impulses with intervals that were originally distributed according to a Gaussian $\varphi(t)$. The interval distribution is denoted by $\varphi_i(t)$ with mean m_i. It can be imagined that the deletion has been effected by Poisson-distributed inhibitory impulses, with a mean frequency of occurrence of μ per unit of time from a source which we shall not specify at the moment, and which interact with the $\varphi(t)$ process in such a way that each subsequent $\varphi(t)$ impulse is annihilated. It can be shown, parenthetically, that the impulse series thus obtained is recurrent. If σ_φ is several times smaller than $1/\mu$, a condition that proved to be fulfilled in the examples so far examined, $\varphi_i(t)$ is very well approximated by a sum of Gaussian distributions with means m_φ, $2.m_\varphi$, $3.m_\varphi$, etc., spreads σ_φ, $\sigma_\varphi \cdot \sqrt{2}$, $\sigma_\varphi \cdot \sqrt{3}$, etc., and multiplied by a weighting factor α, $\alpha(1-\alpha)$, $\alpha(1-\alpha)^2$, etc. Further, $m_i = m_\varphi/\alpha$ and α is related to μ by $\alpha = {}_0\int^\infty \exp(-\mu t)\,\varphi(t)\,dt$; α equals one when there is no inhibition and decreases to zero for increasing strength of inhibition.

In pooling we have used as components $\varphi(t)$, or where applicable $\varphi_i(t)$, and an exponential distribution $\nu \exp(-\nu t)$. The resulting distribution is denoted by $p(t)$ with mean m and spread σ.

An expression for the expectation density function $E(t)$ for the shuffled condition is given in the APPENDIX. $E(t)$ for the unshuffled condition is not given as we have made no use of it in the present paper. We thought it more instructive to illustrate the theory by means of Monte Carlo simulation results. When there is no pooling, as when we are dealing only with a monomodal, a multimodal or an exponential distribution, the underlying processes were assumed recurrent; consequently there is no difference between $E(t)$'s for unshuffled and shuffled series.

PRELIMINARY RESULTS

For an exercise in computing interval distributions we refer to Fig. 1. In Fig. 1a a Gaussian $\varphi(t)$ is depicted with mean $m_\varphi = 38$ msec and $\sigma = 3.5$ msec. If impulses with this interval distribution and arriving via channel (a) are mixed with impulses via channel (b), which are exponentially distributed and have a mean interval duration $1/\nu = 90$ msec or $1/\nu = 18$ msec, one has distributions $p(t)$ as given in Fig. 1b and 1c. In the former the total number of impulses in a given period is constituted for the greater part from those of channel (a), and in the latter for the greater part of channel (b) as $18 < 38 < 90$. If, instead of pooling, inhibition comes into play with $1/\mu = 72$ msec, which implies that about half the impulses in channel (a) are deleted, a distribution $\varphi_i(t)$ as in Fig. 1d results. Only the first two peaks are shown; the subsequent ones are considerably smaller in amplitude. The curve in Fig. 1e holds when both inhibition with $1/\mu = 72$ msec and pooling with $1/\nu = 90$ msec are present. This set of parameter values has been used to characterise neuron 17–8 to which we shall revert in the next section. Fig. 1f represents a small sample of a Monte Carlo simula-

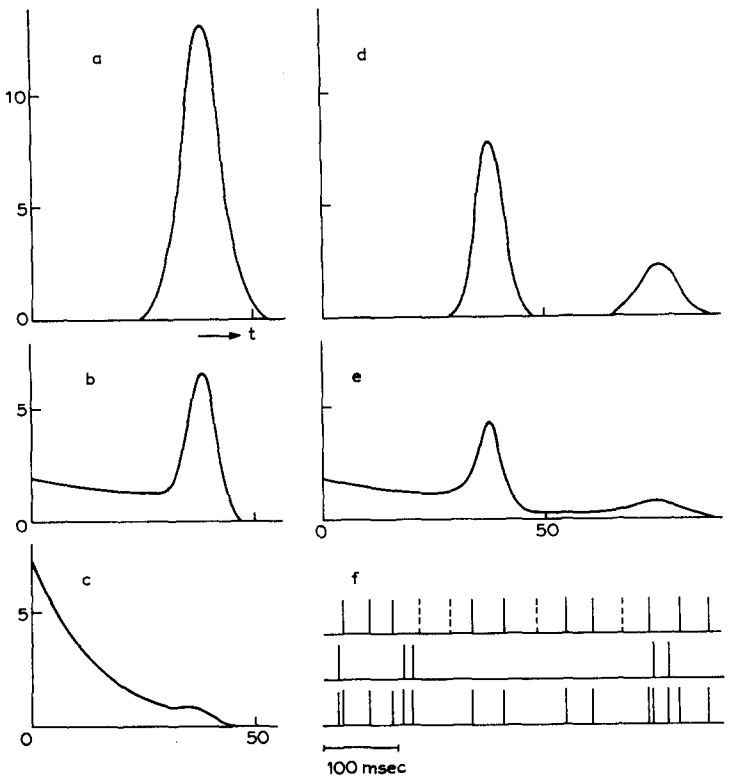

Fig. 1. For explanation see text.

tion belonging to the situation of Fig. 1e. The first series applies to channel (a), the second to channel (b) and the third to the pooled series. Inhibition in the first series is symbolized by dashed impulses.

One of the easiest ways of illustrating the non-recurrent character of inter-event intervals in a qualitative way is by means of so-called joint interval histograms [5, 6]. In Fig. 2b and 2c the abscissa of each point equals the duration of an interval t_n and the ordinate the duration of the immediately preceding interval t_{n-1}. In the underlying case we have pooled a purely periodic series of 100 intervals with period T ($= m_\varphi$; $\sigma_\varphi \to 0$) and 100 exponentially distributed intervals with mean $1/\nu = T$. The distribution of the intervals obtained is drawn in Fig. 2a, and the percentage of intervals of duration T is given by the hatched column. A negative correlation between adjacent interval durations is clearly visible as a clustering of points along the diagonal in Fig. 2b.

A further indication as to dependency between intervals follows from comparison with Fig. 2c obtained from the same collection of intervals after they have been shuffled. It seems that the interdependency has not markedly extended further than next-to-next intervals.

This can be judged from Fig. 2d and 2e where t_n versus t_{n-2} and t_n versus t_{n-3} have been plotted. These pictures do not differ very much from Fig. 2c, at least much less than Fig. 2b does.

We must confess that if $\sigma_\varphi \neq 0$ and $1/\nu \neq m_\varphi$, the differences between joint interval histograms for shuffled and unshuffled series are less clearly visible. For this reason, and because Poggio and Viernstein did not make use of it, we shall not continue to present data in this way.

COMPARISON WITH EXPERIMENTAL DATA

Fig. 3a gives p(t) of cell 39–3 during spontaneous activity, adapted from Fig. 1

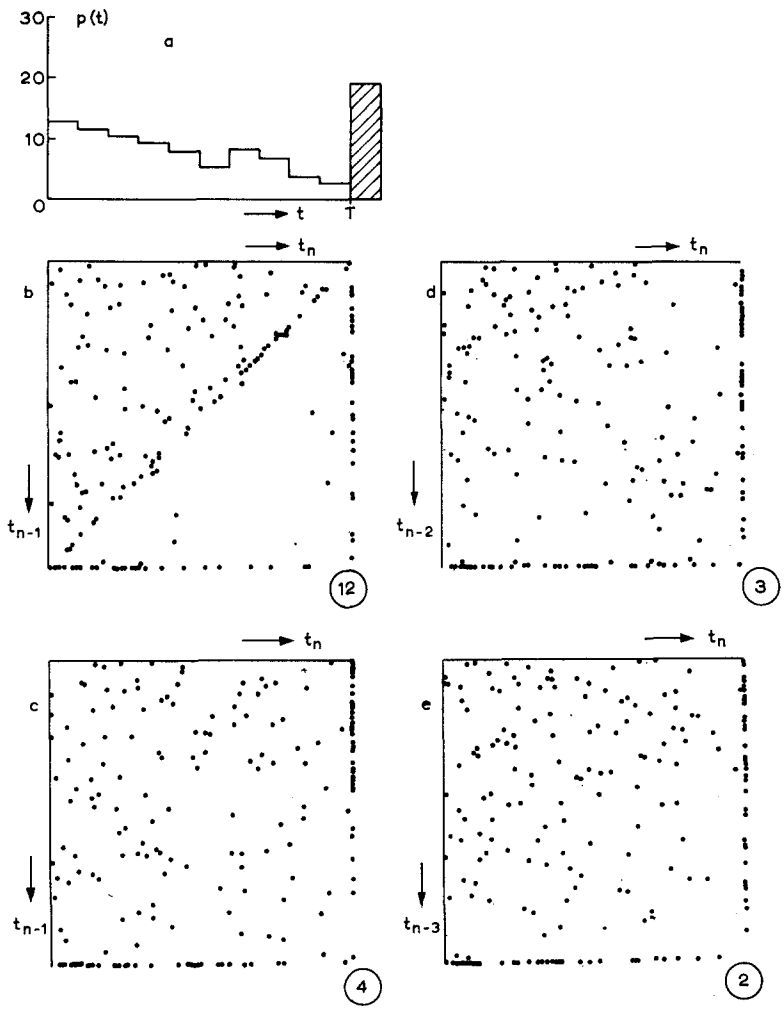

Fig. 2. (a) Interval distribution p(t) of a periodic impulse series with period T after being pooled with impulses the interval durations of which were exponentially distributed with mean T. Results from Monte Carlo simulation. Intervals of duration T are symbolized by a hatched column and equal 19% of the total number of 197 intervals. Abscissa : time, t, in arbitrary units. Ordinate: % of impulses per 0.1 T. b–e, Joint interval histograms. (b) For adjacent intervals of original series: c, the same after randomizing of intervals. Numbers in circles indicate number of times that an interval of duration T was followed by an interval of equal duration. d–e, The same as a, but for intervals further apart.

of Poggio and Viernstein[4], and Fig. 3b p(t) from a Monte Carlo simulation of the model with $m_\varphi = 35.3$ msec, $\sigma_\varphi = 5.7$ msec, $\alpha = 0.68$ and no pooling: $\nu = 0$. E(t) of the cell is drawn as a smoothed curve, from Fig. 12 of the said publication[4]. The points are from the same simulation. E(t) of the shuffled series was not given by

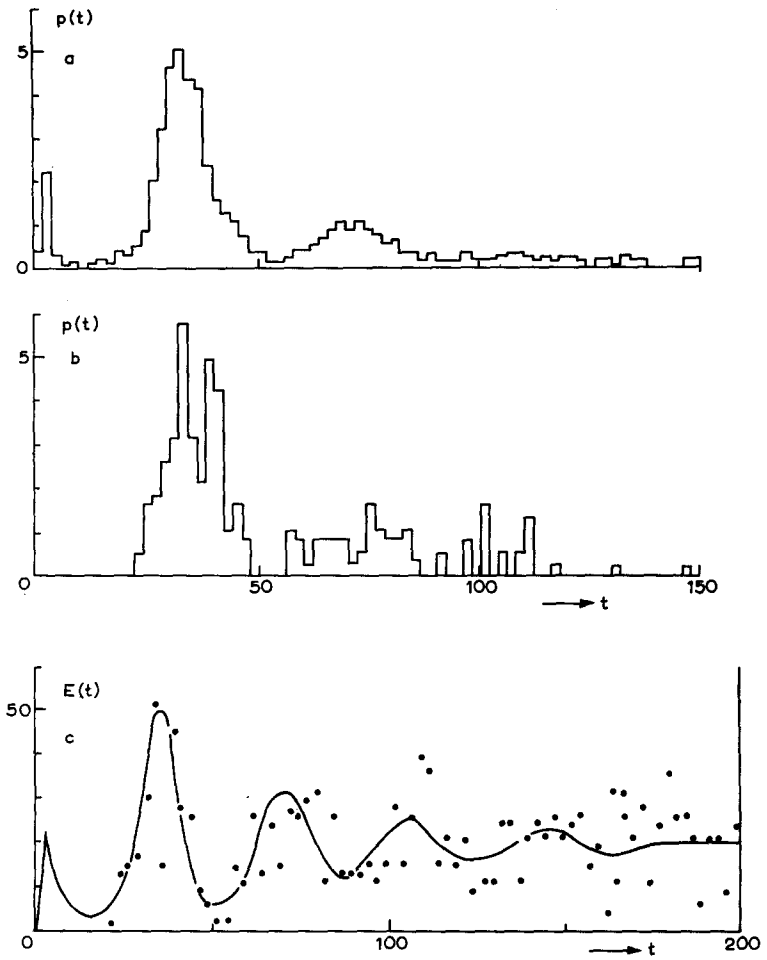

Fig. 3. (a) Interval distribution p(t) of thalamic neuron, after Ref. 4; (b) of model from simulation (200 intervals). Ordinate: % per msec. (c) Expectation density function E(t). Curve (smoothed data) for neuron; points (at multiples of 2.5 msec) for model. Ordinate: occurrence per sec. Abscissae: time t in msec.

Poggio and Viernstein[4] but can be computed from p(t). In doing this we have found hardly any difference from the drawn curve, valid for the original sequence. This might be expected in view of the low values of the serial correlation coefficients ($r_1 = +0.17$, higher orders being still less positive). As the data from the simulation originated from a recurrent process, no differences between E(t)'s for shuffled and unshuffled conditions other than those due to the finite sample length can occur, and

we have omitted the shuffling procedure. Upon stimulation of the cell, or in terms of the model, after the introduction of pooling, the situation changes drastically.

Fig. 4a shows p(t) of the same cell during driven activity, Fig. 4b p(t) from a

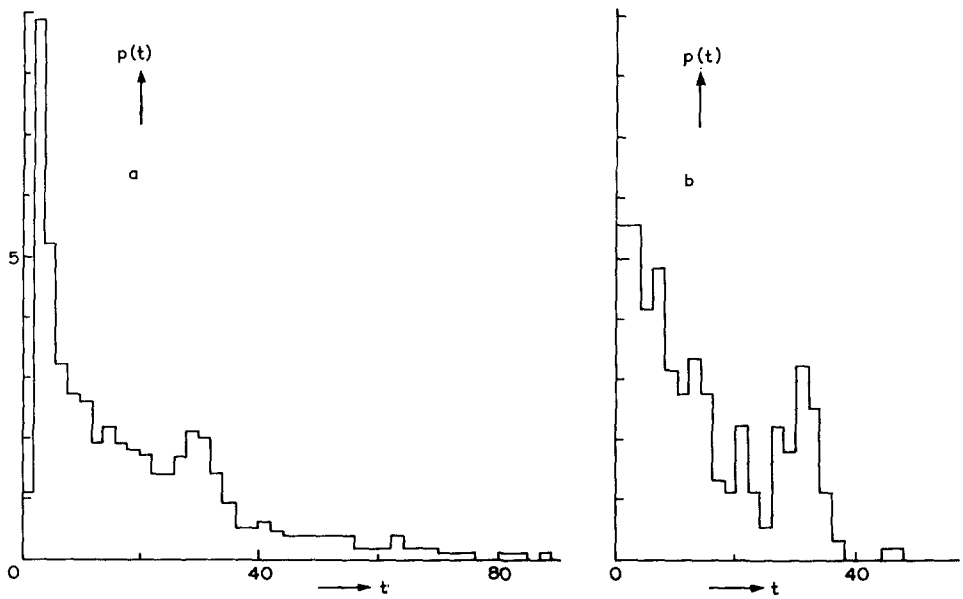

Fig. 4. (a) Interval distribution p(t) of thalamic neuron, after Ref. 4; (b) of model from simulation (200 intervals). Abscissa: time t in msec. Ordinate: % per msec.

simulation with $m_\varphi = 32.5$ msec, $\sigma_\varphi = 2.5$ msec, $\alpha = 1$ (no inhibition) and $1/\nu = 28.5$ msec. The total number of impulses in the simulation therefore consisted of about the same number from each of the two channels. E(t) of the cell is drawn as a smoothed curve in Fig. 5a; the points are from the simulation. The small number of intervals used has resulted in large statistical fluctuations. Nevertheless, the mean of E(t) is about the same for the model as for the cell, and the maxima, at multiples of 32.5 msec, are present in a well preserved form. E(t) of the nervous discharge intervals after shuffling was again computed from p(t) and is given as a smoothed curve in Fig. 5b. Points are from a simulation of 300 intervals. The oscillations are heavily damped and contrast with the unshuffled situation of Fig. 5a.

In Fig. 6a p(t) of cell 17–8 during spontaneous activity is depicted, adopted from Fig. 14 of Ref. 4. Fig. 6b holds for a simulation with $m_\varphi = 38$ msec, $\sigma = 3.5$ msec, $\alpha = 0.66$ and $1/\nu = 90$ msec.

The relatively large proportion of short intervals, shorter than the model value of around 38 msec, we have again identified as being the result of pooling. The interval durations of 50 msec and upwards were generated in the model by inhibition. This gives rise to a slight excess of durations of about 2×38 msec not found in that abundance in the experimental distribution. E(t) is given in Fig. 7a, as a smoothed curve for the cell and as points for the model. Fig. 7b gives E(t) after shuffling. As in

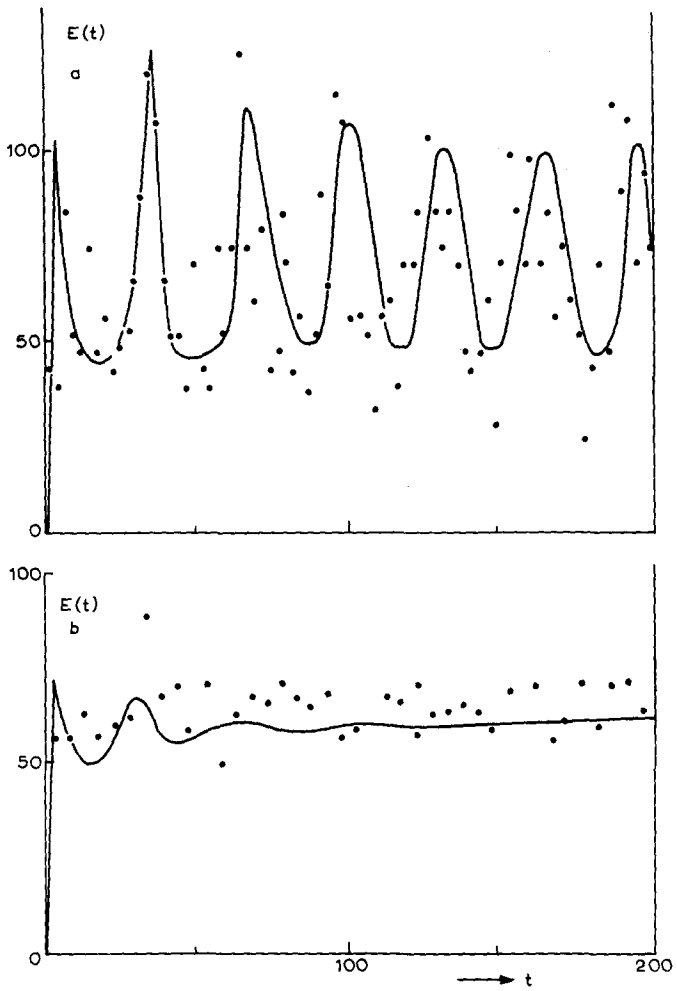

Fig. 5. (a) Expectation density function E(t). Curve (smoothed data) for same neuron as Fig. 4a; points (at multiples of 5 msec) for same model as Fig. 4b. (b) Same as (a) but after randomizing of intervals. Abscissa: time t in msec. Ordinate: occurrence per sec.

Fig. 5a and 5b, the differences between E(t) for original and randomized series are considerable after pooling.

In Fig. 8a the E(t) of cell 38–10 is represented as points, redrawn from Fig. 6 of Ref. 4. The curve is theoretical for $m_\varphi = 32$ msec, $\sigma = 4$ msec and $\alpha = 0.73$ without pooling. A close agreement has been found. This enables us to predict that p(t) of neuron 38–10, not published by Poggio and Viernstein[4], will not differ much from the theoretical one drawn in Fig. 8b. The mean frequency of discharge, $1/m_i = \alpha/m_\varphi = 22.8$ c/sec, is not much larger than 19.6 c/sec found for the cell.

A last example is provided by the spontaneous discharge of cell 34–3, the p(t) of which is given in Fig. 9. The points are from theory with $m_\varphi = 37$ msec, $\sigma_\varphi = 4$ msec, $\alpha = 0.90$ and $\nu = 0$. In order to reveal the theoretically expected third

peak between 100 and 120 msec, a semilogarithmic scale has been used. For E(t) of the cell we refer to Fig. 10a, where the fully drawn curve is valid for the original series and the dashed curve for the shuffled sequence and obtained from Fig. 15 of Ref. 4. The finding that both E(t) functions are characterised by the same cyclic fluctuation has, according to Poggio and Viernstein[4], furnished conclusive evidence

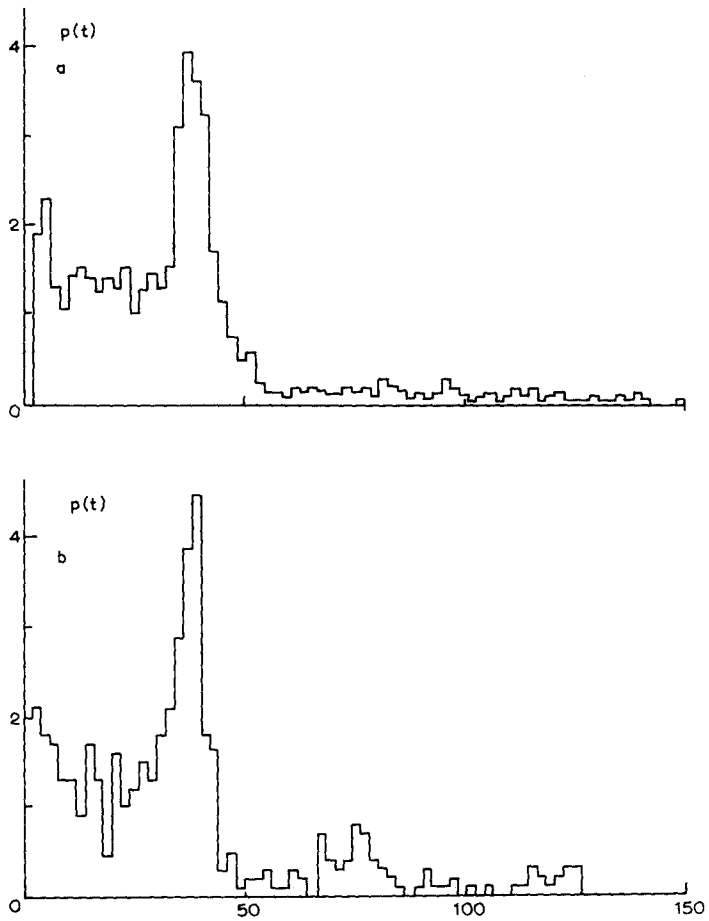

Fig. 6. (a) Interval distribution p(t) of thalamic neuron, after Poggio and Viernstein[4]; (b) of model from simulation (200 intervals). Abscissa: time t in msec. Ordinate: % per msec.

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hat, in this example, the periodic pattern has only secondary relations with the particular sequential order of the interval between impulses in the original neural sequence. It does, therefore, not come as a surprise, that E(t) of the model (Fig. 10b), shuffled and unshuffled being identical, bears a close resemblance with both the experimentally found E(t)'s.

DISCUSSION

The interval histograms of impulse series of thalamic lemniscal neurons,

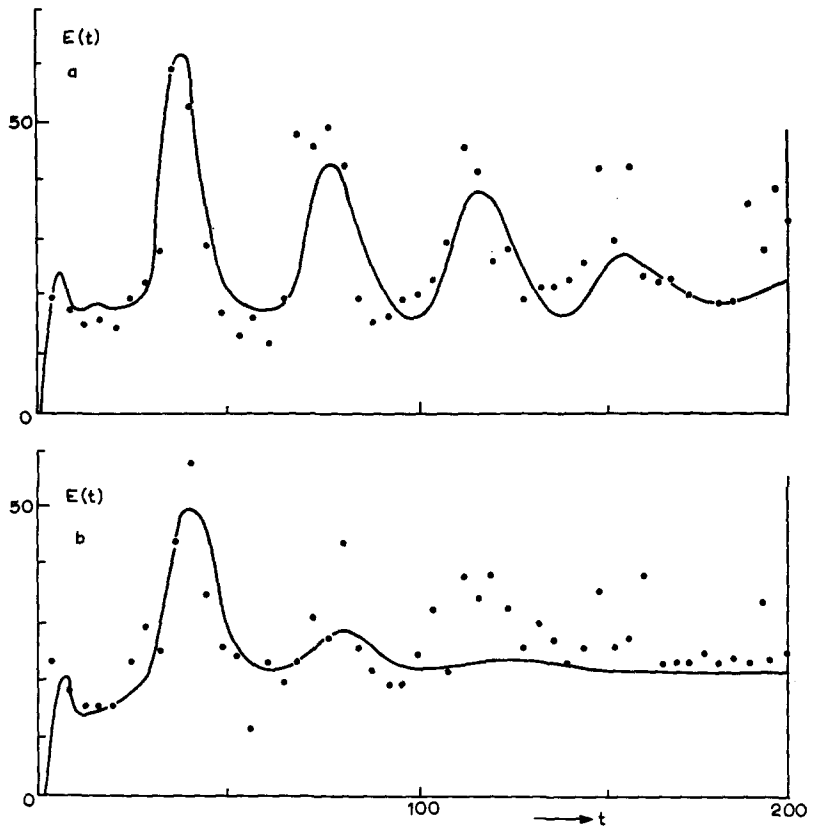

Fig. 7. (a) Expectation density function E(t). Curve (smoothed data) for same neuron as Fig. 6a; points (at multiples of 4 msec) for same model as Fig. 6b. (b) Same as (a) but after randomizing of intervals. Abscissa: time t in msec. Ordinate: occurrence per sec.

reported by Poggio and Viernstein[4], and which were frequently of various and uncommon shapes, could, to a fair extent, be embraced by a model incorporating maximally 4 parameters. A small number of parameters which are to be ascertained is indeed quite a necessary restriction for a model if it is not to fail in its very purpose: organizing experimental data in a condensed form.

The assumption is that a neuron is influenced by two separate channels, one having a rhythmic discharge, and the other carrying an irregular or burst-like sequence of impulses. All impulses impinging upon the cell contribute to the response. It is further supposed that if no intentional stimulation is present, the input with a monomodal interval distribution $\varphi(t)$ with mean m_φ, or in certain circumstances with a multimodal or long-tailed distribution, is of main importance. Upon driving, this factor remains present, not much changing its characteristics, but it is partly represented in the response because of the invasion of impulses with a mean frequency ν from the other channel. This is suggested by the following observation. The cited paper was primarily concerned with spontaneous activity, but for 4 neurons results for driven activity were also given. Among these, neuron 39–3 was studied most extensively. The relevant parameter values, which gave a good fit as to the interval distribu-

tions, equalled for spontaneous activity $1/m_\varphi = 38$ c/s and $\nu = 0$: that is, there was no activity in the second channel. For the driven state $1/m_\varphi = 31$ c/s and $\nu = 35$ c/s: the activity in the second channel was of the same order of magnitude as in the first channel. For another neuron, 39–2, not dealt with in this paper, we found for no stimulation (0 degrees of flexion of wrist) and during stimulation (45° degrees) $1/m_i$ changing from 14.5 c/s to 21 c/s, and ν changing from 4.2 c/s to 12.3 c/s, that is by a factor of nearly three. As amply discussed, a more stringent test for the model is

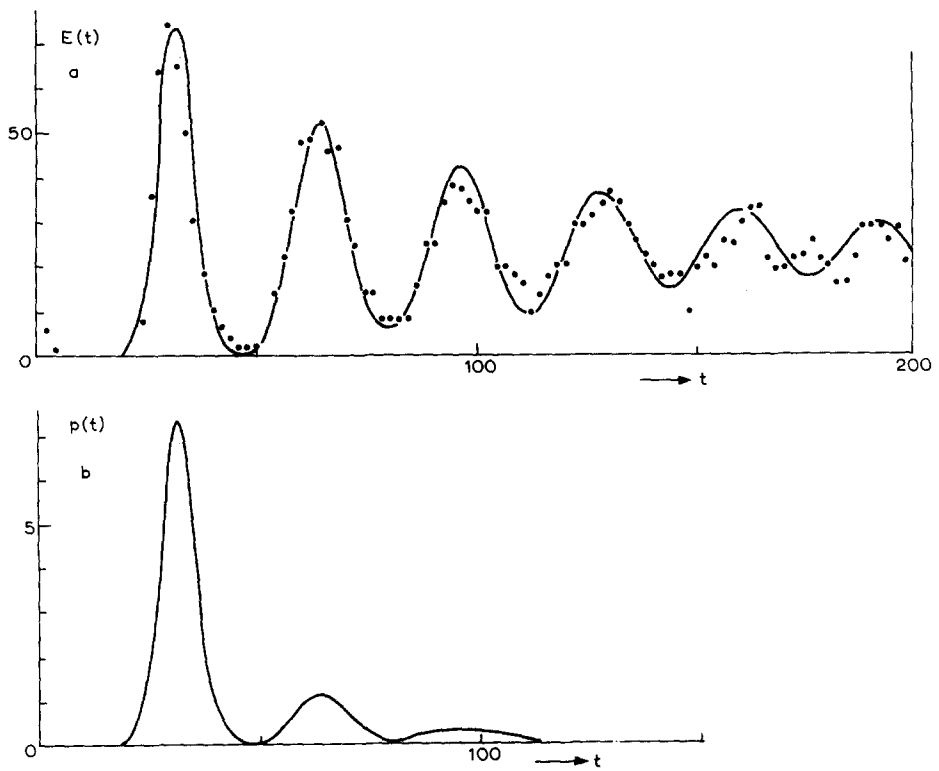

Fig. 8. (a) Expectation density function E(t). Points (at multiples of 2 msec) for thalamic neuron. Curve from theory, with interval distribution p(t) as shown in (b). Abscissa: time t in msec. Ordinate: occurrence per sec (a), % per msec (b).

provided by comparing the expectation density function E(t) for both the original and the shuffled series of impulses.

Before coming to this property we wish to emphasize that at least two other classes of models for probabilistic nervous discharge, developed during the last decade, can account for the observed histograms.

We refer to the concept of a fluctuating threshold and to one that is based on the additive summation of miniature potentials, with a threshold for discharge as well. With an appropriately chosen time course of recovery, arrival times of the summating unit potentials, etc., a huge variety of interval distributions can be generated

although a relatively large number of parameters will probably be required. A more serious drawback of these models is that independence between successive discharges is nearly always postulated in order to make an analytical solution possible. Conse-

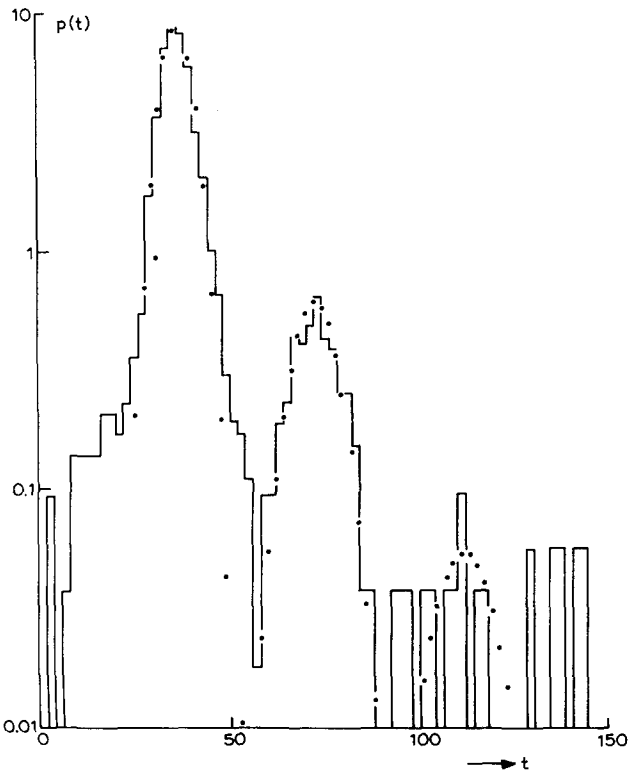

Fig. 9. Interval distribution p(t) of thalamic neuron; points from theory. Abscissa: time t in msec. Ordinate: % per msec.

quently, there is no difference in E(t) before and after shuffling. Indeed, as long as the interval distribution of an impulse series is considered to be the only property of neural activity, implying independence between interval durations, a choice between models is irrelevant.

By heuristic argument in the INTRODUCTION, and by means of the joint probability histogram, we have shown that, if two recurrent series of impulses are pooled, the output is not recurrent. Later on, we made use of the quantity E(t) to examine dependence between intervals. In the absence of short intervals, a situation that corresponds in our model to a single input dominance, no or only small differences in the shape of E(t) for shuffled and unshuffled series are expected. This is borne out for neuron 39–3, Fig. 3c and neuron 34–3, Fig. 10. For neuron 38–10, Fig. 8, an indirect indication can be obtained, as for the original series only E(t) was given and not E(t) after randomizing, nor p(t), from which the latter E(t) might have been computed. As the mean of the predicted interval distribution almost equals the mean of the

experimental interval durations, we have reason to believe that here too the theory is correct.

If short intervals do happen to be present, equivalent to a notable influence of the second channel in the theory, differences with respect to E(t) are anticipated. This is confirmed by the two examples tested: neuron 39–3, Fig. 5 and neuron 17–8, Fig. 7. The effect is optimal if the number of impulses per unit of time is about the same in both channels. For neuron 39–3 the condition is met, and the difference between both modes of E(t) is greater than for neuron 17–8. Judging from the two states of neuron 39–3, and especially from the 4 states of neuron 39–2, not only ν but also m_φ and σ_φ as well as the coefficient of inhibition α seem to change for different stimulus intensities. This complicates the picture, and hinders a more definitive judgement of the adequacy of the model. A search for neurons for which the favoured

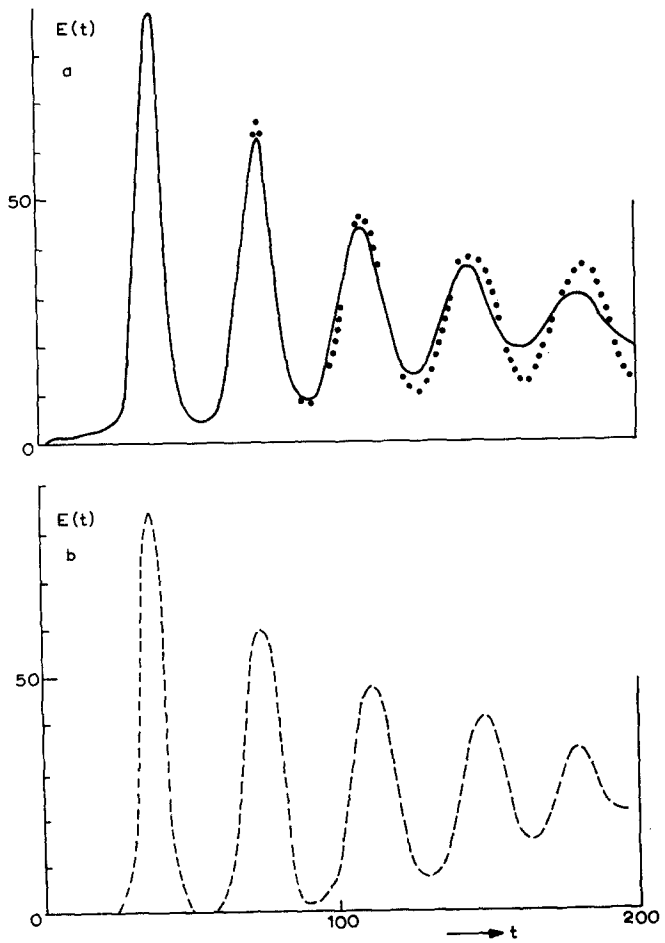

Fig. 10. Expectation density functions E(t). (a) Continuous curve for thalamic neuron; dashed curve, same after randomizing of intervals. (b) From theory. Abscissa: time t in msec. Ordinate: occurrence per sec.

interval duration m_φ remains the same in different circumstances, would allow a better decision.

The phenomenon of inhibition, as we have deliberately interpreted the long-tailed character of some interval distributions, obscures still another possible relationship. If one of the two participating input processes has a truly monomodal distribution of intervals, one might evaluate the influence of the other process, *i.e.* its mean frequency ν, from $1/m = 1/m_\varphi + \nu$.

As indicated, 1/m stands for the mean frequency of the response and $1/m_\varphi$ is equal or nearly equal to the frequency of the periodicity in $E(t)$. The value of ν obtained in this way is verified by comparing the theoretical value of $p(t)$ for $t = 0$ (APPENDIX), and $p(o)$ as found from extrapolation of experimentally recorded interval distributions, if these are of the 'pooled' type. The correlation between the mean impulse frequency (1/m) and the cyclic frequency ($1/m_\varphi$) did not differ significantly from zero. This observation led Poggio and Viernstein[4] to the suggestion that they may reflect two different aspects of neuronal behaviour, and this is, in fact, identical with our main assumption.

On at least two occasions the concept of pooling has been envisaged in theoretical neurophysiology. Cox and Smith[2,3] studied the statistics of motor endplate miniature potentials under the assumption that many independent sources trigger the quantal release of transmitter substance either completely deterministically or in a random way. Amassian *et al.*[1] described cuneate proprioceptive discharges with interval distributions (their P2 type) characterised by a peak at the very brief interval end of the distribution and a second peak at a later interval, that is of a shape that we have termed the pooled type. They found that distributions with a high incidence of very brief intervals in the overall run showed powerful inverse conditioning for such intervals, that is, the relative incidence of a very brief interval was reduced following an interval of similar duration, but was increased following a long interval. This property was encountered in the joint interval histograms of the PRELIMINARY RESULTS. The systemic increase in the duration of the most probable 'conditioned' intervals (t_n) accompanied by a decrease in the duration of the 'conditioning' interval (t_{n-1}) was also present in their 'no coincidence required' model, in which among others two periodical impulse series of different frequency were mixed electronically. They even provided a biological prototype of pooling by driving a cuneate postsynaptic hair field neuron by two different periodic trains (with periods of 90 and 101.5 msec) of electrical stimuli applied to neighbouring areas of skin. In spite of the transformation that the stimuli have undoubtedly endured before reaching the cuneate nucleus, the observed distribution fitted the theoretically expected shape remarkably well, namely an equiprobable distribution of intervals which extends out to the shorter of the two periods followed by a peak of intervals between 88 and 92 msec, and of a type similar to $p(t)$ in our Fig. 2a.

In order not to complicate matters unnecessarily, we have considered a process built up from two well-known basic functions. In doing so we have purposely refrained from an attempt to fit $p(t)$ and $E(t)$ as far as detailed aspects are concerned. This relates primarily to deficiencies between theoretical and experimental curves for small

values of the variable t. Recovery effects in neurons will manifest themselves in the absence of very small interval durations of the order of 1 msec. This property is not taken into account in the model. If so wished this may, to some extent, be remedied in the theory by introducing a dead time after a response, and also by taking in one of the channels an exponential distribution of intervals but including a dead time. On the other hand, several neurons in the driven state, *e.g.* 39–3, seem to possess exaggerated burst activity in that after very few responses of duration 0–2 msec, there is an abundance of intervals of 2–4 msec duration. This phenomenon is readily incorporated into the model by taking an interval distribution in the second channel equal to the sum of two exponential distributions, one with a very small and the other with a longer time constant ($1/\nu$), as suggested by Smith and Smith[7] in another context for cortical neurons.

As to the other channel a refinement is possible as well by assuming a non-recurrent monomodal distribution of intervals with a certain first order serial correlation coefficient r_1. Upon pooling, this coefficient should then change to values actually found for thalamic neurons and that range from +0.4 to –0.1 (Table I of Ref. 4). We have omitted this factor, because the outcome for these values of r_1, as reflected in the shape of $E(t)$, is not very large. This may follow from the fairly good fit of those $E(t)$'s where obviously no pooling was at stake: neuron 39–3, 38–10 and 34–3. For the last neuron, $r_1 = +0.4$ was found, the largest value of all spontaneously active neurons listed. It can be shown that the second maximum of $E(t)$ at $t = 2 \times 37$ msec (Fig. 10) is 7% smaller for $r_1 = +0.4$ than for $r_1 = 0$, the value we have implicitly used when assuming recurrency. A difference of this order of magnitude is observable between $E(t)$ for the unshuffled and shuffled sequence in Fig. 10a.

Another point of discussion deals with a result obtained by Werner and Mountcastle[10] who made an extensive study on the relation between the mean and the standard deviation of intervals during spontaneous activity and during different states of driven activity of the same neuron. They found values with a mean of 0.93 and 0.52 for the relative spread RS ($= \sigma_\varphi/m_\varphi$ and σ/m in our terminology). There was a linear regression between the mean and standard deviation for consecutive sampling periods for both states of the neuron. The slope of the curve through the points, the regression coefficient RC, differed considerably and was equal to 1.52 for spontaneous and equal to 0.63 for driven activity. From this they concluded that qualitative different factors influencing the two modes of activity are likely to exist. Our model is in harmony with this albeit with the annotation that a gradual transition between different modes of activity is expected. A test of the theory, at least for those neurons for which a change in RS and RC is accompanied by a change in the shape of the 'pooled type' interval distribution and for which m_φ is reasonably constant, is derived from the following argument. If the state of a neuron is indeed determined primarily by the proposed pooling mechanism the RC, $p(t)$ being fitted or even more easily m and σ and thus the RS, can be computed independently from $RC = (\partial\sigma/\partial\nu)/(\partial m/\partial\nu)$. Preliminary computations based on data of neuron 17–2 and 34–1 suggest this corollary to be correct, but further investigation is needed to settle this point.

Up to now we have implicitly taken the additive interaction between two impulse

series as being an intrinsic nervous structural property. In conclusion we shall touch upon a differently nuanced application of pooling which formally results in the same outcome. Suppose the normal attribute of a nerve cell is a more or less regular discharge. Now, a microelectrode, intended to record single unit activity, may become influenced by cells in the neighbourhood. As a result, extra impulses may appear on the record, intermingled with the genuine ones and not always well distinguishable from them. If this is so, and if upon stimulation the activity of the nerve cell under consideration and of others increases (1/m larger), it is not unlikely that the influence of the intervening cells or cross-talk (to identify with ν) will also become enhanced. Another application of the theory is the following. A threshold-operating device is often utilized to sharpen up nervous discharges into uniform rectangular or needle-like pulses. The trigger level must not be set too high in order to catch all spikes. To avoid this, the threshold may have been set too low, so that false triggering sometimes occurs because of baseline fluctuations. This again is equivalent to pooling of two sorts of pulses.

SUMMARY

1. In the literature interval distributions of thalamic nerve cell activity have been reported, that sometimes showed a preponderance of brief intervals followed by one or more peaks at a longer interval. These results have been compared with those of a model.

2. The model assumes that impulses via two separate channels impinge upon a nerve cell, and that each impulse gives rise to a response. The intervals between impulses in one channel are distributed according to an exponential or exponential-like function, those in the other channel according to a monomodal (or multimodal) function.

3. Interval distributions and expectation density (autocorrelation) functions of the model, based mainly on Monte Carlo simulations, were compared with those experimentally obtained.

4. Some implications of the double input concept are discussed, and methods are indicated for a more thorough investigation of the adequacy of the model.

APPENDIX

Pooling of an impulse series with interval distribution $\varphi(t)$, and mean m_φ, and an impulse series with distribution $\nu \exp(-\nu t)$, results in an impulse series with distribution $p(t)$ given by:

$$p(t)\,(1 + \nu m_\varphi) \exp(\nu t) = \nu^2 \int_t^\infty \left[\int_{\bar{t}}^\infty \varphi(\bar{\tau})\, d\tau \right] d\bar{\tau} + 2\nu \int_t^\infty \varphi(\bar{t})\, d\bar{t} + \varphi(t)$$

whereas

$$p(o) = \{\nu^2 m_\varphi + 2\nu + \varphi(o)\}/(1 + \nu m_\varphi)$$

The mean m and standard deviation σ can be estimated from:

$$m = m_\varphi/(1 + \nu m_\varphi)$$

$$\sigma^2 (1 + \nu m_\varphi)^2 \nu^2 = \nu^2 m_\varphi^2 - 2 + 2(1 + \nu m_\varphi) \int_o^\infty \exp(-\nu t)\, \varphi(t)\, dt$$

$E(t)$ of the series after randomizing follows from:

$$E(t) = p(t) + \sum_{n=1}^{\infty} p_n(t) \text{ with}$$

$$p_n(t) = {}_0\int^t p_{n-1}(\bar{t})\, p(t - \bar{t})\, d\bar{t} \text{ and } p_0(t) = p(t)$$

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