Effects of Lateral Inhibition on Fluctuations of the Impulse Rate

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ABSTRACT  Inhibition from neighboring eccentric cells has an effect on the variability of firing of a given eccentric cell. The reduction in the average impulse rate which is caused by inhibition decreases the variance of the impulse rate. However, this reduction of the average rate increases the coefficient of variation of the impulse rate. Inhibitory synaptic noise should add to the low frequency portion of the variance spectrum of the impulse rate. This occurs because of the slow time course of inhibitory synaptic potentials. As a consequence, inhibition decreases the signal-to-noise ratio for low frequency modulated stimuli.

INTRODUCTION

I have shown in the preceding paper (Shapley, 1971) that, for Limulus eccentric cells, stimulated by spots of light which act as purely excitatory stimuli, the variability of neuronal discharge is caused by fluctuations of the generator potential.

As is the case in many other neurons, an eccentric cell can also be influenced by neuronal interaction; illumination of neighboring ommatidia in the Limulus eye causes inhibition of the impulse discharge (Ratliff et al., 1963). This lateral inhibition is similar to postsynaptic inhibition in other nervous systems (Purple, 1964; Eccles, 1964). The effects of inhibitory interaction on randomness in the impulse firing of the Limulus cells should be similar to the effects of inhibition on other neurons. The effects of inhibition on the variability of neuronal discharge have hardly been studied in other systems.

In this paper, I will present results concerning the effects of lateral inhibition on randomness in impulse firing of eccentric cells. The time course, size, and rate of occurrence of excitatory and inhibitory postsynaptic potentials are important in determining the properties of variability in impulse firing. These factors which influence variability will differ from animal to animal, and from cell to cell within the same animal. For this reason, it is
obvious that details of the statistical properties of the activity of *Limulus* visual sensory neurons need not be identical to the characteristics of nerve cells performing different functions in other animals. Nevertheless, there should be general usefulness for the methods of analysis and the qualitative conclusions of this research on the stochastic component of neuronal response resulting from postsynaptic inhibition.

**METHODS**

These experiments were done mainly on single nerve fiber preparations from the horseshoe crab optic nerve. Techniques for *Limulus* optic nerve fiber recording have been described in the previous paper (Shapley, 1971).

For one part of this investigation, antidromic electrical stimulation of the optic nerve was used to produce lateral inhibition of a single fiber whose activity was monitored. The method used was similar to that described by Tomita (1958) and Lange (1965). The optic nerve was stimulated in air with a bipolar electrode made out of platinum wire. Brief pulses from a pulse generator (Tektronix 161) were passed through an isolation transformer and thence to the stimulating electrodes. Supramaximal electric shocks produced volleys of antidromically conducted nerve impulses in most of the optic nerve fibers. A single fiber was dissected from the nerve at a point closer to the eye than the stimulating electrodes so that it was spared the electrical stimulus.

A typical experiment proceeded as follows. A response of a single unit to a 20 sec light stimulus was recorded. After 2 min the response of the same unit to an identical light stimulus was recorded while the steady antidromic electrical shocks were being produced. The alternating sequence, first control, then inhibited fibers, was repeated 5 to 10 times in order to obtain sufficient data.

In other experiments I measured the effect of naturally evoked lateral inhibition; i.e., lateral inhibition produced by neighboring spots of light. For these experiments the light stimulus on the test receptor was provided by a small single optical wave guide. At a nearby region of the horseshoe crab eye a bundle of light guides was aligned to stimulate a group of receptors. I attempted to place this larger inhibitory spot in order to get the maximum inhibitory effect. The inhibitory light was turned on at the same moment as the test light. Control and inhibitory runs were interleaved, as above.

Measurement of nerve impulse intervals, computation of impulse rate from pulse intervals, calculation of variance spectra—all were performed as previously described (Shapley, 1971). As in the previous paper, eccentric cells were selected for analysis in the event that their responses were statistically stationary. This excluded those cells (a small fraction) whose variability changed with time during an experimental run or from one run to another.

**THEORETICAL BACKGROUND**

There is a fairly comprehensive mathematical model for the operation of *Limulus* eccentric cells (Knight et al., 1970). A schematic diagram of the model is shown in Fig. 1. The different component processes which determine the response of the cell are labeled in the block diagram. These are: Generator
Lateral Inhibition

Lateral inhibition of a given cell's activity is produced by the firing of nerve impulses by neighboring eccentric cells in the Limulus compound eye. Knight et al. (1970) have shown that the inhibitory synaptic potential resulting from a single nerve impulse in an inhibitory nerve fiber is biphasic, with a brief depolarizing phase and a prolonged inhibitory hyperpolarization. The time constant for decay of the lateral inhibitory synaptic potential is about one-third of a second, as opposed to about one-half second for decay of a self-inhibitory synaptic potential. The unit lateral inhibitory postsynaptic potential can be considered to be the impulse response of the lateral inhibitory synapse. Toyoda measured both the impulse response and frequency response of the lateral inhibitory synapse (which are related to each other by the Fourier transform). The two functions are shown in Fig. 2. The temporal characteristics of lateral inhibition play an important part in determining its effect on neuronal variability, as will be shown in the ensuing discussion.

Variance-Firing Rate Relation

The primary effect of inhibition is to lower the mean firing rate by reducing the average level of membrane depolarization. Such a change in the average
rate of firing will affect the variance of the impulse rate. This can be viewed in two ways, in the time domain and in the frequency domain. One can consider that the length of an interval between nerve impulses is an averaging interval; fluctuations of the membrane potential which are rapid enough to be averaged out during the pulse interval will have only a small effect on pulse firing variability—the longer the interval, the more high frequency components will be averaged out. An alternative way of considering the same effect is to view the impulse-firing mechanism as a filter which has a high frequency cutoff set by the mean firing rate. For instance, as the impulse rate decreases, the bandpass of the filter is narrowed, and, consequently, higher frequency components are filtered out from the impulse rate. Although the latter approach has some limitations, it has proved to be useful for obtaining analytical predictions of the effect of mean impulse rate on the variability of the impulse rate.

The view of an integrate-and-fire mechanism as a linear filter must be applied with caution because of the phenomenon of side bands, or aliasing. These terms refer to

![Image of Figure 2](image-url)

**Figure 2.** Lateral inhibition—frequency response and impulse response. The points were measured by imposing sinusoidal variations in firing of fibers in the optic nerve and measuring the amplitude and phase of the resulting modulation of the lateral inhibitory synaptic potential. The smooth curve is measured similarly, but with the impulse rate of the inhibited cell as the modulated variable. The insert is the impulse response, the Fourier transform of the measured frequency response. This figure is adapted from Dodge (1968).
the appearance of difference frequency components in the firing rate spectrum when
the firing rate is modulated at frequencies which exceed half the mean firing rate.
Aliasing does not affect the filter theory of the impulse-firing mechanism, because it is
an empirical fact that the side band components do not contribute much variance to
impulse rate fluctuations in eccentric cells.

In order to compute the effect of changing the average impulse rate, we
must consider the filtering action of the current-to-firing rate mechanism.
This involves the contributions of the integrate-and-fire mechanism and self-
inhibition. As derived by Knight (1969) and Knight et al. (1970) the fre-
quency response for the current-to-firing rate process is,

\[
S(f) = \frac{(1 + K_s)(B(f))}{1 + K_s \left[ 1 - \frac{(1/\tau_s f_0)(1 - e^{2\pi f/f_0})}{(e^{2\pi f/f_0} - 1)(1 - e^{-2\pi f_0/2\tau_s})} \right]}
\]

(1)

\( S(f) \) depends on the mean firing rate \( f_0 \), and the self-inhibitory coefficient,
\( K_s \), and time constant, \( \tau_s \). \( B(f) \) is the frequency response of an integrate-and-
fire device; it depends on \( f_0 \).

\[
B(f) = \frac{1 - e^{-2\pi f/f_0}}{2\pi f/f_0}.
\]

I have been able to simplify the analytic expression for \( S(f) \) by means of an
approximation.

If we assume that \( \tau_s f_0 \gg 1 \), which is true over a useful range of the re-
sponse of eccentric cells, then \( e^{2\pi f_0/\tau_s} \approx 1 + 1/\tau_s f_0 \), and we can write

\[
S(f) \approx \frac{(1 + K_s)B(f)}{1 + B(-f)2\pi f/\tau_s}.
\]

In fact, \( S(f) \) can be further approximated to yield

\[
S(f) \approx \frac{1 + K_s}{1 + 2\pi f/\tau_s} B(f)
\]

(2)

where the dependence on the mean firing rate is entirely contained in \( B(f) \).¹
That equation (2) is a good approximation for \( S(f) \) is shown in Fig. 3. \( S(f) \) is
computed for nominal values of \( K_s \) and \( \tau_s \), and two values for \( f_0 \): 10 adrians
(impulses/sec) and 20 adrians. The amplitude and phase of the complex

¹ The approximation, equation (2), turns out to be a refinement of Stevens' original calculation (1964)
for the frequency response of a neuron with self-inhibition. It is identical with Stevens' expression
except for the important factor \( B(f) \).
valued frequency response \( S(f) \) are shown. The approximation for \( S(f) \) based on equation (2) is plotted as points (+) on the solid curve. The latter is computed from the exact expression, equation (1), which has been shown to fit observed frequency responses. What the approximation ignores is the discrete nature of self-inhibition, the fact that self-inhibitory potentials are phased to the firing of nerve impulses. That it is a good approximation for typical parameter values tells us that the self-inhibitory potentials are long enough so that we can safely ignore the discreteness at moderate firing rates.

The approximate expression for the frequency response is a product of two parts: \( B(f) \) which depends on the mean impulse rate, and a function which

does not vary with mean rate. The approximation allows us to predict the effects of changes in mean rate in terms of a single function, \( B(f) \).

We can do this by considering the variance spectrum of the impulse rate, \( \varphi_\nu(f) \). As shown previously, the impulse rate variance spectrum is produced by filtering the variance spectrum of the generator potential, \( \varphi_\sigma(f) \), through the current-to-firing rate mechanism. This is expressed in the following equation

\[
\varphi_\nu(f) = |S(f)|^2 \cdot \varphi_\sigma(f).
\]

Suppose the generator potential variance spectrum remains the same, but
the mean impulse rate is changed. Call the original variance spectrum of the impulse rate \( \varphi_{N1}(f) \), and the variance spectrum after the rate has been changed \( \varphi_{N2}(f) \). Using the approximation of equation (2) and the same notation as for the spectra, \( B_1(f) \) for the original impulse rate and \( B_2(f) \) for the changed rate, we obtain the following expression

\[
\frac{\varphi_{N2}(f)}{\varphi_{N1}(f)} = \left| \frac{B_2(f)}{B_1(f)} \right|^2
\]

or

\[
\varphi_{N2}(f) = \varphi_{N1}(f) \left| \frac{B_2(f)}{B_1(f)} \right|^2.
\]  \hspace{1cm} (3)

The variance can be calculated by integrating the variance spectrum with respect to frequency.

With the use of equation (3) we can calculate the change in variance with average impulse rate, all other variables held fixed. Given \( \varphi_{N1}(f) \) at a particular average impulse rate, we can predict the variance (and shape of the variance spectrum) for other mean impulse rates. The curve relating variance with average impulse rate is shown in Fig. 4. The variance increases monotonically with mean firing rate, other things being equal.

In order to check whether this method of calculating the variance–firing rate relation is theoretically correct, I simulated the problem with one of the neuronal analogues which are described in Appendix I. The neuronal analogue is an electronic device which was designed to simulate the mathematical model of the eccentric cell which was diagrammed in Fig. 1. The generator potential variance spectrum, \( \varphi_{o}(f) \), for the neuronal analogue was held fixed while the impulse rate was varied by varying a constant voltage which was added to the noisy simulated generator potential at the summing point of the analogue. The variance and variance spectrum were computed from the impulse rate produced by the analogue. The points marked with an X on Fig. 4 are the values of the variance at different average impulse rates. The analytically calculated curve fits the points fairly well; this indicates that the assumptions used for the calculation are valid.

It is also interesting to consider the effect of varying the average impulse rate on the coefficient of variation of the impulse rate. This relation is also shown in the graph of Fig. 4; it was derived from the variance–firing rate curve. While the variance decreases with decreasing impulse rate, it decreases more slowly than the mean rate; this results in a net increase of the fraction standard deviation/mean, which is the coefficient of variation. Therefore, reductions in average impulse rate decrease the variance of neuronal firing while increasing the coefficient of variation.
Lateral Inhibition As a Noise Source

Besides its effect on the average impulse rate, lateral inhibition should add some extra randomness to the membrane potential of the eccentric cell. During natural stimulation by light, a group of inhibitory cells fire nerve impulses asynchronously and, to some extent, randomly in time. The summed inhibitory synaptic potential should fluctuate because of this effect. The inhibitory synaptic noise is independent of the generator potential, so the variances of the two fluctuating components should add.

The characteristics of the summed inhibitory synaptic potential should depend on two factors: statistical properties of the occurrence of nerve impulses in inhibitory neurons, and the time course of the unit inhibitory synaptic potentials.

The point process which underlies the summed lateral inhibitory potential

![Figure 4](image-url)

Figure 4. Variance (σ²) and coefficient of variation (σ/m) as functions of mean impulse rate. Variances at different impulse rates of eccentric cell analogue are denoted x. The smooth curve for variance is calculated by filtering the impulse rate variance spectrum at one average rate (16.1 impulses/sec or adrians) by the appropriate filter characteristic for each average impulse rate. The coefficient of variation points (open circles) is calculated from the variance points, and the curve from the variance curve. Note the slope of these curves: positive for the variance, negative for the coefficient of variation.
is a superposition of the impulse trains from each of the nerve fibers which have a synaptic effect. The statistics of this point process, which depends critically on the fact that the individual fibers are almost periodic, have an influence on the variance of the summed synaptic potential. This effect is discussed by Dodge et al. (1970). Summarizing this work we can say that the variance spectrum of the superimposed pulse train will have peaks at the average firing rates of the individual fibers, and at higher harmonics of these average rates. It will therefore differ from a Poisson point process whose variance spectrum is flat.

The inhibitory potential, like all summed synaptic potentials, can be viewed as filtered shot noise. The shots are the presynaptic nerve impulses and the filter is the synapse; the unit inhibitory postsynaptic potential is the impulse response of the synaptic filter. The shape of a typical lateral inhibitory postsynaptic potential is shown in Fig. 2; also shown in that figure is the frequency response of the inhibitory synapse. The low pass character of this filter tends to reduce high frequency periodic components in the summed inhibitory potential.

A consequence of the low pass characteristic of the lateral inhibitory synapse is that whatever inhibitory fluctuations there are must be very low frequency fluctuations. So we expect to see additional low frequency components in the impulse rate variance spectrum in an eccentric cell which is influenced by lateral inhibition.

We can get definite predictions for this complicated phenomenon, the effect of inhibitory interaction on neuronal variability, by using the analogue of the eccentric cell (described in Appendix I). Typical neuronal firing in response to purely excitatory stimuli can be simulated. Then a good imitation of naturally occurring lateral inhibition can be produced by feeding a multiple fiber pulse train recorded from a Limulus eye into the inhibitory synapse of the analogue.

The results of such an analogue experiment are summarized in the variance spectra of Fig. 5. The control spectrum, characteristic of firing which results from purely excitatory stimuli, shows the low frequency cutoff imposed by self-inhibition and the high frequency cutoff resulting from the integrate-and-fire mechanism. The spectrum of the inhibited impulse rate shows an increase in the size of low frequency components because of added inhibitory “noise” and a lowered high frequency cutoff as a result of the reduction of average impulse rate. If our model is correct, the same kind of change in the pattern of neuronal randomness should be observed in Limulus eccentric cells which are inhibited by light-evoked lateral inhibition. Observations on these effects are presented in the next section.
RESULTS

Effect of Reduction in Mean Rate

Inhibition produced by antidromic electrical stimulation reduces the variance of the impulse rate. When the antidromic shock rate is high enough, i.e. greater than 10/sec, the steady-state summed inhibitory potential ought to be practically constant, with very small ripple at the shock rate. Therefore, the change in variance with "antidromic inhibition" should be a measure of the effect on variance of changing the average impulse rate.

The data from such an experiment are displayed in Fig. 6. Two sample records of impulse rate are shown: the lower record is control firing in response to a purely excitatory light stimulus, the upper record is firing in response to the same stimulation by light while the cell is also undergoing steady inhibition elicited by antidromic electric shock of the optic nerve.

The variance of the antidromically inhibited impulse rate is 60\% of the variance of the control rate. This drop in variance is associated with a reduction in average impulse rate of 5.2 adrians. The magnitude of the variance reduction predicted by the filter model for the impulse firing mechanism is 59\% of the control. The agreement, both qualitatively and quantitatively, of the mathematical model with this experimental result is strong support for the theory.

What seems at first a simpler and more straightforward method for controlling the firing rate, namely DC current injection through a microelectrode, has proved to have more complicated effects than antidromic inhibition. This seems to occur because DC current injected at the cell soma affects the nearby photoreceptor membrane while the inhibitory synaptic potential, which occurs at a point far from the photoreceptor, does not. The inhibitory potential occurs at the point of synaptic contact between eccentric cells,
which is close to the impulse firing mechanism and far from the cell soma and photoreceptor membrane (Purple, 1964).

**Lateral Inhibition Produced by Light**

Lateral inhibition produced by stimulating a neighboring group of receptors with light has a more complex effect than the mere reduction in average impulse rate produced by antidromic inhibition. A record of data from an experiment which demonstrates this is shown in Fig. 7. The impulse rate of a *Limulus* optic nerve fiber is shown. At time zero a small light illuminated the test receptor. At 4 sec a large spot of light stimulated a neighboring group of receptors and the test cell is inhibited by their activity. Both the pattern and magnitude of the variability in the firing rate were changed by the light-evoked inhibition.

The nature of the effects produced by lateral inhibition can be seen by examination of variance spectra of the impulse rate. Impulse rate spectra for control and inhibited firing are shown in Fig. 8 for two cells which are representative of the many cells on which these measurements were made. The change in the shape of the variance spectra, because of the presence of
FIGURE 7. Lateral inhibition produced by illumination of neighboring receptors. Shown is the response to excitatory stimulation by light, of 19 sec duration, and superimposed inhibitory flash, of 6 sec duration starting 4 sec after the onset of the excitatory stimulus. In this case the variance is increased by the presence of inhibition.

FIGURE 8. Impulse rate variance spectra for control and inhibited firing. Spectra are shown for two different cells. The control spectra are the response of each cell to a purely excitatory stimulus (small steady light). The spectra labeled inhibited are from the response of the cell to the excitatory stimulus presented simultaneously with a stimulus which evoked lateral inhibition (large neighboring spot of light).
lateral inhibition, is very much in agreement with the theoretical predictions advanced in the previous section; to see this, compare Fig. 8 with Fig. 5.

In one of the cases shown, the variance increased during inhibition, in the other it decreased during inhibition. This occurred because the naturally evoked inhibition produced two opposing influences on the variance. Lateral inhibition tends to decrease variance by its reduction of the mean rate, and increase variance by adding an additional noise source to the membrane potential. These two opposing influences can sometimes result in a net increase in variance though more often the balance is on the side of a reduction. Because these effects take place at opposite ends of the variance spectrum, they may be clearly seen in the spectra of Fig. 8.

In both these experiments, reduction of the mean impulse rate by inhibition caused a filtering out of higher frequency components. In opposition to this effect, the noise from inhibition added to low frequency components in the fluctuations of the impulse rate.

Relation between Variance Spectrum and Frequency Response

In the previous paper (Shapley, 1971, equation 3) proportionality was demonstrated between the variance spectrum of the impulse rate, \( \Phi_N(f) \), and the squared amplitude of the frequency response for the transduction from light to impulse rate, \( N(f) \). In those experiments there was no lateral inhibition because the stimuli were restricted to single ommatidia. Lateral inhibition markedly affects the relation between the frequency response, \( N(f) \), and the variance spectrum of steady-state fluctuations.

Fig. 9 shows the results of an experiment designed to measure this effect. The variance spectrum in Fig. 9 is the spectrum of the impulse rate in response to a large spot of steady light intensity. On the same scale, plotted as a smooth curve, is the squared amplitude of the response to sinusoidal modulation of the light at all modulation frequencies. A large spot of light was used in these experiments to provide a substantial amount of lateral inhibition.

In this experiment \( \Phi_N(f) \) and \( |N(f)|^2 \) do not have the same shape, although for experiments in which the stimulus is a small spot of light, \( \Phi_N(f) \) is roughly proportional to \( |N(f)|^2 \). The result of this experiment is consistent with the characteristics of lateral inhibition mentioned in the section on theoretical background. As a component of the response to modulated light, inhibition subtracts from the response to low frequency modulation while enhancing the response to midrange frequencies. As a noise source inhibition adds to the low frequency components of the variance spectrum.

The squared amplitude of the frequency response, \( |N(f)|^2 \), shows very marked peaking under the conditions of large spot illumination; this is the amplification phenomenon reported and explained by Ratliff et al. (1967, 1969).
Under these conditions the variance spectrum is relatively flat out to the cutoff frequency. This result implies that, in terms of the impulse rate, lateral inhibition reduces the signal-to-noise ratio for low frequency modulated stimuli while maintaining, or even increasing the signal-to-noise ratio for stimuli at the tuning frequency, the peak frequency of the frequency response.

![Graph](image)

**Figure 9.** The relation between frequency response of the light-to-impulse rate process and the variance spectrum: the effect of lateral inhibition. $|N(f)|^2$ is the smooth curve and $\phi_N(f)$ is the jagged curve in the upper graph. Below are the respective autocorrelations. Deviations between the spectra are obviously large and significant at low frequencies and at the peak frequency of the frequency response (corresponding to deviations in the autocorrelations at 0.4–0.5 sec, and at 0.15 sec, respectively). The reasons for these discrepancies are commented upon in the text.

**Discussion**

Lateral inhibition in eccentric cells tends to lower variance of the impulse rate by reduction of average pulse rate; at the same time it tends to increase the variance by adding low frequency fluctuations to the membrane potential.

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2 I am using the term signal-to-noise ratio in an unconventional way. By signal-to-noise ratio at a given frequency, I mean the ratio $(|N(f)|^2/\sigma_N^2(f))^{1/2}$. This is the signal-to-noise ratio of the signal plus noise passed through a filter optimally tuned to the frequency $f$; it is a measure of the optimal performance of which a system is capable. In an uninhibited eccentric cell, typically this ratio is a constant. The usual definition of a signal-to-noise ratio is $|N(f)|/\sigma_N$. 
of the neuron. Both these effects are predicted from a phenomenological model of the eccentric cell which has been described above.

The competing effects of lateral inhibition most often result in a net decrease in variance of the impulse rate. The coefficient of variation of the impulse rate, the standard deviation/mean, is invariably increased by the introduction of inhibition.

There are several neuronal models in the literature which contain notions about the sources of neuronal variability similar to the eccentric cell model presented here (Stein, 1967; Gerstein and Mandelbrot, 1964; Geisler and Goldberg, 1966; Calvin and Stevens, 1968). Such models include the assumption that noise in the membrane potential, probably due to randomly arriving synaptic potentials, causes the randomness in neuronal firing. They differ somewhat in degree, but not in kind, from models which involve triggering single nerve impulses off presynaptic pulses arriving on several convergent channels—the pooling models of Bishop et al. (1964) and ten Hoopen (1966). All these models possess a common property, namely that postsynaptic summative inhibition will tend to make the impulse rate relatively more variable, i.e. increase the coefficient of variation, other things being equal. This assertion is proved for one particularly tractable neuronal model, the Gerstein-Mandelbrot model, in Appendix II.

Although the conclusion that relative variability increases with postsynaptic inhibition is implicit in many theories of neuronal mechanisms, it has not been emphasized before. The increased relative variability due to postsynaptic inhibition may be a price the nervous system has to pay for the increased discrimination and tuning, both spatial and temporal, provided by inhibition (Ratliff, 1965; Ratliff et al., 1967, 1969).

However, randomness introduced by inhibition also may serve to mask signals which are not physiologically important. For instance, lateral inhibition in eccentric cells decreases the signal-to-noise ratio (as defined in the section on Results) for low frequency flicker. But it tends to maintain or increase the signal-to-noise ratio at the peak frequency of the frequency response. The *Limulus* eye is sharply tuned to a modulation frequency of 3 hz, while the fluctuations introduced by inhibition are mainly concentrated in the frequency range of zero to 1 hz. So, while variability is designed into the *Limulus* visual system, it still may not degrade the transmission of signals which are important. This may be a design principle in other nervous systems.

**APPENDIX I**

*Analogue Eccentric Cells*

The effects on eccentric cells of mixed dynamic excitation and inhibition are complex. In order to simulate these effects, F. A. Dodge has designed electronic analogues of eccentric cells. These machines were used to perform the analogue experiments
whose results were shown in Figs. 4 and 5. The analogues conform to the block diagram of Fig. 1.

Each section of the analogue includes a network which imitates, with electrical components, the dynamic behavior of the corresponding part of an eccentric cell. The analogue possesses a summing point which is the output of an operational amplifier. This summing amplifier has as inputs the "generator potential" section, the "current" input, "self-inhibition," and "lateral inhibition."

The output of the summing amplifier drives a voltage-to-frequency converter (FM) which is an integrator circuit in series with a monostable, fast recovery, multivibrator. The output of the multivibrator is the impulse output of the analogue; these pulses are fed back through the "self-inhibition" network to the summing amplifier, or to the "lateral inhibition" network of other analogue eccentric cells.

The generator potential section consists of five stages of low pass RC filtering. The self-inhibition is a single time constant low pass filter; i.e., it produces a decaying exponential for each pulse the analogue fires as a result of stimulation. The lateral inhibition section is somewhat more complicated since it must reproduce a biphasic impulse response. It consists of two different low pass filters in parallel, both feeding yet another filter. The faster of the two parallel stages is inverted before being added to the final filter in order to provide the early positive phase of lateral inhibition. The strengths of self-inhibition and lateral inhibition are set by potentiometers which control how much inhibition each impulse exerts.

The noisy generator potential was simulated with the use of a photomultiplier tube as a white noise generator; the photomultiplier output was fed into the generator potential section.

APPENDIX II

Inhibition and the Gerstein-Mandelbrot Model

WITH THE HELP OF BRUCE KNIGHT

Gerstein and Mandelbrot (1964) proposed that variability in neural impulse firing reflects the random bombardment of excitatory and inhibitory synaptic potentials on the neuron. They assumed that synaptic potentials are very brief, that they are integrated up to a threshold, and that each individual synaptic potential is so small that many are required to sum up to the firing threshold. They derived a probability density function for the impulse intervals, which they wrote:

\[ P(t) = Kt^{-3/2} \exp \left\{ -\frac{a}{t} - bt \right\} \]

\( K \) is a normalization constant. The parameter, \( a \), measures the height of the threshold relative to the size of a single synaptic potential, and the parameter, \( b \), measures the difference between the rate of occurrence of excitatory and inhibitory synaptic potentials; i.e., the net rate of drift towards threshold. In order to understand the effects of inhibition, one needs to calculate the coefficient of variation of the Gerstein-Mandelbrot model. This reduces to the problem of calculating the first and second moments of the probability density function.
In order to calculate the moments of $P(t)$ we have to evaluate integrals of the form

$$K \int_0^\infty dt \, t^{n-1/2} \exp \left\{ -a/t - bt \right\} = \overline{t}^{n+1}$$

where $n = 0$ for the calculation of $\overline{t}$, $n = 1$ for calculation of $\overline{t}^2$.

We simplify the problem by introduction of the parameter, $\gamma$, such that $t = \gamma \tau$ and $\gamma = \sqrt{a/b}$. Then, $a/t + bt = a/\gamma \tau + b \gamma \tau = \sqrt{ab} (1/\tau + \gamma)$. Also, let $z/2 = \sqrt{ab}$.

The integrals for the calculation of the moments become

$$K \gamma^{n+1/2} \int_0^\infty d\tau \, \tau^{n-1/2} \exp \left\{ -\frac{z}{2} \left( \frac{1}{\gamma \tau} + \tau \right) \right\} = \overline{\tau}^{n+1}.$$

It is possible to show, using the substitution, $\xi = \frac{1}{\tau}$, that

$$\int_0^\infty d\tau \, \tau^{n-1/2} \exp \left\{ -\frac{z}{2} \left( \frac{1}{\gamma \tau} + \tau \right) \right\} = \int_0^\infty d\tau \, \tau^{n-1/2} \exp \left\{ -\frac{z}{2} \left( \frac{1}{\gamma \tau} + \tau \right) \right\}$$

or, if we say

$$F_n = K \int_0^\infty d\tau \, \tau^{n-1/2} \exp \left\{ -\frac{z}{2} \left( \frac{1}{\gamma \tau} + \tau \right) \right\},$$

then $F_n = F_{n-1}$ and in particular $F_1 = F_{-1}$. This implies that $\overline{t} = \gamma = \left(\frac{a}{b}\right)^{1/2}$ since calculation of the first moment involves $\gamma F_0$ and calculation of the normalization integral involves $F_{-1}$.

In order to calculate the second moment, $\overline{t}^2$, we must do a little more. Differentiating with respect to $z$, we can establish the identity

$$F_{n+1} = -2F_n' - F_{n-1}.$$

It is also possible to show that

$$F_n(z) = \sqrt{2\pi} \, \varepsilon^{-z} / \sqrt{z}$$

and to calculate from the above identity

$$F_1(z) = \sqrt{2\pi} \, \varepsilon^{-z} \left(1 + \frac{1}{z}\right)$$

this leads finally to the conclusion that

$$\overline{t} = \gamma^2 \left(1 + \frac{1}{z}\right)$$
where \( z = 2 \sqrt{ab} \) or
\[
\bar{t}^2 = \frac{a}{b} \left( 1 + \frac{1}{2 \sqrt{ab}} \right).
\]
The variance of the intervals is
\[
\sigma^2 = \bar{t}^2 - (\bar{t})^2 = \gamma^2 \left( 1 + \frac{1}{z} \right) - \gamma^2 = \gamma^2 / z = \frac{1}{2} \frac{a^{1/2}}{b^{3/2}}
\]
and the coefficient of variation is
\[
\frac{(\sigma^2)^{1/2}}{\gamma} = \frac{1}{(4ab)^{1/4}}.
\]
As Gerstein and Mandelbrot pointed out, when \( b = 0 \), i.e. when there is no net drift to threshold because inhibition on average balances out excitation, the moments become infinite. A consequence they did not explore is the divergence of the coefficient of variation as net drift approaches zero.

This calculation shows that with \( a \) constant, if \( b \) is decreased by the introduction of more inhibition, the coefficient of variation will be increased. The quantitative dependence of coefficient of variation on inhibition is not the same for the Gerstein-Mandelbrot model as for the eccentric cell model; the reason is that the Gerstein-Mandelbrot model has identical time constants for excitation and inhibition and the departure from this condition in the \textit{Limulus} cells has significant effects on variability. Nevertheless, it is interesting that postsynaptic inhibition should have the same qualitative effect, an increase of the coefficient of variation, for two such different models of neuronal fluctuations.

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