*ON TUNING AND AMPLIFICATION BY LATERAL INHIBITION**

By Floyd Ratliff, B. W. Knight, and Norma Graham†

ROCKEFELLER UNIVERSITY

Communicated December 16, 1968

Abstract.—Lateral inhibition in a neural network generally attenuates the amplitudes of the responses to sinusoidal stimuli—both spatial and temporal. For an inhibitory influence with an abrupt onset and an exponential decay in time, and with a Gaussian distribution in space (the forms often assumed in theoretical calculations), the attenuation is greatest at low temporal and spatial frequencies. The attenuation diminishes with increasing frequencies until ultimately the amplitudes of inhibited responses become equal to, but never exceed, the amplitudes of the uninhibited.

For an inhibitory influence with a delay to the maximum in time or with eccentric maxima in space, however, the amplitudes of inhibited responses to certain intermediate frequencies may be greater than those of the uninhibited responses. This "amplification" results because the delay and the spatial separation "tune" the network to particular temporal and spatial frequencies; the inhibition is turned on at the trough of the response and off at the crest, thus tending to produce the greatest possible amplitude. The amplification has been observed in one neural network, the retina of the lateral eye of *Limulus*. The basic principles are general, and the effects may be expected in any system with negative feedback.

The theory developed here illustrates some effects of spatial and temporal distributions of inhibitory influences. It is based on earlier experimental analyses of interactions among receptor units (ommatidia) in the retina of the compound lateral eye of the horseshoe crab, *Limulus*. In the steady state [1, 2] the mth ommatidium, when illuminated alone, discharges optic nerve impulses at a rate e_m. Because of the lateral inhibition, illuminating the rest of the eye will produce a generally lower rate r_m, which is given by the linear equation

$$r_m = e_m - \sum_{n \neq m} k_{mn}(r_n - r^0{}_{mn}), \tag{1}$$

where the r_n are the rates of discharge of the elements other than r_m; k_{mn} are constants specifying the inhibition for particular spatial separations of m and n, independent of rate of discharge; and the summation extends over all elements for which the rate of discharge is above the threshold of effectiveness $r^0{}_{mn}$. Further analyses have extended the theory to include the dynamics of lateral inhibition.[3, 4] Such a translationally invariant linear system may be characterized by its response to sine-wave input. The response is a sine wave of the same frequency, generally differing in amplitude and phase. The relationship of the amplitude and phase of the output to that of the input is commonly called the "transfer function" of the system.

The diagonal lines in Figure 1 illustrate the steady-state operation of a linear

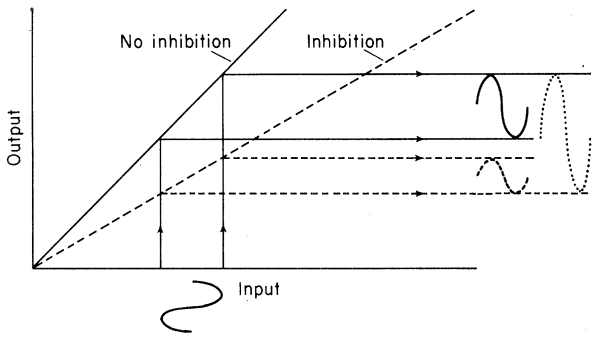

FIG. 1.—Steady-state input-output curves for a network with no inhibition (*solid diagonal line*) and with inhibition (*dashed diagonal line*). Calculated on the basis of these steady-state curves, the two outputs for a sinusoidally modulated input would not exceed the limits indicated by the pair of horizontal solid lines (no inhibition) and the pair of horizontal dashed lines (inhibition).

neural network, such as that represented by equation (1), in which the lateral influence is inhibition (to simplify the illustration, effects of thresholds of inhibition are omitted). Also shown are the responses to a sinusoidal modulation of the input. (For a retinal network, an example of an input sinusoidally modulated in time is a flickering light where the intensity is a sinusoidal function of time t; an example of an input sinusoidally modulated in space, in one dimension, is a pattern of striations where intensity changes sinusoidally along the spatial axis x, perpendicular to the stria.) If the modulation is very slow in time or very much spread out in space (long wavelength in t or x), the temporal characteristics of the inhibitory influences or the spatial characteristics of the inhibitory field may be neglected. Under these conditions any output, inhibited or uninhibited, would be given simply by drawing a reflection of the input from the appropriate steady-state input-output curve, as illustrated.

Thus, for very low frequency inputs, the difference between maxima and minima in the response is less with inhibition than without inhibition. Accordingly, the expectation has been that the amplitude of the response of an inhibited system cannot exceed the comparable response without inhibition. Indeed, as the frequency increases, the amplitude of the inhibited response to a sine wave increases and must eventually become the same as the uninhibited. This happens because the wavelength of the stimulus at the higher frequencies is short compared to the extent of the inhibitory field or the duration of the influence.

As a result of the attenuation of the amplitudes of the responses to low frequencies, inhibition will produce a low-frequency cutoff in the transfer function. In general, there is also a high-frequency cutoff resulting from other mechanisms (Fig. 5), and so the network is "tuned" to the intermediate frequencies. Note, however, that the limit on this best transmission is fixed by the difference between the maximum *uninhibited* response and the minimum *inhibited* response. If the inhibition could be turned completely off at the crests of the modulation of the input and completely on at the troughs, the output would be amplified as indicated by the dotted curve in Figure 1. A tuning of the system to particular intermediate wavelengths in either space or time can actually lead to such an amplification.

In order to make a comparison of various functions easier, the following modification of equation (1) is used:

$$r(x,t) = e(x,t) - \int_{-\infty}^{\infty} dx' \int_{-\infty}^{t} dt' k(x - x', t - t') r(x',t'). \qquad (2)$$

Here $r(x,t)$ is the response at spatial position x and time t, $e(x,t)$ is the stimulus, and $k(x - x',t - t')$ is the amount of inhibition exerted by the ommatidium at x' at time t' on the ommatidium at x at time t.

In this model the amount of inhibition exerted by one point on another depends on the response at the first point. A reasonable alternative is a system where the inhibition depends on the stimulus at a point, rather than on the response.[5] This is expressed by integration over e rather than r:

$$r(x,t) = e(x,t) - \int_{-\infty}^{\infty} dx' \int_{-\infty}^{t} dt' k(x - x',t - t')e(x',t'). \quad (3)$$

In line with earlier terminology,[6] we will call equations (2) and (3) "recurrent" and "nonrecurrent" systems, respectively.

A recent investigation[7] of the spatial distribution of inhibition in the *Limulus* eye showed that inhibition is greatest, not at points immediately adjacent to the inhibiting ommatidium,[8,9] but at some distance from it. This observed distribution of the inhibition k as a function of distance x from the inhibited ommatidium is closely approximated by the difference between a broad Gaussian distribution and a narrow one.

For this and for a simple Gaussian inhibitory field, the transfer functions for responses to spatial sinusoids by both recurrent and nonrecurrent networks were calculated by the usual techniques of linear systems analysis. As expected (Fig. 2), the responses to low spatial frequencies are always depressed by inhibition, and for high frequencies the inhibited response approaches that of the uninhibited. For intermediate frequencies, however, there is a difference in the behavior of the two networks. One amplifies the response (i.e., the ratio goes above unity) and the other does not. Note that there is little difference between the recurrent and nonrecurrent networks.

Mathematically there is a straightforward answer to the question of what

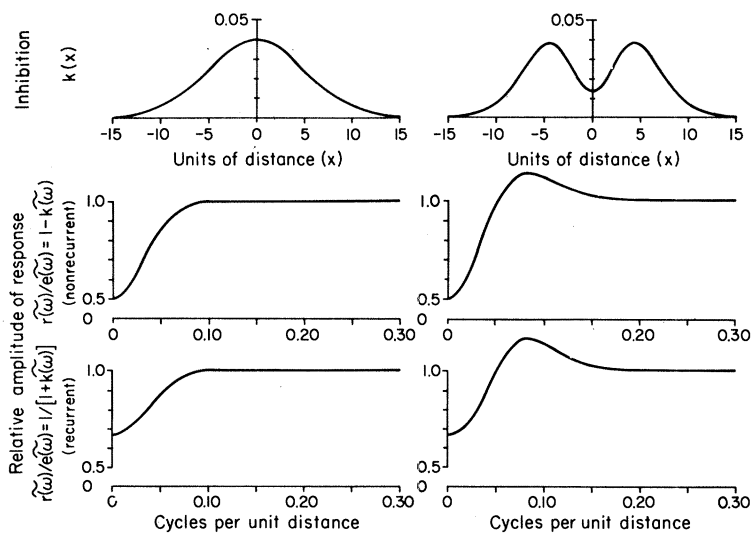

FIG. 2.—Normalized transfer functions for examples of symmetrical unimodal (*left graph*) and symmetrical bimodal (*right graph*) inhibitory fields $k(x)$ in a nonrecurrent network (*upper graph*) and a recurrent network (*lower graph*).

produces amplification in the spatial case. Since the stimulation is constant as a function of time, $r(x,t)$ and $e(x,t)$ are the same for all t and can be written as $r(x)$ and $e(x)$. Equation (2) for a recurrent system becomes

$$r(x) = e(x) - \int_{-\infty}^{\infty} r(x') \left[\int_{-\infty}^{t} k(x - x', t - t') dt' \right] dx'. \quad (4)$$

The inner integral is a function only of the distance $x - x'$, indicating the total amount of inhibition being contributed by point x'. This will be called $k(x - x')$. It is equivalent to the coefficient k_{mn} in the usual steady-state equations (1). Equation (4) now becomes:

$$r(x) = e(x) - \int_{-\infty}^{\infty} r(x') k(x - x') dx'. \quad (5)$$

By taking Fourier transforms of both sides and dividing by the transform of the input, one obtains

$$\frac{\widetilde{r(\omega)}}{\widetilde{e(\omega)}} = \frac{1}{1 + \widetilde{k(\omega)}}, \quad (6)$$

where $\widetilde{r(\omega)}$ is the Fourier transform of $r(x)$ as a function of frequency ω and similarly for $\widetilde{e(\omega)}$ and $\widetilde{k(\omega)}$. Therefore $\widetilde{r(\omega)}/\widetilde{e(\omega)}$ is the transfer function of the system. In general, the Fourier transforms $\widetilde{r(\omega)}$ and $\widetilde{e(\omega)}$ are complex numbers with the absolute values representing the amplitude (crest-trough distance) of the response and the angular coordinate in the complex plane representing the phase of the response. However, in this case, $\widetilde{r(\omega)}$ and $\widetilde{e(\omega)}$ have the same phase because k is symmetric, so that the ratio $\widetilde{r(\omega)}/\widetilde{e(\omega)}$ is the real ratio of peak-trough distances.

The nonrecurrent equation (3) can be transformed in the same way to give

$$\frac{\widetilde{r(\omega)}}{\widetilde{e(\omega)}} = 1 - \widetilde{k(\omega)}. \quad (7)$$

Now assume that the total amount of inhibition $\widetilde{k(0)}$ (which equals the integral of $k(x)$ over all x) is less than unity so that the absolute value of $\widetilde{k(\omega)}$ is always less than unity. With this assumption, the condition for amplification can be easily stated: Amplification occurs if and only if $\widetilde{k(\omega)}$ is negative for some ω.

The following analysis of the effects of the inhibitory time course on the responses to stimuli that vary in time, but are uniform in space, bears close formal similarities to the above analysis. Equation (5) is replaced by

$$r(t) = e(t) - \int_{-\infty}^{t} k(t - t') r(t') dt', \quad (8)$$

and equations (6) and (7) follow, as before, where now $\widetilde{k(\omega)}$ is the Fourier transform of the inhibitory time course $k(t)$ rather than of the spatial distribution of inhibition.

The one evident difference from the spatial case is that k no longer is symmetric. In equation (8), only the past history of r, and not its future, influences its present value so that where $\tau < 0$, $k(\tau) = 0$. This means that the point at which the sinusoidal response reaches its crest may differ from that of the stimulus

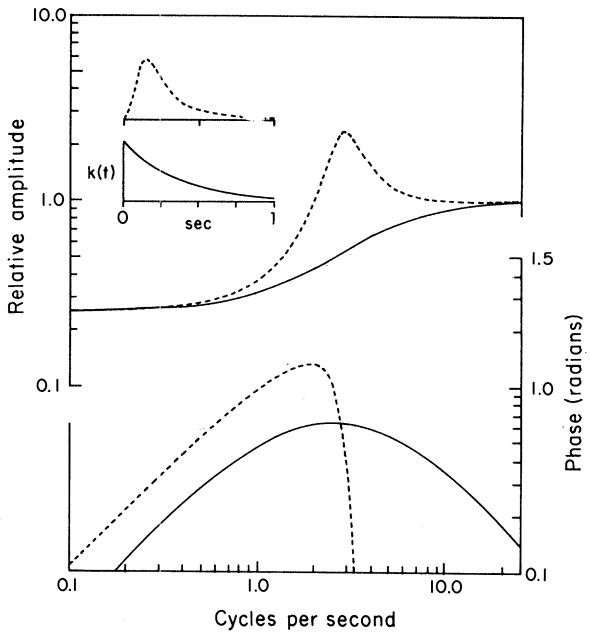

FIG. 3.—The effect of a delay to the maximum inhibition. Normalized transfer functions showing amplitude (*upper graph*) and phase (*lower graph*) for the two inhibitory time courses shown in the inset, an immediate rise to the maximum followed by an exponential decay, and a gradual rise to the maximum followed by a gradual decay. Recurrent network.

by a phase shift. This is reflected in a complex-valued transfer function whose angular coordinate represents the phase shift. Two examples of inhibitory time courses and the resulting transfer functions for a recurrent system are shown in Figure 3. The phase advance at low frequencies, like that shown in the figure, is typical of inhibitory feedback, as inhibition is already shutting off the response by the time the stimulus reaches its maximum.

As is evident from the examples in Figure 3, if $k(t)$ has a maximum away from $t = 0$, then amplification may occur at a frequency about reciprocal to twice the time to the peak of the inhibition. Qualitatively, the reason is the same as for the spatial case above.

A variety of time courses for the inhibitory influences were examined by varying the parameters in the following general expression:

$$k(t) = \begin{cases} 0 \text{ for } t < \tau_l \\ K\dfrac{1}{n!}\left(\dfrac{t-\tau_l}{\tau_d}\right)^n \exp\left(-\dfrac{t-\tau_l}{\tau_d}\right) \text{ for } t \geq \tau_l \end{cases} \tag{9}$$

where K is the total or steady-state inhibition, τ_l is the latency before onset of inhibition, τ_d is the relaxation time for final decay, and n indexes the order of onset ($n = 0$ abrupt, $n = 1$ linear, $n = 2$ parabolic, etc.). The time courses in Figure 3 are $n = 0$ and $n = 3$ from this family. The parameters τ_d and n are less easily grasped than the peak time (the time until the maximum inhibition) and spread time (the "standard deviation") of the time course defined by

$$\tau_s = \left[\overline{(t-\bar{t})^2}\right]^{1/2}, \tag{10}$$

which also characterize the time course.

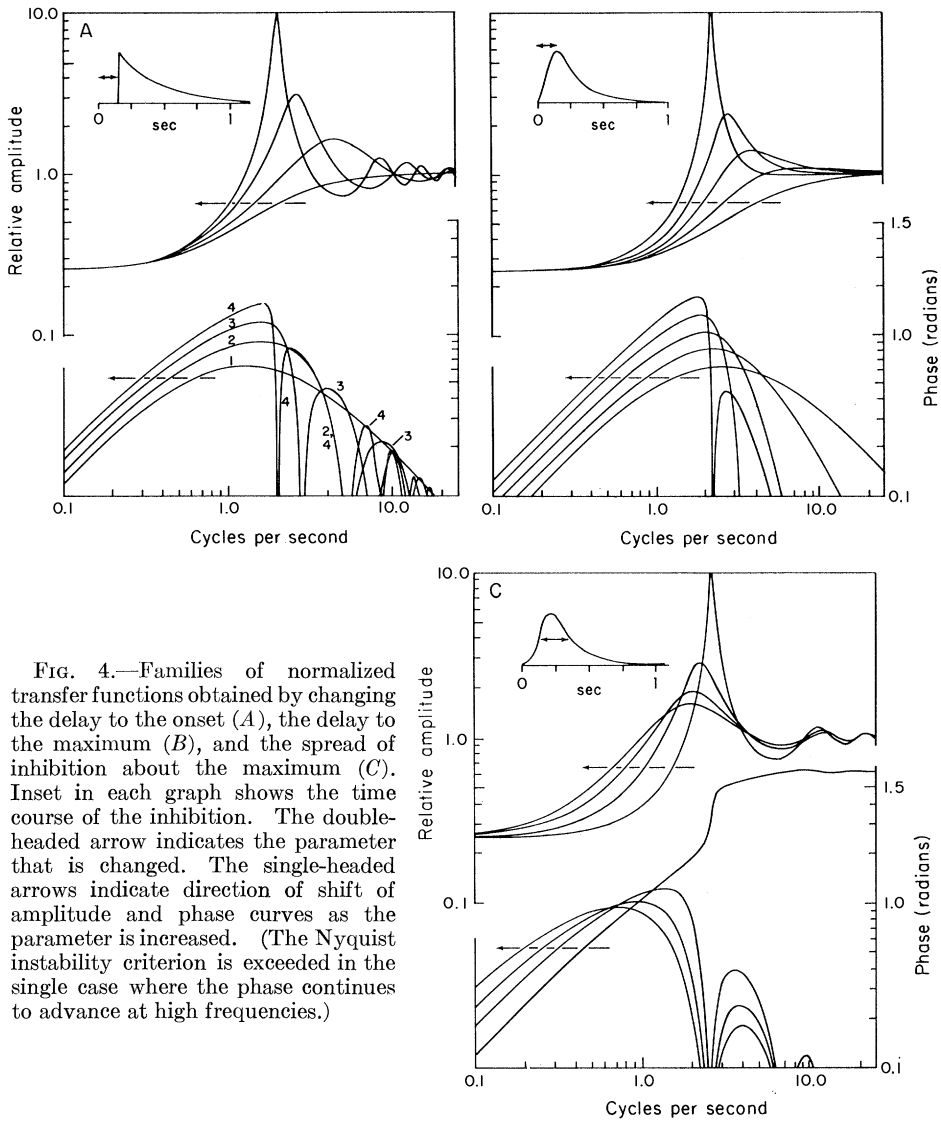

FIG. 4.—Families of normalized transfer functions obtained by changing the delay to the onset (A), the delay to the maximum (B), and the spread of inhibition about the maximum (C). Inset in each graph shows the time course of the inhibition. The double-headed arrow indicates the parameter that is changed. The single-headed arrows indicate direction of shift of amplitude and phase curves as the parameter is increased. (The Nyquist instability criterion is exceeded in the single case where the phase continues to advance at high frequencies.)

The temporal transfer function changes, as expected, with inhibitory latency, peak time, and spread time (Fig. 4). A longer latency (A), or a later peak (B), or a narrower spread (C) gives a stronger amplification maximum, and a longer latency also enhances secondary extrema in the transfer function.

This theory of the response of an inhibitory network to temporal stimuli may be checked experimentally in the eye of *Limulus*. The total inhibitory influence in this case is composed of self-inhibitory (k_s) and lateral inhibitory (k_l) components:

$$k(t) = k_s(t) + k_l(t), \tag{11}$$

$$\widetilde{k(\omega)} = \widetilde{k_s(\omega)} + \widetilde{k_l(\omega)}. \tag{12}$$

Both k_s and k_l may be measured directly[10] and the measured functions may be matched fairly well to ones coming from time courses in the equation (9) family by the following choice of parameters:

For self-inhibition, $K = 3$, $\tau_l = 0$, $\tau_d = 0.5$ sec, $n = 0$.
For lateral inhibition, $\tau_l = 0.1$ sec, $\tau_d = 0.3$ sec, $n = 0$.

The total lateral inhibition, determined by the size of the flickering spot illuminating the eye, is $K = 0$ for a small and $K = 3$ for a large spot. Figure 5*A* shows the generator-spikes transfer function for small and large spots predicted from equation (6). (The falling-off of the small-spot curve near 10 cps is due to a complication that arises when the driving frequency approaches the mean interspike frequency.[11]) With the large spot (and the resulting lateral inhibition) there is amplification of responses to intermediate frequencies.

In the *Limulus* eye, there is a conversion from light stimulus to generator potential that occurs prior to the inhibitory network. Its transfer function can also be measured directly[10] and is plotted in Figure 5*B* (for the same mean light intensity as in *A*). Since the output of the transfer function in *B* is the input to that in *A*, multiplying the transfer functions in *A* and *B* together gives a predicted transfer function for the complete light-spikes conversion which is plotted in Figure 5*C*. Also plotted in *C* is a transfer function for the complete conversion that was measured directly from another preparation under similar conditions.[12] In the phase data (not shown), the agreement between theory and experiment is equally good.

The principles underlying tuning and amplification are general, and similar effects may be expected to occur in any system with negative feedback. For example, Kelly[13] observed a similar amplification in the

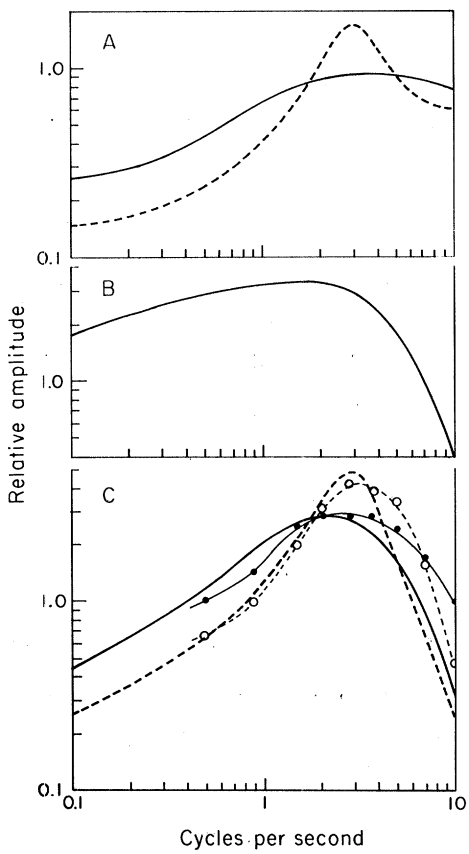

FIG. 5.—Comparison of theoretical and experimental results.

(*A*) Theoretical generator to spikes transfer function (*solid line*) for no lateral inhibition—that is, a small spot of illumination; and the corresponding transfer function (*dashed line*) for lateral inhibition—that is, a large spot of illumination.

(*B*) Observed light to generator transfer function.

(*C*) Theoretical light to spikes transfer functions (*A* times *B*) for small spot (*heavy solid line*) and for large spot (*heavy dashed line*). Experimental results for small spot (*filled data points, thin solid line*) and for large spot (*open circle data points, thin dashed line*).

temporal frequency response of the human eye. (Although he attributed the observed effects to ocular tremor, he noted that any other retinal mechanism capable of providing the necessary spatiotemporal interactions would account equally well for the effects.) A similar amplification has also been observed in the transfer function of xerography.[14] It is worth noting, in conclusion, that there is a possibility that reversible variations in the tuning of neural networks in the central nervous system could provide a means for the storage and retrieval of information.

The transfer function shown in Figure 5*B* is based on an experiment carried out by Jun-ichi Toyoda. We also wish to acknowledge the assistance of F. A. Dodge, Jr., Norman Milkman, and H. K. Hartline.

* This research was supported in part by a research grant (B864) from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service, and by a research grant (GB-6540X) from the National Science Foundation.

† Present address: Department of Psychology, University of Pennsylvania, Philadelphia.

[1] Hartline, H. K., and F. Ratliff, "Inhibitory interaction of receptor units in the eye of *Limulus*," *J. Gen. Physiol.*, **40**, 357–376 (1957).

[2] Hartline, H. K., and F. Ratliff, "Spatial summation of inhibitory influences in the eye of *Limulus*, and the mutual interaction of receptor units," *J. Gen. Physiol.*, **41**, 1049–1066 (1958).

[3] Ratliff, F., H. K. Hartline, and W. H. Miller, "Spatial and temporal aspects of retinal inhibitory interaction," *J. Opt. Soc. Am.*, **53**, 110–120 (1963).

[4] Lange, David, H. K. Hartline, and F. Ratliff, "The dynamics of lateral inhibition in the compound eye of *Limulus*. II," in *The Functional Organization of the Compound Eye*, ed. C. G. Bernhard (New York: Pergamon Press, 1966), pp. 425–449.

[5] Békésy, G. von, *Sensory Inhibition* (Princeton, N.J.: Princeton University Press, 1967).

[6] Ratliff, F., *Mach Bands: Quantitative Studies on Neural Networks in the Retina* (San Francisco, Calif.: Holden-Day, 1965).

[7] Barlow, R. B., Jr., thesis: "Inhibitory fields in the *Limulus* lateral eye," The Rockefeller University (1967).

[8] Ratliff, F., and H. K. Hartline, "Fields of inhibitory influence of single receptor units in the lateral eye of *Limulus*," *Science*, **126**, 1234 (1957).

[9] Ratliff, F., and H. K. Hartline, "The responses of *Limulus* optic nerve fibers to patterns of illumination on the receptor mosaic," *J. Gen. Physiol.*, **42**, 1241–1255 (1959).

[10] Toyoda, J., B. W. Knight, and F. A. Dodge, Jr., "A quantitative description of the dynamics of excitation and inhibition in the eye of *Limulus*," manuscript in preparation.

[11] Borsellino, A., R. E. Poppele, and C. A. Terzuolo, "Transfer functions of the slowly adapting stretch receptor organ of crustacea," in *Cold Spring Harbor Symposia on Quantitative Biology*, vol. 30 (1965), pp. 581–586.

[12] Ratliff, F., B. W. Knight, J. Toyoda, and H. K. Hartline, "The enhancement of flicker by lateral inhibition," *Science*, **158**, 392–393 (1967).

[13] Kelly, D. H., "Effects of sharp edges in a flickering field," *J. Opt. Soc. Am.*, **49**, 730–732 (1959).

[14] Neugebauer, H. E. J., "Development method and modulation transfer function of xerography," *Applied Optics*, **6**, 943–945 (1967).